Effects of Low Voltage Pulsed Current on Edema Formation in Frog Hind Limbs Following Impact Injury

James L Karnes
Frank C Mendel
Dale R Fish

The purpose of this study was to test the effect of low voltage pulsed current (LVPC) on posttraumatic edema formation in frog hind limbs. Feet of 26 anesthetized bullfrogs were systematically injured by weight drop. One hind limb of each animal was randomly selected to receive continuous 100-pps LVPC at 90% of motor threshold; the opposite hind limb served as a control. A series of four 30-minute treatments (interrupted by 30-minute rests) was begun minutes after injury. Changes from pretrauma limb volumes were determined before and after each treatment and at 8, 17, 20, and 24 hours posttrauma. Analysis of variance revealed no significant treatment effect. Similar studies utilizing high voltage pulsed current (HVPC) at 90% of motor threshold revealed significant curbing of edema formation in frogs. Waveform (LVPC versus HVPC) seems to influence the efficacy of electrotherapy for edema control. [Karnes JL, Mendel FC, Fish DR. Effects of low voltage pulsed current on edema formation in frog hind limbs following impact injury. Phys Ther. 1992;72:273–278.]

Key Words: *Edema; Electrotherapy, electrical stimulation; Injuries; Wounds.*

High voltage pulsed current (HVPC) is a type of electrical stimulation (ES) characterized by dual monophasic pulses, delivered at relatively high voltages, but with each pulse pair lasting only a few microseconds, followed by relatively long interpulse intervals.[1] Conversely, *low voltage pulsed current* (LVPC) can be either biphasic or monophasic, but has much longer pulse durations and is delivered at relatively low voltages. The vast majority of stimulators used in physical therapy clinics, including those used for pain control and most neuromuscular electrical stimulators, may thus be classified as LVPC units.

Both HVPC and LVPC are used in clinics for different patient problems, although why one form and not another is used for a specific application is not known and seems arbitrary. For example, HVPC has been advocated for acute edema control,[2] but its effectiveness has not been demonstrated. Bettany et al[3–5] recently showed that cathodal HVPC significantly inhibited edema formation in frog hind limbs following impact or hyperflexion injury. Following injury, they performed four 30-minute treatments at intensities of 90% of motor threshold (ie, sensory ES) and showed that this type of ES, in an animal model, curbed edema. In the absence of a clear understanding of how HVPC inhibits edema, we hypothesized that, given the same conditions (ie, 10% less than motor threshold), LVPC would also be successful in inhibiting edema formation. We therefore studied the effects of cathodal LVPC on edema

JL Karnes, PT, is Assistant Professor, Program in Physical Therapy, Division of Rehabilitation Sciences, D'Youville College, 320 Porter Ave, Buffalo, NY 14201-1084 (USA). He is also a doctoral candidate in the Department of Anatomical Sciences, State University of New York at Buffalo. Address all correspondence to Mr Karnes.

FC Mendel, PhD, is Associate Professor, Department of Anatomical Sciences, State University of New York at Buffalo, Buffalo, NY 14214.

DR Fish, PhD, PT, is Associate Professor, Department of Physical Therapy and Exercise Science, and Director, Electrotherapy Research Laboratory, State University of New York at Buffalo.

This study was undertaken with the approval of the State University of New York at Buffalo Institutional Laboratory Animal Care Committee.

This article was submitted June 17, 1991, and was accepted September 9, 1991.

formation in frog hind limbs using the methods of Bettany et al.[3,4]

Rationale for Frog Model

Edema-causing injuries frequently happen in humans, but such injuries vary in severity and anatomical location and occur in people who differ in age, sex, health, and a host of other variables. This variability requires that studies of the effects of ES on edema in humans have large sample sizes to reduce the confounding influences of variability in such factors as age, sex, health, severity and site of injury, and time elapsed from injury to initiation of treatment. Such studies are expensive and time-consuming. Thus, to better control variables and reduce time and cost, nonhuman models, namely rats, have been used extensively to probe the effectiveness of various treatments, especially those involving anti-inflammatory medications, on posttraumatic swelling.[6] In most such studies, the animals' paws are injured after administration of anesthesia and limb volumes are measured repeatedly by plethysmography (ie, immersion of limb and measurement of displaced water). Unfortunately, small mammals, including rats, do not readily tolerate prolonged anesthesia. Their high metabolic rates preclude prolonged anesthesia without intravenous feeding; heat and water loss are also difficult to counteract without directly affecting their vascular systems, which may affect their microcirculation.

If anesthetized just for trauma, the animals must either be restrained after they wake, a very stressful situation for most animals, or allowed free movement, which may itself influence limb volumes by way of displacing fluids via "muscle pumping." Free movement may also subject animals to pain and the injured body part to further injury or manipulation (eg, massage or licking), all of which may influence limb volumes. Limb volumes must be determined on relaxed, perfectly still limbs (ie, on anesthetized animals). Treatment, especially sensory-level ES, is also delivered more effectively and with less evoked stress when the animal is anesthetized. Repeated use of anesthetics with small animals within 1 day or even once a day, however, often results in death.

To avoid some of the problems associated with human trials or trials involving small mammals, we chose bullfrogs as our experimental model. Bullfrogs can be anesthetized (through their skin) for an entire day without interdicting their vascular systems, and pain, stress, and movement ("muscle pump" activity) are eliminated as confounding factors. Repeated limb volume measurements can be easily accomplished and strong sensory-level treatments can be administered without inducing stress or discomfort. Ordinary room temperature is within tolerance of free-ranging bullfrogs and is probably near the high end of their preferred range; heat loss, therefore, is less a problem at room temperature for anesthetized poikilothermic (cold-blooded) frogs than for anesthetized homeothermic (warm-blooded) small mammals. Water loss is easier to control for amphibians than for small mammals because anesthetized amphibians breathe through their skin and therefore lose little moisture from their respiratory trees; simply keeping them moist effectively negates water loss.

Anesthesia, of amphibians or mammals, slows heart rate and probably most other physiologic responses, including responses to trauma. Observations of traumatized anesthetized animals (amphibians or mammals), however, indicate that fairly typical physiologic responses do occur, albeit at a rate that may be different from that of fully alert animals, and that those responses for each class of vertebrate are similar in kind and in function and therefore that the animals share similar physiologic processes. Just as axons of giant squids have served to reveal many principles of mammalian neurophysiology[7] and eggs of other invertebrates have served as a model for mammalian fertilization,[8] so may experiments using hind limbs of bullfrogs suggest the clinical utility of ES.

Method

Subjects

Twenty-six bullfrogs, *Rana catesbeiana*, weighing 382.5 to 573.7 g, were used. All procedures related to animal use were approved by the State University of New York at Buffalo Institutional Laboratory Animal Care Committee.

Instrumentation

Instruments used in this study, for the most part, were patterned after those used by Bettany et al.[3,4] To summarize, a 352.5-g metal rod was dropped through a tube from a height of 66 cm to cause trauma to the plantar aspects of the frogs' feet. To distribute the impact of the rod, a sheet of Plexiglas®* (4×2.5×0.3 cm) was placed between the tube and the frogs' feet.

A silanized plethysmograph, modified after that described by Singh and Mourya,[9] was used to measure limb volumes. It consisted of an immersion reservoir connected by a rubber tube to an overflow spigot. To test the reliability of the measurements obtained with the plethysmograph, four frog limbs were each immersed 30 times and the displaced water weighed to the nearest 0.1 g. The coefficient of variation averaged 0.87% for these 120 measurements, yielding an intraclass correlation coefficient of .995.

Treatments were administered via the immersion technique (water into which a limb was immersed served as the distal electrode) using dual-channel NTRON muscle stimulators† set at 100 pps. These stimulators were

*Rohm & Haas Co, Independence Mall W, Philadelphia, PA 19105.

†Model 8100, Henley International Inc, 104 Industrial Blvd, Sugar Land, TX 77478.

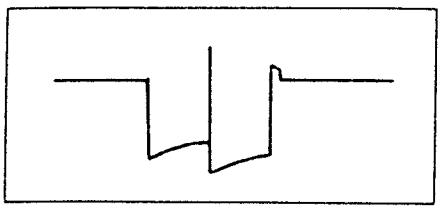

Figure 1. *Stimulation waveform. The standard biphasic pulses were converted via an internal bridge rectifier to double-peaked monophasic pulses of negative polarity with an "effective" pulse duration of 620 to 630 microseconds.*

previously modified such that standard biphasic pulses were converted via an internal bridge rectifier to dual monophasic pulses of negative polarity (Fig. 1). "Effective" pulse duration was 620 to 630 microseconds, because the interphase duration was virtually zero. Self-adhering carbon-rubber electrodes[‡] (25×18 mm) were applied to the skin overlying the frogs' hips and to the inside walls of beakers. Stimulator voltage outputs from all subjects were visualized on a dual-trace storage oscilloscope[§] in conjunction with a voltage monitor.

Procedure

Frogs were anesthetized in 3-aminobenzoic acid ethyl ester (3 g of anesthetic per liter of water) for 20 to 30 minutes and then placed in anesthesia-soaked cloth slings in which they were held and suspended throughout most of the 24-hour test period. Slings simplified handling and provided a means of uniform support for frogs during plethysmography, treatment, and rest and also rendered all four limbs in dependent positions.

Lines were painted on both legs of each frog 4 cm proximal to the lateral malleoli. Pretrauma limb volumes were obtained via plethysmography by immersing the frog's legs to these lines. Displaced water, equivalent to limb volumes, was collected and weighed,[‖] with each gram equal to 1 ml. Trauma was then inflicted as described earlier.

Following trauma, each hind limb was immersed to its premarked line in separate 1-L beakers containing tap water. Positive electrodes were applied to the skin overlying the hips, and negative electrodes were applied to the inside walls of each treatment beaker in which limbs were immersed. Electrical stimulation to each limb was controlled by separate stimulator channels. One hind limb was randomly selected to receive ES; the other hind limb served as a control. Treatments began within 5 to 12 minutes of trauma.

Animals received four 30-minute treatments separated by 30-minute rest periods. Stimulation intensity of treated limbs was increased to the point of visible muscle contractions, then reduced 10%. Use of the oscilloscope made this reduction of stimulation intensity quite precise. To match brief contractions induced in the treated limbs, stimulation intensities of the control limbs were increased to a point of brief visible muscle contraction, but then brought quickly to zero. This procedure ensured that any possible treatment effect caused by the small muscle "twitch" in the treated limbs would be the same in the control limbs. Limb volumes were obtained before and after trauma, before and after treatments, and at 8, 17, 20, and 24 hours posttrauma by a rater who did not know which limbs were treated. Anesthesia was maintained from the last treatment to 8 hours posttrauma and from 17 hours posttrauma to 24 hours posttrauma by dripping anesthesia on the slings at rates not greater than 60 drops/min (approximately 2 mL/min). From 8 hours to 17 hours posttrauma, animals were placed prone on towels saturated with the anesthetic. This was the only time in which the animals were not hanging in the slings with their hind limbs in a dependent position.

After 24 hours, the animals were sacrificed. Skin from the feet was removed to check for hematomas to confirm that volume changes were due to edema formation and not frank bleeding. Bleeding into the interstitium would increase limb volumes, but would not represent volume changes attributable to edema. Data from six animals were discarded because of the presence of visible hematomas or death.

Data Analysis

A one-way analysis of variance (ANOVA) for repeated measures ($P<.05$) was used to determine the effects of treatment and time. An ANOVA ($P<.05$) was also used to analyze voltage output differences recorded from treatment to treatment.

Results

The Table shows the results of the ANOVA for the treated and untreated limbs. Volumes of hind limbs treated with LVPC were not significantly different over time from those of untreated hind limbs (Fig. 2). Average voltages ranged from 6.4 to 5.8 V across treatments; the ANOVA revealed no significant change in the voltage needed to treat limbs at 90% of motor thresholds through the series of four treatments.

Discussion

The research design used in this study was nearly the same as that used by Bettany et al,[4] who, using a 120-pps continuous train of cathodal HVPC (the first pulse lasting 5 microseconds and the second pulse lasting 8 microseconds, with a 75-microsecond interpulse interval), demonstrated significant inhibition of edema formation. Low voltage pulsed current, at 100 pps with cathodal monophasic pulse pairs lasting 620 to 630 microseconds, however, did not

[‡]Tenzcare, 3M Corp, Bldg 225-5S-01, 3M Center, St Paul, MN 55144-1000.

[§]Tektronix 5103N, Tektronix Inc, Beaverton, OR 97005.

[‖]Mettler E2000, Mettler Instrument Corp, 29 Nassau St, Princeton, NJ 08520.

Table. *One-Way Analysis-of-Variance Results for Effects of Treatment and Time on Changes in Limb Volume*

Source	df	SS	MS	F	P[a]
Treatment	1	38.36	38.36	0.14	.708
Error	38	10222.70	269.02		
Time	11	1479.40	134.49	9.15	<.001
Interaction	11	76.50	6.95	0.47	.920
Error	418	6145.48	14.70		

[a] $P<.05$.

significantly curb edema formation in the frogs' hind limbs.

Frogs differed in body weight, so dropping the same weight from the same height did not inflict uniform injuries across the group; smaller animals received greater injuries than larger animals. Impact forces were not normalized relative to body weight because each animal was used as its own control. Our design required only the assumption that treated limbs, as a group, were injured to the same extent as untreated limbs. Each treated limb had a near-perfect untreated match (ie, its contralateral limb), so we believe we met the requirements of that assumption. Also, even normalized impact forces would fail to produce uniform injuries in all animals because of variation in such factors as age, sex, nutritional and hormonal states, reproductive status, musculoskeletal development, and inherent differences in development of vascular and lymphatic systems.

Comparing and contrasting waveforms and stimulation characteristics of HVPC, as used by Bettany et al,[3,4] and LVPC, as used in this study, may provide some clues as to why the results were so different. Polarity is one such characteristic that may be important. Because plasma and other blood components are negatively charged, it is thought by some that cathodal ES may inhibit edema by repelling those components from sites of edema or retarding the escape of plasma proteins from vascular to extravascular spaces.[2] Such hypotheses have yet to be substantiated with pulsed current, but, because cathodal stimulation was common to this study and those of Bettany et al,[3,4] it can hardly be expected to account for the differences in success of HVPC and LVPC in inhibiting edema formation.

Differences in signal characteristics between the studies of Bettany et al[3,4] and this study also include differences in signal frequency. Bettany et al used 120 pps, whereas we used 100 pps, the highest frequency available from the NTRON stimulators that we used. These frequencies, however, are not very disparate (100 pps is 83.3% of 120 pps). It is unlikely (but theoretically possible), therefore, that this small difference in signal frequency accounted for the different outcomes of HVPC and LVPC.

Pulse duration is another stimulation characteristic that differed between this study and the studies of Bettany et al.[3,4] They delivered HVPC pulse pairs lasting a total of 13 microsec-

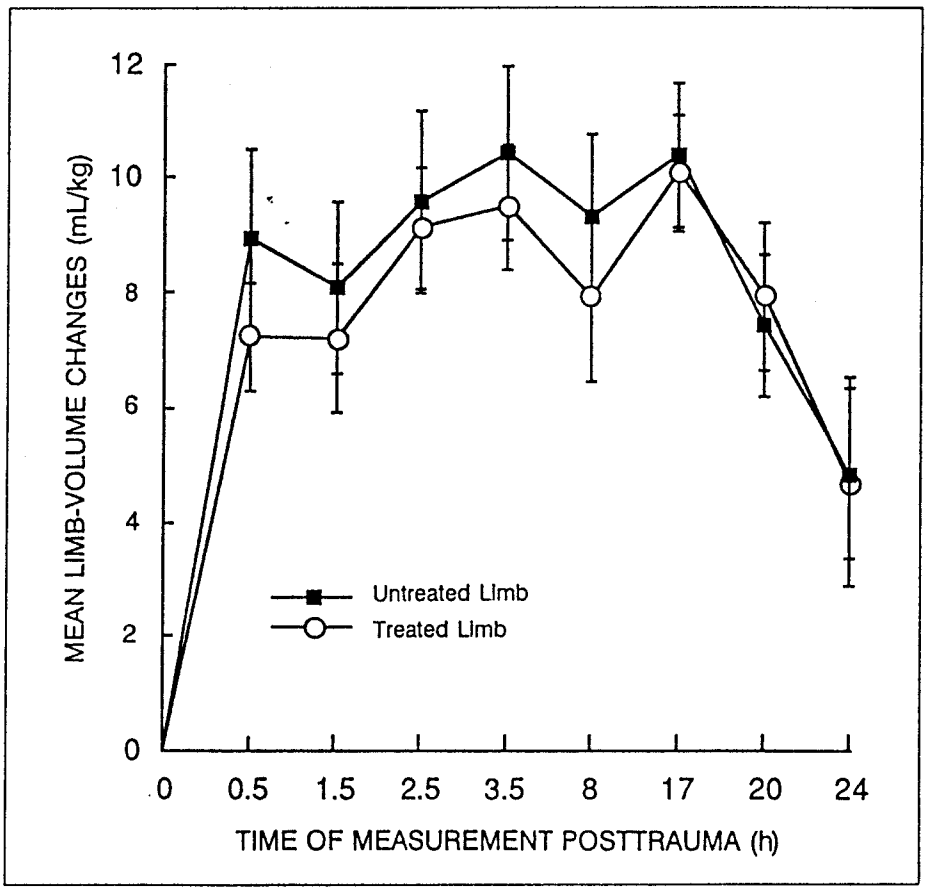

Figure 2. *Analysis of variance of changes in treated and untreated limb volumes over time. Vertical lines depict standard errors. Means for treated limbs were not significantly less than those for untreated limbs (P>.05). Measurements at 0.5, 1.5, 2.5, and 3.5 hours posttrauma represent data collected after treatments 1, 2, 3, and 4, respectively.*

onds, whereas the LVPC used in this study had durations of 620 to 630 microseconds (ie, nearly 50 times longer). Pulse charge, the quantity of electrical energy delivered to tissue with each phase of each pulse,[10] was about 7.5 times higher with LVPC than with HVPC. This large difference in pulse charge is obviously due to the relatively long pulse duration of LVPC. It seems that high-amplitude pulses of very short duration producing small amounts of charge (ie, those characteristic of HVPC) are more effective in inhibiting edema formation than are low-amplitude pulses of long duration producing comparatively large amounts of charge (ie, those characteristic of LVPC, as used in this study). Both kinds of signals, however, were equivalent in the sense that both were delivered at 90% of motor threshold. Unaccountably, sensory stimulation to 90% of motor threshold produced a significant treatment effect with HVPC, but not with LVPC. This finding suggests that the mechanism(s) being activated (or inhibited) by HVPC may not be neuronally mediated. Further evidence in support of this hypothesis follows.

Alon and DeDomenico[1] suggest that ES may affect sympathetic outflow, which in turn could affect edema formation by inducing vasoconstriction and thereby restricting movement of blood constituents from vascular to extravascular compartments at an injury site. Results of investigations into the effects of sensory-level ES on sympathetic activity are anything but uniform. Monitoring such variables as skin temperature,[11–16] peripheral blood flow,[15] and blood pressure and heart rate,[12] investigators have provided indirect evidence that sensory-level ES increased,[11,14] decreased,[13,15] or had no effect[12,15] on sympathetic activity. The LVPC used in this study had pulse widths nearly 50 times those of the HVPC signals used successfully by Bettany et al[3,4] and pulse charges 7.5 times as great. Therefore, if HVPC curbed edema via stimulation of sympathetic neurons, it is likely that LVPC, as used in this study, would have exceeded thresholds of those nerves as well and triggered the same response. That did not occur. Because the HVPC used by Bettany et al[3,4] and the LVPC used in this study were both at 90% of motor threshold, it is unlikely that thresholds of smaller, unmyelinated sympathetic neurons were exceeded. We conclude, therefore, that neither sensory nor sympathetic stimulation, nor indeed neuronally mediated mechanisms, are the means by which sensory-level HVPC curbs edema.

Reed[17] reported that HVPC diminished leakage of labeled dextran from microvessels exposed to histamine. This finding suggests that ES may influence permeability of microvessels and hence could potentially influence edema formation. Reed's findings might be attributable to neurogenic reactions, but fairly typical inflammatory reactions, including increased microvessel permeability, are known to occur in denervated tissue.[18] Further research of the effects of ES on microvessels is essential.

Unlike Bettany et al,[3,4] who found that voltages necessary to cause muscle contractions increased from one treatment to the next, we found no statistical difference in LVPC voltages from the first to the last treatment (ie, no need to increase voltage of LVPC to reach 90% of motor threshold). Increases in the voltage requirement by Bettany et al may, in part, have been due to the ever-increasing depth of anesthesia in their studies. They soaked animals in an anesthetic for long periods (ie, between treatments and limb-volume measurements), possibly causing desensitization of motoneurons such that relatively high voltages were needed to cause muscle contraction.[4] We maintained unconsciousness from 0 to 8 hours and 17 to 24 hours posttrauma by dripping the anesthetic on the animals while they were suspended in cloth slings. Anesthesia may have been maintained at a more constant and less profound level by this method.

Whereas Bettany et al[3,4] were able to obtain voltage outputs directly from their stimulators, the NTRON stimulators used in this study did not have output indicators. To allow comparison with the works of Bettany et al, voltage outputs were read from an oscilloscope placed in series with the stimulators and the frogs. Because of its greater sensitivity, the oscilloscope probably allowed greater accuracy in measuring voltage outputs than did the stimulators used by Bettany et al. Nevertheless, greater precision in measuring voltages cannot account for the large differences in voltage between first and last treatments in the studies of Bettany et al and the relatively uniform voltages across treatments (ie, not significantly different from the first to the last treatment) we administered.

Hind limbs were required to be in a dependent position at least for plethysmography and treatment, as the hind limbs were immersed to determine volume displacement and for administration of treatment, respectively. Such positioning alone is known to increase limb volumes in anesthetized frogs.[19] Therefore, it seems reasonable to expect dependent positioning to exacerbate posttraumatic edema formation. Both feet of each frog were traumatized equally so that net increases in limb volume included swelling induced by trauma as well as by positioning. Whereas dependent positioning is contrary to conventional clinical practice, orienting limbs in virtually any other position might be construed as therapeutic. Efficacy of ES for edema control might be underestimated using our current model because dependent positioning may mask a small, but positive, treatment effect. That is, we are now imposing a more stringent test of efficacy of ES to ensure that positioning is not a factor. Thus, when we report that ES results in significant treatment effects,[20] such effects occur despite the challenge of dependent positioning.

We used the immersion technique in this study because it eliminated problems associated with surface electrodes (eg, uneven contact with skin, particularly on small, irregularly shaped body parts of small vertebrates, and difficulties in applying electrodes for long

periods). Frogs were kept moist and anesthetized by anesthetic-laden water that was continuously dripped over them during rest periods between treatments. Moreover, measuring limb volumes by plethysmography requires repeated immersions in water. This repeated exposure to moisture would probably result in dissolution of electrode gel/adhesive. Reapplication of electrodes would require frequent manipulation of injured limbs and would potentially influence limb volumes.

Our model, like any other, has limitations. Frogs and humans, as vertebrates, share significant and fundamental aspects of their physiology. In physiologic responses such as inflammation, frogs have long been studied and used as models for humans,[21] and many basic tenets of electrotherapy have been determined on frogs and applied to humans with good fidelity.[22] The physiology of frogs and humans also differs in significant ways; thus, the results of studies of frogs cannot be applied directly to humans. We believe, however, that our kinship with frogs (and hence our shared physiology) is sufficiently close that results of studies on frogs are predictive of similar results in humans, enough at least to serve as bases for clinical hypotheses.

Continuous cathodal HVPC, at 120 pps and 90% of motor threshold, has been shown to be effective in controlling edema formation. Low voltage pulsed current, as applied in this study, was not effective. We conclude, therefore, that not all forms of ES are effective in controlling edema formation. We still have no clear understanding of why HVPC is effective and LVPC, as applied in this study, is not effective in controlling edema when both are administered at 90% of motor threshold, but we are beginning to suspect non-neuronally mediated processes. To date, then, the only form of ES that has been shown to significantly curb edema formation in nonhuman models is HVPC.

Conclusion

Continuous cathodal low voltage stimulation of 620 to 630 microseconds at 100 pps and 90% of motor threshold does not significantly inhibit edema formation in frog hind limbs following impact injuries.

Acknowledgments

We thank Keith Taylor, PT, and Robert E Kell for their technical assistance, Kenneth Ottenbacher, PhD, OTR, for statistical consultation, and Henley International for complimentary loan of stimulators.

References

1 Alon G, DeDomenico G. *High Voltage Stimulation: An Integrated Approach to Clinical Electrotherapy.* Chattanooga, Tenn: Chattanooga Corp; 1987.

2 Newton RA. High voltage pulsed galvanic stimulation: theoretical bases and clinical applications. In: Nelson RM, Currier DP, eds. *Clinical Electrotherapy.* East Norwalk, Conn: Appleton & Lange; 1987:165–182.

3 Bettany JA, Fish DR, Mendel FC. High-voltage pulsed direct current: effect on edema formation after hyperflexion injury. *Arch Phys Med Rehabil.* 1990;71:677–681.

4 Bettany JA, Fish DR, Mendel FC. Influence of high voltage pulsed direct current on edema formation following impact injury. *Phys Ther.* 1990;70:219–224.

5 Bettany JA, Fish DR, Mendel FC. Influence of cathodal high voltage pulsed current on acute edema. *J Clin Electrophysiol.* 1990;2:5–8.

6 Riesterer L, Jacques R. The influence of anti-inflammatory drugs on the development of an experimental traumatic paw oedema in the rat. *Pharmacology.* 1970;3:243–251.

7 Young JZ. The giant nerve fibers and epistellar body of cephalopods. *Q J Microsc Sci.* 1936;78:367–386.

8 Balinski BI. *An Introduction to Embryology.* 3rd ed. Philadelphia, Pa: WB Saunders Co; 1970:118.

9 Singh RH, Mourya SP. Development and standardization of a new apparatus for accurate measurement of swelling in paw of small laboratory animals. *Indian J Med Res.* 1972;60:488–490.

10 Alon G. Principles of electrical stimulation. In: Nelson RM, Currier DP, eds. *Clinical Electrotherapy.* East Norwalk, Conn: Appleton & Lange; 1987:29–80.

11 Abram SE. Increased sympathetic tone associated with transcutaneous electrical stimulation. *Anesthesiology.* 1976;45:575–577.

12 Ebersol MJ, Laws ER, Albers JW. Measurements of autonomic function before, during, and after transcutaneous stimulation in patients with chronic pain and in control subjects. *Mayo Clin Proc.* 1977;52:228–232.

13 Owens S, Atkinson ER, Lees DE. Thermographic evidence of reduced sympathetic tone with transcutaneous nerve stimulation. *Anesthesiology.* 1979;50:62–65.

14 Randall BF, Imig CJ, Hines HM. Effect of electrical stimulation upon blood flow and temperature of skeletal muscle. *Am J Phys Med.* 1953;32:22–26.

15 Wong RA, Jette DU. Changes in sympathetic tone associated with different forms of transcutaneous electrical nerve stimulation in healthy subjects. *Phys Ther.* 1984;64:478–482.

16 Dooley DM, Dasprak M. Modification of blood flow to the extremities by electrical stimulation of the nervous system. *South Med J.* 1976;69:1309–1311.

17 Reed BV. Effect of high voltage pulsed electrical stimulation on microvascular permeability to plasma proteins: a possible mechanism to minimizing edema. *Phys Ther.* 1988; 68:491–495.

18 Macleod AG. *Scope Monograph on Aspects of Acute Inflammation.* Kalamazoo, Mich: The Upjohn Co; 1971.

19 Fish DR, Mendel FC, Bettany JA. Research design considerations in studying edema. *Phys Ther.* 1990;70:76–78. Author response to letter to the editor.

20 Taylor K, Fish DR, Mendel FC, Burton HW. Effect of a single 30-minute treatment of high voltage pulsed current on edema formation in frog hind limbs. *Phys Ther.* 1992;72:63–68.

21 Borgens RB, Robinson KR, Vanable JW, McGinnis ME. *Electric Fields in Vertebrate Repair.* New York, NY: Alan R Liss Inc; 1989.

22 Waters RL. History of electrical stimulation. In: *Functional Electrical Stimulation: A Practical Clinical Guide.* Downey, Calif: Rancho Los Amigos Rehabilitation Engineering Center; 1980:1–8.