Combined Electrochemical Treatment for Peripheral Neuropathy

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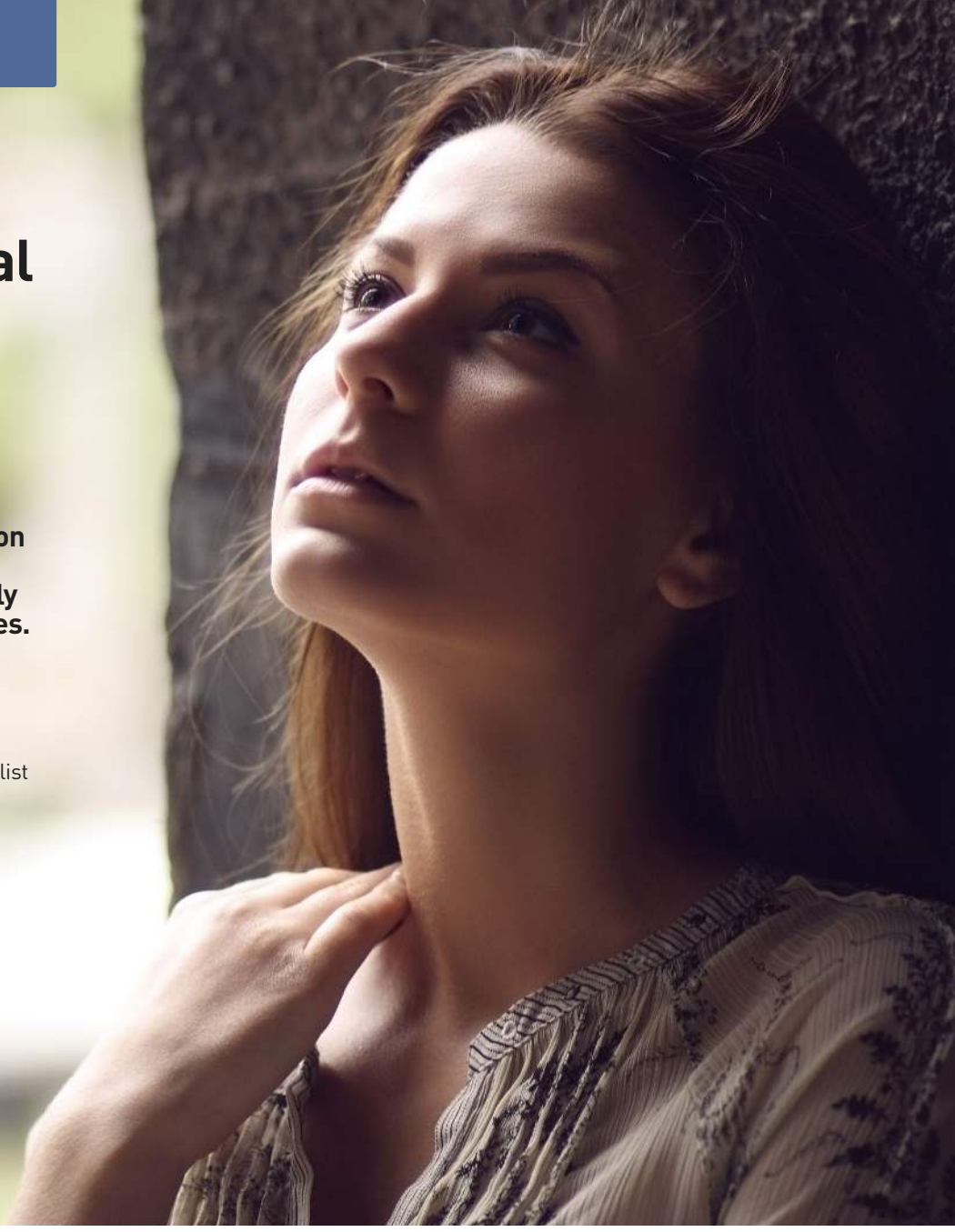
Combined Electrochemical Treatment For Peripheral Neuropathy

This technique uses local anesthetic blocks in conjunction with electric cell signaling treatment (EST) to successfully treat neuropathies of all causes.



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A neuropathy occurs as a result of basic pathologic processes gone awry—either from injury or disease. The incidence of neuropathy increases with age and its prevalence is growing. In fact, the prevalence of peripheral neuropathy may be as high as 2.4% in the United States.[1] A study of people with diabetes estimated the prevalence of diabetic peripheral neuropathy (DPN) in patients with type 2 diabetes to be 26.4%.[2] DPN is often the first indication to the patient that they have diabetes.[3] Morbidity associated with diabetic and other neuropathies is a major reason patients seek medical care and represents a major cost to patients and society.[4,5]

It is compelling to note that the course of DPN, as well as other neuropathies, generally is progressive. To date, most treatments have focused on reduction of symptoms,[6] and, in the case of diabetes, control or slowing of the progression of the underlying disease.

Combined electrochemical treatment (CET) represents a safe and effective therapy for all forms of neuropathy.[7] We have now documented the reversal of the neuropathic process both from clinical observations and from objective functional (neurodiagnostic) testing and anatomic (epidural nerve fiber density [ENFD]) data.[8] Although our clinics have not yet initialized formal double-blinded control studies, our clinical outcomes strongly suggest that the CET protocol is making a substantive difference in patients' lives and certainly warrants more detailed consideration.

This paper will discuss neuropathic pathophysiology, with a focus on DPN. We will discuss how biochemistry and physics act in concert for healing.

Peripheral Neuropathy

Four primary nerve fibers are important in small fiber (sensory) neuropathy: A-delta, afferent C, efferent C, and A-beta. Neuropathic pain occurs when normal signaling between adjacent nerve cells attenuates as a result of insufficient oxygen transport. The hypo-oxidative state associated with neuropathic pain appears to be a primary factor, along with demineralization of the synaptic fluid, necessary for axon signal transport.[9]

Unlike muscles, which use either oxygen or glucose metabolic pathways, nerve cells are limited to the oxidative reductive metabolic system, or Krebs cycle.[10,11] The Krebs cycle requires an immediate defense response to assure neural integrity and survival during a hypo-oxidative state. This defense mechanism also occurs upon exposure to environmental toxins, chemotherapeutic agents, military chemical weapons, insecticides, and other neurotoxic substances. Contraction, which is one such defense mechanism, causes a generalized shrinking of the nerve cells and a widening of the synaptic cleft between these cells.

As the synaptic junctions between the axons of one nerve cell and the dendrites of the next nerve widen, normal signal transmission can become compromised. Signals of normal intensity can no longer bridge this newly widened gap, resulting in a loss of bioelectric integrity. Widening of the synaptic gap makes it more difficult for normal sensations to propagate and causes a general loss of electrical conductivity in the synaptic fluid.[12]

Conductivity relies on minerals and specific neurotransmitters in the synaptic fluid to enable propagation of the nerve signal. These conductive minerals and neurotransmitters are delivered via the perfusion of adjacent tissues with fresh blood. They are kept in suspension by the periodic ionization of successfully transmitted nerve signals across the junction. When nerve signals attenuate because the synaptic cleft widens, necessary conductive minerals and neurotransmitters are no longer held in place by naturally-occurring electrical tension and are slowly leeched away.[12,13]

The initial sensory perception associated with atrophying nerves and enlarged synaptic clefts often is reported by the patient as tingling or electric sensation. This effect most likely is the result of ephatic firing, defined as some nerve signals being misdirected to nearby nerves.[12-14] As the condition worsens, more signals are misdirected or suppressed, leading to increasingly unpleasant sensations such as stinging, burning, and pain. In time, affected nerve signals can become completely suppressed, resulting in numbness.

Ephatic cross firing co-existing with numbness may also explain why patients can have pain, dysesthesia, and numbness at the same locations at the same time. These conditions often result in poor tissue perfusion, insecure gait, balance problems, general muscle weakness, and other mobility issues. From a diagnostic standpoint, specific neurodiagnostic testing can directly measure this effect, as the increased voltage threshold necessary to fire enough nerve axons for the patient to "feel" sensation normally.

The sensory function of afferent A-delta and C fiber is best measured by the A-delta nerve conduction study (NCS), thermal evoked potentials, and functional magnetic resonance imaging (fMRI). Nerve conduction velocity (NCV) testing is less sensitive than A-delta NCS but can also measure all three fibers. A-delta function is effectively measured by A-delta NCS with 95% accuracy.[15] Efferent C fiber function, which is a primary pathology, is best assayed by quantitative sensory testing (QST) such as sweat testing (Sudoscan), thermography, and possibly fMRI, and will be considered in future studies.

In physics, electron behavior is referred to as "organized chaos." This idea unites activities of electrical and chemical medicine, and thus ties disease and curative medicine together conceptually.[16] Although myotomes and dermatomes have been well documented in published biomedical literature, we are unable to find any data detailing existing "maps" for the distal sympathetic C fibers in the body. Still, C fibers are known to have a primary influence in the development of the pathophysiology of diabetes. These efferent fibers control the tone of local arterioles, and, critically, contribute to the pathophysiology of small vascular structures and small nerve fibers (which are viable only as a function of these tiny arterioles). Pathology in the small arterioles and in the nerve fibers combines to adversely affect the distal tissues of the extremities.[17]

Tests of functional improvement are generally considered more robust than anatomic testing. However, ENFD testing is rapidly becoming an accepted standard to measure afferent C fibers and unmyelinated A-delta fibers.[18] Thermal evoked potentials and fMRI also can measure the function of C and A-delta fibers, but ENFD currently is the most practical method. In our clinics, we have employed A-delta NCS and ENFD biopsies.

Despite the many described causes of peripheral neuropathy, the pathophysiology of simultaneous and synergistic decrease in vascular and neuronal function remains constant throughout the process and creates a pathological cascade.

Basis of CET

CET involves the use of local anesthetics to block pain and other nerve

Table 1. Differences Between Electrical and Chemical Nerve Blocks

What do nerve blocks accomplish?	
Electrical—sustained depolarization	**Chemical—hyperpolarization**
Neuron blockade	Neuron blockade
Afferent block results in less perceived pain	Afferent block results in less perceived pain
• Less pain, local muscle relaxation	• Less pain, local muscle relaxation
• Relaxation, more circulation	• Relaxation, more circulation
• More circulation	• More circulation
○ More nutrients/enzymes/hormones	○ More nutrients/enzymes/hormones
○ Less toxic metabolites	○ Less toxic metabolites
• Less neurogenic inflammation	• Less neurogenic inflammation
Efferent block results in local vasodilation	Efferent block results in local vasodilation
• More circulation	• More circulation
○ More nutrients/enzymes/hormones	○ More nutrients/enzymes/hormones
○ Less toxic metabolites	○ Less toxic metabolites
• Less neurogenic inflammation	• Less neurogenic inflammation
They achieve exactly the same physiologic results	

function in the distal lower extremities, followed by electrical cell signaling treatments (EST) to both lower extremities. First, a low-dose, low-volume injection of local nutrient-infused anesthetic (Na+ channel blocker) is injected into the target region, followed by treatment with the EST device.[19] The device combines, and simultaneously delivers, frequency-modulated (FM) and amplitude-modulated (AM) electric cell currents in a pulsed electromagnetic fields (EMFs).[20-22]

The concepts of cell membrane signaling, simultaneous nerve stimulation, and timed muscle activation indicate how physics and pharmacology can work together to promote a physiological environment that favors healing.[20,23] Clinically, we have witnessed extraordinary results with CET that are consistent with plausible and scientifically supportable regenerative and reparative physiologic mechanisms.[21,22]

The effects of the local anesthetic and higher-dose, specific-frequency EST are similar with regard to their ability to block nerve fiber (axon) transmission and promote beneficial effects on nerve cells (Table 1).[24] The afferent block results in less perceived pain; the efferent block promotes increased blood flow through vasodilation. Vasodilation promotes nutrient transfer to the nerve cell and removal of waste products with pH normalization; the reduction in inflammation produces a concomitant reduction in edema and pain.

Key Mechanisms of Action

Patients occasionally ask, "How does the CET treatment fix my numbness?" The answer to this question is most likely that the healing process is enhanced by factors in the local anesthetic beyond simply its ability to block sodium channels, arresting degenerative pathology and promoting healing.

The key physiological mechanisms of action of CET necessary for the treatment of neuropathy include: increasing blood flow and available oxygen, increasing second messenger(s) responsible for regenerative tissue effects, and promoting analgesia and anti-inflammatory effects. At a deeper level, the effects of the local anesthetic (LA) and EST on cyclic adenosine monophosphate (cAMP), a second-messenger molecule, cause the most basic and important mechanism in reversing neuropathy: activating the regenerative processes.[14] The effects of chemically blocking pain also may play a role in early patient compliance. Patients become more motivated to continue treatment because they experience improvements in their symptoms and reduced pain or numbness, particularly allodynia.

Effects on Increased Blood Flow and Oxygen Transport

Peripheral neuropathy is most likely caused by disorders of the circulation,

neural edema (neurogenic inflammation), and altered microcirculation around nerves. Blood flow is among the least discussed and appreciated factor in pain relief. The influence of blood flow, especially its diminution, is not emphasized enough in the chronic pain literature.[25]

CET's promotion of increased blood flow is likely a primary mechanism for its effectiveness. If blood flow is normalized, the local milieu is improved, and healing of A-delta and C fibers can occur. Increasing blood flow to the affected tissue has obvious, well published benefits, such as increasing available oxygen content, increasing availability of nutrients, facilitating the elimination of waste, and the overall normalization of neural transmitters.

EST signals, programmed with the appropriate and time-varying cell signaling parameters, as well as appropriate amplitude, influence the circulatory system via several mechanisms of action. By using specific programming, EST signals produce the following effects on blood flow:

- Slow-frequency nerve stimulation (1-4 Hz) of the sympathetic nervous system to produce vasoconstriction of the blood and lymph vessels, accelerating the centripetal transport of venous blood and lymph
- Slightly faster low-frequency signal stimulation of the sympathetic nervous system to produce vasoconstriction (10 Hz)
- Fast stimulating signal frequencies (100 Hz) to produce vasodilatation via sympathetic function exhaustion of the synaptic neurotransmitters
- Fast non-stimulating frequency signaling (>2,000 Hz), in which multiple electric signals fall within the absolute refractory period of the cell membrane to inhibit the action impulse capability of the cell membrane via sustained cell membrane depolarization.[19]

Specific signaling produces other secondary circulatory effects: facilitation of diffusion processes and balancing of metabolic concentration differences; EST-induced activation of metabolism by increasing the formation of cAMP, particularly in the endothelium; and activation of muscle pump by motor activity, which results in the centripetal transport of venous blood and lymph nodes.[23]

The EST effects of motor neuronal and muscle stimulation produce an increase in metabolism, followed by auto regulatory vascular mechanisms that result in a decrease of local peripheral resistance of the vasculature in the stimulated muscle. Post-EST stimulation leads to an overall relaxation effect and circulatory normalization.[19,20,23]

A simplified schematic of the sympathetic nervous system's control of circulation is illustrated in Figure 1. Variations in the input at control points will affect vascular tone. If the afferent sympathetic signal is increased, with no other influence on the efferent C-fibers, sympathetic tone also will increase. When the efferent C-fibers are blocked, including by electric signaling, the blood flow will increase regardless of the input of the afferent C-fibers. The control exerted will trump afferent signals, as the circuitry is in series.

Second Messenger (cAMP) Formation/Activation: Normalization of Cell Function

EST energy produces a hormone-like effect by triggering an electrical conformation change to the cell membrane G protein. This change influences the activity of adenylate cyclase, resulting in the formation of cAMP. cAMP-induced repair processes are necessary to stabilize the cell membrane and inhibit continued leakage of acids known to trigger pain and inflammatory mediators. By promoting changes to G proteins in cell membranes, EST may ultimately normalize cell function and neuropathic pathology.

Multiple studies support the belief that cAMP will increase from sustained depolarization of the cell membrane.[26,27] Schwartz stated that there are "numerous citations that demonstrate … second messenger formation within the cell at various ion voltage gates when exposed to frequency specific electronic signal currents."[28] This direct effect of EST increases available cAMP for normalization of cellular metabolism, improvement of local blood supply and oxygen, improvement in cell proliferation, increases in local blood flow, and equilibration of differences in metabolic concentration.

Analgesia and Inflammation

Several mechanisms help explain the analgesia produced by EST. Under the influence of rapidly-alternating polarity, ion movement is enhanced, which tends to balance differences in metabolite concentration, leading to pH normalization and reduction in tissue acidosis. Formation of cAMP directs all cell-specific activity toward the repair of cell membranes, inhibiting the release of arachidonic acid from insulted membranes and inhibiting subsequent prostaglandin (pain mediator) cascade.[19,20,23]

Specific parameters of the electric signal energy produce repeated excitation of afferent nerve fibers, effecting neuronal signaling processes in the central nervous system (CNS), thus interfering with local pain perception.[29] Finally, EST assists in cell receptor uptake of beta-endorphin, encephalin, and phyllokinin among other substances, which modulate or inhibit pain impulses in the CNS.

Direct blocking of afferent pain signals occurs in several ways:

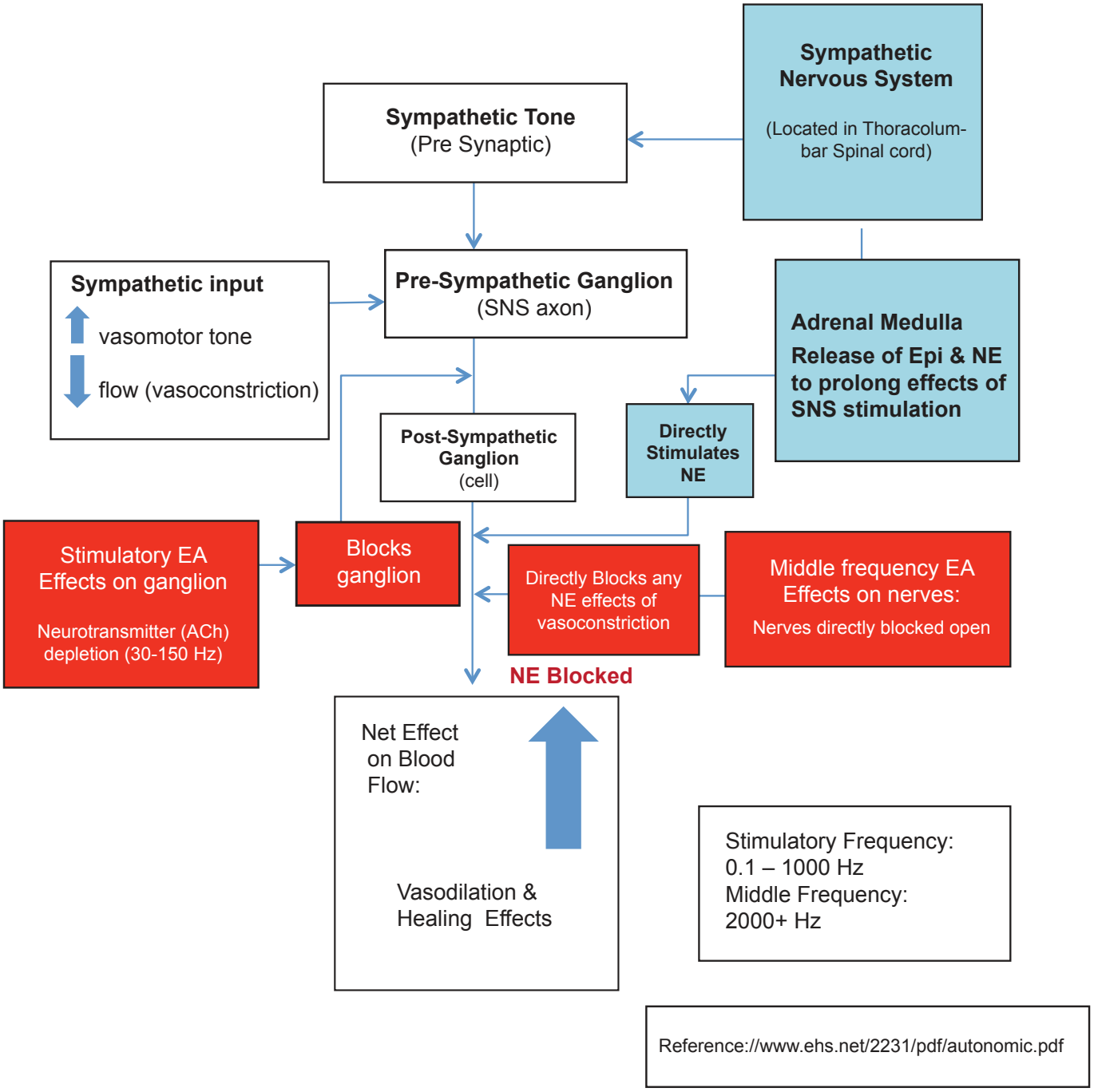


Figure 1. Schematic drawing of nervous system control of vasomotor tone and the influence of EST. **EA**, electroanalgesia; **Epi**, epinephrine; **EST**, electrical cell signaling treatments; **NE**, norephinephrine

- At low, stimulatory frequencies, EST produces Na+ channel exhaustion of neurotransmitters occurs
- At the application of higher doses, higher frequency non-stimulating EST electric cell signals induces a sustained depolarized state across multiple Nodes of Ranvier and blocks axon information (pain signal) transport
- EST "resets" or "reboots" primary and secondary hyperalgesia mechanisms (wind-up)[19,20,23,28]
- EST blocks conduction in both directions, since efferent pain signals can be associated with peripheral sensitization (the so-called "blocking the dieseling effect" analogy).

Pure electric nerve blocks have been performed clinically for years to block pain and increase local blood flow, with success similar to that of chemical blocks.[30]

EST signal energy works to reduce inflammation by initially facilitating

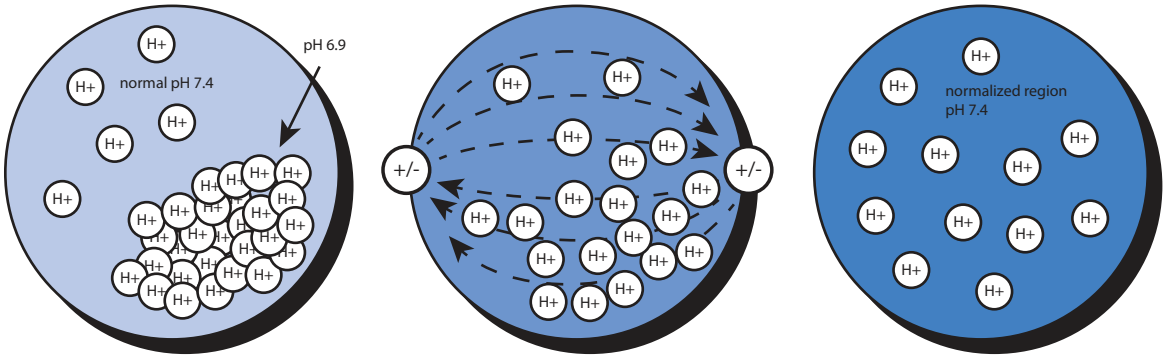


Figure 2. Influence of alternating current (electric field) on the concentration of hydrogen ions. Note how low pH (6.9) creates an area of inflammation. Based on reference 23.

the natural inflammatory process toward a swift, organized, and natural resolution. While complex, all concepts above fit together when taken into the context of electric cell signaling and of normalization of cAMP. However, the basic signaling mechanism could easily be the EST-driven ionic action on cAMP. Through this and the other mechanisms, cellular derangements return to normal in optimum physiological time. An entire focused review has been devoted to the beneficial effects of CET on inflammation.[23] By alternating the electronic signal frequency parameters, intensities, and dwell times of the applied EST treatment energy, the movement of inflammatory mediators and metabolic end-products away from the area of inflammation is enhanced, leading to the reduction of inflammation.

Figure 2 shows the influence of an alternating current on the concentration of hydrogen ions and how an area of inflammation with low pH is normalized under the effects of electric signaling.[23]

Restoring Metabolic Equilibrium

Equilibration of differences in metabolic concentration by alternating-polarity EST will result in an increase in the redistribution of ions and water within tissues.[10,13,19,20,28] This rebalancing results in the dilution of toxic, pain and/or inflammatory mediators; an increase in tissue clearance by an improvement in the efficacy of the local blood flow; and an overall improvement of diffusion and reabsorption between the intra- and extra-capillary fluids.[23]

Distal Phenomena

Axon Circulation

Neuropathies also may result from interference in axon transport by products of glucose metabolism, such as sorbitol.[31] Axon transport problems also are accompanied by inflammation. Some unique factors must be used to explain nerve hypofunction, which depends on how distal that section of nerve is from the CNS. The circulatory concepts of axon transport, including afferent movement of nutrients and efferent movements of waste, appear to be an important factor.

Does decreased axon circulation decrease nerve function, or does decreased nerve function decrease circulation? Perhaps both occur. However, at this time, we cannot identify which is first. Nonetheless, inflammation probably plays a major role in interference of this circulation. The largest manifestation of these disturbances occurs at the distal aspect of the nerve axon.[32-35]

Synergistic Interaction Of EST and Anesthetics

Local anesthetics are known to depress mitochondrial function by hyperpolarization, a "locking down" of the cell's voltage channels.[14,32] However, EST has been shown to increase the number, size, and overall activity of mitochondria.[33,34] Increased mitochondrial activity allows for substantially more energy for bioutilization and regeneration of cells. This physiologic benefit of EST is extremely important, because increasing production and use of energy are central to the healing process.

Clinical Markers and Results

Formal studies and clinical experience with CET have shown improvement in 80% to 85% of patients with peripheral neuropathy, and a major functional improvement in 75% of patients.[7,21] The difficulty in defining improvement arises because neuropathy is more multidimensional than chronic pain in its presentation. Symptoms include pain, dysesthesia, paresthesia, as well as loss or impairment of sensory function, numbness, dry skin, gait instability and fall risk, erectile dysfunction, and incontinence.[35] Signs of peripheral neuropathy include decreased vibration, reflexes, protective sensation to pain,

Table 2. Relationship of Symptom score (NRS) to Neuralscan Score (NS)			
	NS improved	**NS same or not improved**	**Totals**
NRS improved	16	11	27
NRS same or not improved	4	3	7
Totals	20	14	34
McNemar's odds Ratio = 2.7			

This lower odds ratio reflects the fact that while A-delta nerve condution study can predict clinical improvement; other nerves (afferent and efferent C fibers, and A-beta fibers) also play roles in an individual patient's progress. Because objective improvements of A-delta nerves have been observed, there would also likely be improvements in afferent and efferent C-fibers resulting from improvements in the microvascular environment. A-beta improvement is measured by a reduction in allodynia, but no objective test exists.

pressure, and thermal stimulation, as well as decreased proprioception. All of these symptoms can be measured but can be difficult to reproducibly quantify from provider to provider and clinic to clinic.

Objective Testing

The effectiveness of interventions can only be self-reported by patients. However, numerous difficulties exist in describing, standardizing, and quantifying pain and the other aspects of neuropathic symptoms in clinical evaluations. Objective measures of improved neurological function and regeneration should satisfy even the most skeptical of government regulators, stakeholders and third party payers, and should pave the way for more widespread usage of CET and EST. Three diagnostic tests have demonstrated reproducible functional and anatomic objective improvement of neurological function after the CET protocol in treating peripheral neuropathy.

NCV

Cernak et al reported trends in increased amplitude and decreased latency of motor function when patients treated with CET were tested at least 1 month post-procedure—3.8% of peroneal motor nerves, and 49% of tibial motor nerves, showed improvement.[12] Sensory function in the peroneal and sural nerves showed a 36% improvement (including those with no recordable responses). When sensory nerves did show a pretreatment response, however, they improved in 82% of patients. In some cases, nerves that had no response did, in fact, begin to have a measurable NCV. Since a placebo effect would be unlikely in this setting, Cernak et al stated that "These trends in motor nerve function may represent a decline in neurological morbidity of DPN as nerve function improves. In both sensory nerves tested … over 40% of patients did show an improvement in peroneal sensory nerve conduction while more than 31% showed an improvement in their sural sensory nerve."[21]

spf (A-delta) NCS

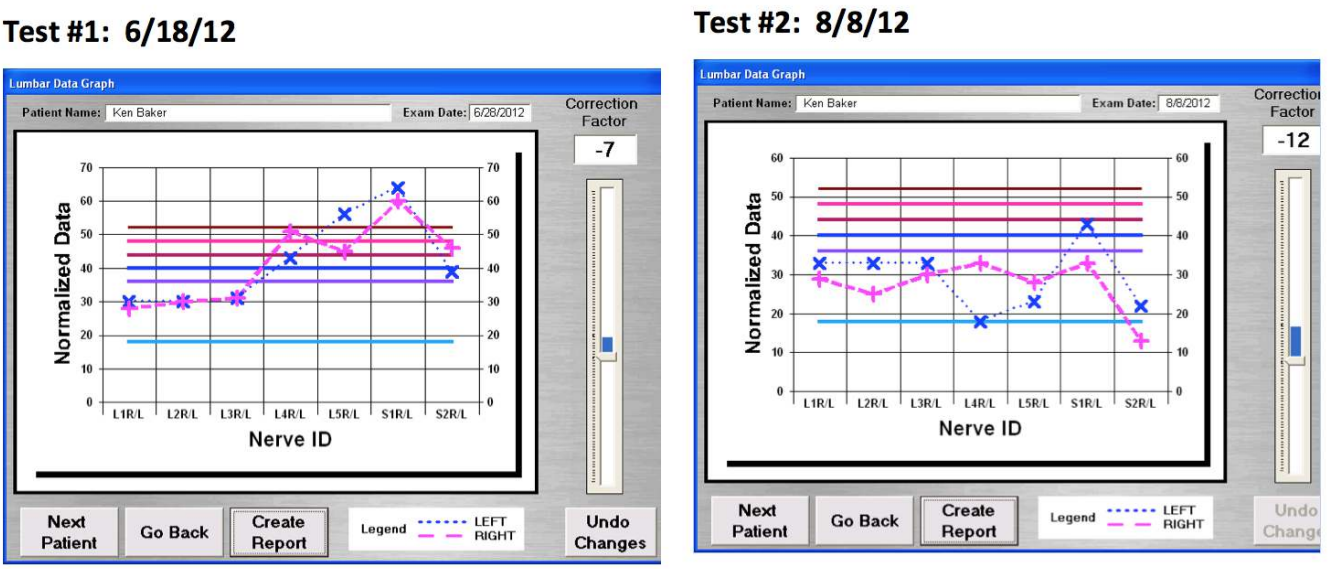
spf A-delta NCS testing is based on the behavior of A-delta nerves in the pain processing system and has gained traction in the medical community over the past 15 years. The A-delta NCS system has 2 components: an electrical stimulator that generates neuroselective signals specific to A-delta nerves; and a detector that records in real-time the micro-voltage changes of the threshold action potential signal at muscles. The A delta-NCS measures the voltage required to fire peripheral A-delta nerves, and has been shown to be reproducible with localization of nerve root injury sensitivity of about 95% and a specificity of 62%.[15]

The spf A-delta test device is capable of assessing a wide variety of polyneuropathies and compressive/entrapment syndromes. Regional mapping techniques in the hands and feet can be easily employed. In peripheral neuropathies, standard dermatome points measured at L4, L5, S1, S2 and in the feet appear hypoesthetic.

The spf-NCS technology can objectively track the progress of the patient by repeat testing. The A-delta NCS score Deviation Index is a numerical means of measuring outcomes and the extent of a neuropathy. Improvements in nerve function are represented by decrease in hypoesthesia and are identified as positive numbers; worsening results, as negative numbers. Numbers close to 0 indicate little or no change in A-delta nerve function (Figure 3, page 54). In the example, the Neural scan score improved by +34. Table 2 (above) shows the relationship between symptom relief and test score improvement.

ENFD Skin Biopsies

ENFD punch biopsies are gaining wide acceptance for diagnosing and following patients with neuropathy.[18] The test measures the density of intra-epidermal nerve fibers at various sites in the leg. The measurements usually are taken in the lateral mid-foot, 10 cm above the lateral malleolus, and 10 cm above the lateral epicondyle. Loss of nerve fibers



Clinical course: The patient is a 72-year-old male who presents with pain and numbness in the toes and bottoms of his feet. Cause of his neuropathy was either idiopathic or pre-diabetic. Over the course of 6-weeks, the patient had improvement in his symptoms, including numbness, by 80% to 90%. His sleep improved as well. He discontinued his medications and continued to improve after August 2012. He remains almost symptom free through mid-2015.

Figure 3: Example of Neuralscan with clinical improvement. Normal nerves lie between bottom single line and the lowest line in the left (hypoesthetic) set. In this case, the Neuralscan score has improved significantly, which is readily seen by comparing the graphs. Improvement in objective testing correlates well with the patient's clinical improvement; notable is the fact that this patient, a functional medicine advocate, takes optimal care of himself.

is associated with increased neuropathic pain. In our experience, nearly half of patients with a painful condition had evidence of small fiber neuropathy as noted with the skin biopsy.[36] The diagnostic efficiency of skin punch biopsy is about 88%, whereas findings on routine nerve conduction studies and electromyography typically are normal.[37]

One laboratory, Corinthian Research Lab, has developed the Prevalence Registry in Small Fiber Treatment in Neuropathic Evaluations (PRISTINE). Various clinics using the CET neuropathy protocol have registered their pre- and post-treatment biopsy results. Data in this registry are helping to improve our understanding of the relationship between clinical profiles and reduced ENFD in patients with neuropathic pain (Table 3). In a preliminary analysis, definitive epidermal nerve regrowth is demonstrated in 50% (11 of 22) of biopsied nerves, and 75% of patients showed at least 1 nerve regrowth. After 3 months, nerve regrowth was present in 63% of all nerves biopsied. These results are remarkable when one considers that there could not be a placebo effect because of the natural history of this disease. Neuropathies of all kinds are represented here and a significantly larger study is underway.

Safety of CET

CET has a remarkable track record of safety. Clinics that have used our protocol for patients with neuropathic pain in the feet and legs have rarely, if ever, observed side effects. In our experience, there has been an occasional allergy to bupivacaine, which is easily solved by switching to xylocaine with no loss of efficacy. Occasional mild, superficial burns have been reported from adhesive-type electrodes when excessive power density is applied. These problems have been resolved by using a venturi-type vacuum cup electrode system. There have been no reports of infection to date.

In a study comparing CET to pregabalin (Lyrica), Carney demonstrated that CET is "superior" to treating diabetic nerve pain; CET "decreased the average pain score 54% more than pregabalin (P=0.00006), and was 62% more effective than pregabalin in reducing the average pain score by 50% (P=0.003)" without side effects.[22]

Summary

The time has come for a paradigm shift in the approach to chronic disease. Although complex, the basic mechanisms of cell signaling could easily

Table 3. Comparison of Epidural Nerve Fiber Biopsy in 8 patients (Preliminary)

#	NRS pre	NRS post	NFI max	NFI post	#CET	#EA	ENFD Pre-Treatment			ENFD Post-Treatment				Results	
							foot	calf	thigh	Time from last treatment	foot	calf	thigh	# improved/ total biopsied	At least one improved
AS	8	0	24%	2%	0	19	0	0.1	11	0	0	0	5.9	0/3	no
EB	5	3	28%	10%	16	20	0	0	3.5	0	0	0	4.7	1/3	yes
MB	10	3	62%	29%	16	15	0	0.5	3.4	5 mos	0.1	0.2	4.5	2/3	yes
LC	10	5	49%	52%	20	15	0	0	2.9	3 mos	0	0	1.6	0/3	no
JD	10	1	8%	4%	20	20		1.6		3 mos	0.5	3.2	6.1	1/1	yes
EG	8	2	80%	44%	20	36[a]	0.7	2.3	0.3	6 mos	0.9	2.3	3.4	2/3	yes
JS	9	2	48%	24%	16	11	0	1.7	4.8	3 mos	3.4	3.1	5.4	3/3	yes
DY	5	3	54%	30%	20	10	5.5	8.3	11.8	6.5 mos	6.4	10.3	5.3	2/3	yes

[a]over 15 month period

Of the total number of nerves biopsied, 11 of 22 showed nerve growth. Six of the 8 patients (total # of patients) had at least 1 nerve growth. Ten of 16 nerves biopsied after 3 months showed nerve growth.

CET, Combined Electrochemical Treatment; **EA**, electroanalgesia; **ENFD**, Epidermal Nerve Fiber Density; **NFI**, neuropathy function index; **NRS**, numerical pain/numbness (symptom score)

be the normalization of cAMP, which leads to the opening of voltage-gated channels in pain neurons and the sympathetic nervous system. Vessels then vasodilate, increasing local circulation, allowing incoming nutrients and a "washing out" of waste products. This cascade eliminates the primary chemical causes of local pain. In addition, signaling cAMP also leads to decreased firing of afferent C-fibers, which in turn decreases ephatic cross firing of afferent A-delta fibers.

We postulate that signaling the distal nerve axons to normalize function and circulation may be precisely what is required to rebalance the system and break the pathogenic cycles of neuropathy. In the CET neuropathy protocol, electrodes are placed on the gastrocnemius, which has the largest-diameter blood vessels, and on the feet. In this way, circulatory and signaling phenomena work synergistically to effect tissue healing.

Preliminary results have been promising when EST is used in conjunction with spine blocks, including epidural, paravertebral, and medial branch blocks using local anesthetics only. This approach has the potential to be superior to current practice, because the combination of local anesthetics and EST does not require the injection of particulate matter (from steroids) near the medullary arteries. Slowing, stopping, and even reversing the progression of the neuropathic process has been observed clinically. Even in patients whose symptoms do not seem to be reversed, we have seen evidence of stabilization and/or slowing of the progression of disease. As a result, the issue of early intervention is critically important.

One question that our experience and observations have not been able to answer is when neuropathy becomes irreversible. Some patients with symptoms for greater than 10 years have experienced substantial improvement. Longitudinal studies certainly are indicated, and correlation of outcomes with length of time of known neuropathic symptoms must be done.

CET and EST are an important first step in the overall treatment picture, but they should not be expected to stand alone. Nutritional support, diet, exercise, and other lifestyle changes all are necessary for successful long-term outcomes.

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Richard Sorgnard, PhD (molecular biology), is Executive Director for Morhea Technologies, LLC, a medical technology development and engineering

firm in Las Vegas, Nevada.

Peter Carney, MD, is a neurosurgeon who now focuses his practice on the accurate diagnosis and treatment of patients with chronic pain. For the last 5 years he has had a special interest in the use of the principles of quantum mechanics to treat patients with painful peripheral neuropathy (PPN). His recent work documents that the principles of quantum mechanics not only treats PPN more effectively and more safely than pharmacological methods but also demonstrates that these principles help to regenerate nerves destroyed by PPN.

As a pioneer in Integrative Medicine, Robert Milne, MD, recognized the potential of using complementary methods. Dr. Milne's interest in complementary medicine began when his young daughter became very ill and was unable to be helped with prescription drug medicines. Dr. Milne received his undergraduate degree from the University of Southern California. After three years in the Peace Corps in Paraguay, he attended the University of Missouri-Columbia School of Medicine where he received his medical degree. He spent three years of residency at the University of Texas-Southwestern, John Peter Smith Hospital, where he was chief resident and in addition was awarded Board Certification in Family Practice. Dr. Milne has published several books and has also traveled extensively to Europe in his continued search for methods to help his patients. He holds 2 patents on medical devices, the Elast Allergy Testing Device and Micro-Vibration Therapy (MVT) for the treatment of pain. He is also a frequent lecturer on Integrative Medicine.

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