Papers on Wound Healing

Increased Blood Flow to the effected Treatment Area and Wound Healing while using electrical stimulation.

Effects of aging on neurogenic vasodilator responses evoked by transcutaneous electrical nerve stimulation: relevance to wound healing.

Khalil Z, Merhi M
J Gerontol A Biol Sci Med Sci. 2000 Jun; 55(6):B257-63.
National Ageing Research Institute, University of Melbourne, Victoria, Australia.

We have previously shown an age-related decline in the modulation of skin vascular reactivity by sensory nerves that correlates with a decline in wound repair efficacy. This study was designed to examine the possibility that improving the functional ability of aged sensory nerves using noninvasive transcutaneous electrical nerve stimulation (TENS) could also accelerate tissue repair. TENS of the sciatic nerve, combined with measuring blood flow responses in the rat hind-footpad using laser Doppler flowmetry, was used to establish the vascular effects. Following TENS (using parameters 20V, 5 Hz for 1 min), similar increases in vascular responses were obtained in both young (13.2+/-0.9 cm2) and old rats (11.6+/-2.3 cm2). In contrast, capsaicin-pretreated rats showed markedly diminished responses. Sympathetic fibers did not appear to modulate these sensory nerve responses. In the second part, a thermal wound was induced (using a CO2 laser) in the interscapular region of old rats (under anesthesia). In the active treatment group, TENS was applied twice daily for the initial 5 days, and the sham group received inactive TENS. Using the healing endpoint as the time when full wound contraction occurred, the active group required 14.7+/-0.2 days for complete healing, a significant improvement over the sham group (21.8+/-0.3 days). We contend that low-frequency TENS can improve the vascular response of old rats. In addition, wound healing in aged rats can be accelerated by peripheral activation of sensory nerves at low-frequency electrical stimulation parameters.

Epidural spinal cord electrical stimulation in diabetic critical lower limb ischemia.

Petrakis IE, Sciacca V
Title Abbreviation: J Diabetes Complications.
1999 Sep-Dec; Volume Issue: 13(5-6):293-9.
First Department of General Surgery, Policlinico Umberto I, University of Rome, La Sapienza, Rome, Italy.

Spinal cord stimulation (SCS) has been suggested to improve microcirculatory blood flow to relieve ischemic pain and to reduce amputation rate in patients with peripheral arterial occlusive disease (PAOD). The aim of this study was to evaluate the specific prognostic parameters in the prediction of successful SCS, in diabetic patients, performing a retrospective data analysis. To perform this evaluation, 64 diabetic patients (39 men, 25 women; mean age, 69 years) classified as Fontaine's stage III and IV, with PAOD, were treated with SCS for rest pain and trophic lesions with dry gangrene, after failed conservative or surgical treatment. In clinical controls, pedal transcutaneous oxygen tension (TcPO(2)), ankle/brachial blood pressure index (ABI), and toe pressure Doppler measurements were utilized to select and follow-up the patients. After 58 months of follow-up (range, 20-128 months), pain relief

greater than 75% and limb salvage were achieved in 38 diabetic patients. A partial success was obtained in nine patients with pain relief greater than 50% and limb salvage for at least 6 months. The method failed in 17 patients or the device was removed due to technical problems, and the limb was amputated in these patients. TcPO(2) was assessed on the dorsum of the foot. Clinical improvement and SCS success were associated with increase of TcPO(2), before and after implantation. Limb salvage was achieved in the patients who had significant TcPO(2) increase within the 2 weeks of the testing period, independently of the stage of the disease. A TcPO(2) increase of more than 50% in the first 2 months after implantation was predictive of success, and was related to the presence of adequate paresthesias in the painful area during the trial period. TcPO(2) significantly increased after long-term follow-up in all patients with limb salvage (from 22.1 to 43.1 mm Hg in the rest pain patients, from 15.8 to 36.4 mm Hg in those with trophic lesions of less than 3 cm(2), and from 12.1 to 28.1 in those with trophic lesions of greater than 3 cm(2), ($p < 0.01$). ABI did not changed under stimulation. In diabetic patients with PAOD, the SCS increases the skin blood flow, is associated with significant pain relief, and could be proven an excellent alternative therapy, improving the life quality. Significant TcPO(2) increase within the 2-week test period, is a predictive index of therapy success and should be considered before the final decision in terms of cost effectiveness, before the permanent implantation.

Effects of transcutaneous nerve stimulation on the microcirculation in chronic leg ulcers.

Cosmo P, Svensson H, Bornmyr S, Wikstrom SO
Scand J Plast Reconstr Surg Hand Surg. 2000 Mar; 34(1):61-4.
Department of Plastic and Reconstructive Surgery, Malmo University Hospital, Sweden.

The purpose of this study was to find out to what extent transcutaneous electrical nerve stimulation (TENS) affects the blood flow in and around chronic lower leg ulcers, as measured with a new technique, laser Doppler imaging (LDI). Fifteen patients, mean age 73 years (range 38-85) with chronic leg ulcers of various causes participated in the study. The duration of the ulcers ranged from 3 months to 16 years. Low-frequency (2 Hz; 10-45 mA) TENS was given for 60 minutes. The changes in blood flow were measured every 5 minutes by LDI. After 60 minutes, mean blood flow had increased in the ulcer by 35%, and in the intact skin surrounding the ulcer by 15%. Even 15 minutes after the TENS had finished there was still a mean blood flow increase of 29% in the ulcer and 9% in the skin. The present results show that TENS has a stimulating effect on local blood circulation in and around chronic ulcers.

Effect of transcutaneous nerve stimulation on microcirculation in intact skin and blister wounds in healthy volunteers.

Wikstrom SO, Svedman P, Svensson H, Tanweer AS
Scand J Plast Reconstr Surg Hand Surg. 1999 Jun; 33(2):195-201.
Department of Plastic and Reconstructive Surgery, University Hospital MAS, Malmo, Sweden.

Healthy non-smoking volunteers participated in two experimental studies in which the circulatory changes induced by transcutaneous nerve stimulation (TENS) were quantified by two different methods. In experimental series 1 (intact skin), nine volunteers were given TENS on the left lower leg for 60 minutes on three occasions at different frequencies each time (2 Hz, 100 Hz, and sham). Changes in blood flow were assessed by laser Doppler imaging

technique every five minutes. The mean blood flow increased by 40% during low frequency TENS and by 12% during high frequency TENS. There was no change in mean blood flow during sham stimulation. In experimental series 2 (blister wound), the circulatory changes induced by TENS were studied by intravital video microscopy and computerised image analysis in standard blister wounds on the lower leg. The microcirculatory blood flow, measured as red blood cell velocity (RBC-V) in 5-14 individual capillaries in each wound, was assessed before and during 45 minutes of TENS (2 Hz and 100 Hz). Mean RBC-V increased by 23% during low frequency TENS (n = 6) and by 17% during high frequency TENS (n = 8). The results show that: laser Doppler imaging and intravital video microscopy techniques can be used to study events at the microcirculatory level; the blister wound is an interesting new standard wound for use in clinical studies; and TENS stimulates the peripheral circulation.

Prognostic factors in the prediction of chronic wound healing by electrical stimulation.

Cukjati D, Robnik-Sikonja M, Rebersek S, Kononenko I, Miklavcic D.
Med Biol Eng Comput. 2001 Sep;39(5):542-50.
Faculty of Electrical Engineering, University of Ljubljana, Slovenia.

The aim of the study is to determine the effects of wound, patient and treatment attributes on the wound healing rate and to propose a system for wound healing rate prediction. Predicting the wound healing rate from the initial wound, patient and treatment data collected in a database of 300 chronic wounds is not possible. After considering weekly follow-ups, it was determined that the best prognostic factors are weekly follow-ups of the wound healing process, which alone were found to predict accurately the wound healing rate after a minimum follow-up period of four weeks (at least five measurements of wound area). After combining the follow-ups with wound, patient and treatment attributes, the minimum follow-up period was reduced to two weeks (at least three measurements of wound area). After a follow-up period of two weeks, it was possible to predict the wound healing rate of an independent test set of chronic wounds with a relative squared error of 0.347, and after three weeks, with a relative squared error of 0.181 (using regression trees with linear equations in its leaves). Regression trees with a relative squared error close to 0 produce better prediction than with an error closer to 1. Results show that the type of treatment is just one of many prognostic factors. Arranged in order of decreasing prediction capability, prognostic factors are: wound size, patient's age, elapsed time from wound appearance to the beginning of the treatment, width-to-length ratio, location and type of treatment. The data collected support former findings that the biphasic- and direct-current stimulation contributes to faster healing of chronic wounds. The model of wound healing dynamics aids the prediction of chronic wound healing rate, and hence helps with the formulation of appropriate treatment decisions.

Choosing an adjunctive therapy for the treatment of chronic wounds.
Houghton PE, Campbell KE.

Ostomy Wound Manage. 1999 Aug;45(8):43-52; quiz 53-4.
St. Joseph's Health Center, School of Physiotherapy, University of Western Ontario, London, Canada.

Adjunctive therapies such as ultrasound, laser, ultraviolet light, superficial heating, pulsed electromagnetic fields, and electrical stimulation have all been indicated in the treatment of chronic wounds. The purpose of this article is to outline the issues a healthcare professional must consider when

choosing the best adjunctive therapy for a chronic wound. It summarizes the effects of therapeutic modalities on the wound healing process, analyzes the clinical research evidence, discusses practical considerations, and reviews indications, contraindications, precautions, and safety considerations. Finally, an algorithm is presented to help guide the clinician in selecting a modality. In summary, research evidence exists in the literature that suggests these adjunctive therapies can directly stimulate new tissue growth, augment wound tissue strength, improve local circulation and oxygenation, reduce edema, and/or inhibit bacterial growth. Electrical stimulation and ultrasound are the only therapeutic modalities that currently have sufficient clinical research evidence to support their use in the treatment of chronic wounds. Practical issues such as cost, time and training required, and patient and therapist safety concerns, will ultimately influence the selection of these modalities.

Effect of electrical stimulation on chronic wound healing: a meta-analysis.
Gardner SE, Frantz RA, Schmidt FL.

Wound Repair Regen. 1999 Nov-Dec;7(6):495-503.
Colleges of Nursing, The University of Iowa, Iowa City, IA 52242-7066, USA.

The purpose of this meta-analysis was to quantify the effect of electrical stimulation on chronic wound healing. Fifteen studies, which included 24 electrical stimulation samples and 15 control samples, were analyzed. The average rate of healing per week was calculated for the electrical stimulation and control samples. Ninety-five percentage confidence intervals were also calculated. The samples were then grouped by type of electrical stimulation device and chronic wound and reanalyzed. Rate of healing per week was 22% for electrical stimulation samples and 9% for control samples. The net effect of electrical stimulation was 13% per week, an increase of 144% over the control rate. The 95% confidence intervals of the electrical stimulation (18-26%) and control samples (3.8-14%) did not overlap. Electrical stimulation was most effective on pressure ulcers (net effect = 13%). Findings regarding the relative effectiveness of different types of electrical stimulation device were inconclusive. Although electrical stimulation produces a substantial improvement in the healing of chronic wounds, further research is needed to identify which electrical stimulation devices are most effective and which wounds respond best to this treatment.

A comparative study of the effect of ultrasound and electrostimulation on wound healing in rats.

Taskan I, Ozyazgan I, Tercan M, Kardas HY, Balkanli S, Saraymen R, Zorlu U
Plast Reconstr Surg. 1997 Sep;100(4):966-72.
Physical Therapy and Rehabilitation Center, Medical Faculty of Inonu University, Istanbul, Turkey.

A comparative study has been carried out to investigate the effects of electrical stimulation and ultrasound on wound healing. Eighty-four female rats were divided into four groups depending on the treatment received. The first group was given electrical stimulation of 300 microA direct current, 30 minutes daily, starting with negative polarity and then changed after 3 days of treatment. Group 2 received sham electrostimulation treatment. The third group received 0.1 W/cm2 pulsed ultrasound using the moving applicator technique for 5 minutes a day. Group 4 received sham ultrasound treatment. A total of 7 days of treatment was given to all groups. Histopathologic and biochemical analyses on the fourth and seventh days and wound breaking

strength on the twenty-fifth day were performed for all groups. By accelerating the inflammatory phase, electrical stimulation had progressed the proliferative phase of wound healing earlier than ultrasound had done. Both electrical stimulation and ultrasound have positive effects on proliferative phases, but electrical stimulation was superior to ultrasound at the maturation phase. There was no difference between the two experimental groups on the mast cell reduction effect. Although ultrasound treatment may seem to be efficient in terms of time, when the effects of electrical stimulation and ultrasound on wound healing with the methods employed in our study are considered, it is concluded that electrical stimulation is a means of treatment superior to ultrasound in wound healing.

Effects of electrical stimulation on wound healing in patients with diabetic ulcers.

Baker LL, Chambers R, DeMuth SK, Villar F.
Diabetes Care. 1997 Mar;20(3):405-12.
Department of Biokinesiology and Physical Therapy, University of Southern California, Los Angeles 90033,

OBJECTIVE: To evaluate the effects of two stimulation waveforms on healing rates in patients with diabetes and open ulcers. The hypothesis was that stimulus waveforms with minimal polar characteristics would provide significant healing for this patient sample. RESEARCH DESIGN AND METHODS: This was a prospective study that enrolled 80 patients with open ulcers. Patients received stimulation with either an asymmetric biphasic (A) or symmetric biphasic (B) square-wave pulse. Amplitudes were set to activate intact peripheral nerves in the skin. Two other groups received either very low levels of stimulation current (MC), or no electrical stimulation (C). When combined these groups were referred to as the control group. Treatment was carried out daily until the wound healed, the patient withdrew from the study, or the physician changed the overall wound management program. Average healing rates were calculated from weekly measures of the wound perimeter and were used for statistical comparison through a one-way analysis of variance. RESULTS: Stimulation with the A protocol significantly increased the healing rate, enhancing healing by nearly 60% over the control rate of healing. Stimulation with the B protocol did not increase the healing rate when compared with control subjects. CONCLUSIONS: Electrical stimulation, given daily with a short pulsed, asymmetric biphasic waveform, was effective for enhancement of healing rates for patients with diabetes and open ulcers.

Promotion of wound healing with electrical stimulation.

Kloth LC, McCulloch JM.
Adv Wound Care. 1996 Sep-Oct;9(5):42-5.
Program of Physical Therapy, Marquette University, Milwaukee, Wis, USA.

Clinicians involved in the conservative care of chronic wounds have many treatment interventions from which to choose, including debridement/irrigation, dressings, pressure-relieving devices, hyperbaric or topically applied oxygen, whirlpool/pulsed lavage, ultrasound, topical antibiotics, and cytokine growth factors. All except the last two interventions are physical treatments that create a wound-tissue environment conducive to healing. Unfortunately, many chronic wounds heal very slowly, do not heal, or worsen despite the best efforts of caregivers to promote tissue repair. An intervention commonly used to treat chronic wounds, especially by physical therapists, is electrical stimulation (ES). The rationale for use of

this method is based on the fact that the human body has an endogenous bioelectric system that enhances healing of bone fractures and soft-tissue wounds. When the body's endogenous bioelectric system fails and cannot contribute to wound repair processes, therapeutic levels of electrical current may be delivered into the wound tissue from an external source. The external current may serve to mimic the failed natural bioelectric currents so that wound healing can proceed. Certain chemotaxic factors found in wound substrates contribute to tissue repair processes by attracting cells into the wound environment. Neutrophil, macrophage, fibroblast, and epidermal cells involved in wound repair carry either a positive or negative charge. When these cells are needed to contribute to autolysis, granulation tissue formation, anti-inflammatory activities, or epidermal resurfacing, ES may facilitate galvanotaxic attraction of these cells into the wound tissue and thereby accelerate healing.

Physical modalities in wound management: UVC, therapeutic heating and electrical stimulation.

Kloth LC.
Ostomy Wound Manage. 1995 Jun;41(5):18-20, 22-4, 26-7.

In spite of efforts to create an optimum wound environment for healing, there are times that a wound may not heal, may heal very slowly, or may worsen. In these cases, a series of treatments with an appropriate physical agent can be added to the patient's care plan to augment tissue reparative processes. Three modalities that have received support in the literature for use in wound healing are ultraviolet "C" radiation (UVC), therapeutic heating, and electrical stimulation. Treatment goals for UVC are hyperplasia and enhanced re-epithelialization or desquamation of the leading edge of periulcer epidermal cells, granulation tissue formation, sloughing of necrotic tissue, and bactericidal effects. Treatment goals for therapeutic heating are increased blood perfusion with subsequent increased delivery of oxygen to the tissues (avoiding the dessication of wound tissues). The treatment goal for electrical stimulation is to attract negatively or positively charged cells into the wound area, such as neutrophils, macrophages, epidermal cells and fibroblasts that in turn will contribute to wound healing processes by way of their individual cellular activities.

Experimental wound healing with electrical stimulation.

Reger SI, Hyodo A, Negami S, Kambic HE, Sahgal V
Title Abbreviation: Artif Organs.
1999 May; 23(5):460-2.
Department of Physical Medicine and Rehabilitation, The Cleveland Clinic Foundation, Ohio 44195, USA.

The effect of alternating current (AC) and direct current (DC) stimulation was studied on experimental pressure ulcer healing in a new monoplegic pig model. The study was conducted in 30 healthy young Hanford minipigs. The rate of wound healing, histology, vascularization, collagen formation, microbiology, perfusion, and the mechanical strength of the healed wounds were studied. Normal pigskin was compared to denervated control and denervated AC and DC stimulated healed skin. Hind limb denervation was by right unilateral extradural rhizotomies from the L2 to S1 nerve roots. Reproducible uniformly controlled Stage III or higher tissue ulcers were created. When compared to the control wounds, both the AC and DC stimulated wounds showed reduced healing time and increased perfusion in the early phases of healing. DC

stimulation reduced the wound area more rapidly than AC, but AC stimulation reduced the wound volume more rapidly than DC. The electrical stimulation did not reduce the strength of the healing wounds below those of the nonstimulated controls. The applied current appears to orient new collagen formation even in the absence of neural influences.

Electric muscle stimulation for pressure sore prevention: tissue shape variation.

Levine SP Kett RL Cederna PS Brooks SV
Arch Phys Med Rehabil (1990 Mar) 71(3):210-5

This study measured changes in tissue shape and deformation at the seating interface produced by electric muscle stimulation (EMS) of the gluteus maximus. The purpose of the study was to investigate the application of EMS for pressure sore prevention. Limitations of pressure measurements for analysis of load distribution are discussed and a rationale developed for using tissue shape and deformation to further characterize the seating interface. Ultrasonic imaging of the seating interface is described under three conditions: buttocks suspended, external load applied with no EMS, and external load applied with bilateral EMS of the buttocks. Results show that low level stimulation of the gluteus maximus produces substantial changes in the shape of the loaded buttocks and an external contour more nearly shaped like the suspended buttocks. It is concluded that EMS produces buttock tissue undulation and shape reconfiguration which may assist in preventing pressure sores over the seating surface.

Adjuvant therapy for ulcer care.

Frantz RA
Clin Geriatr Med (1997 Aug) 13(3):553-64

Adjuvant therapies, specifically electrotherapy, hyperbaric oxygen, ultrasound, and hydrotherapy, are considered increasingly for use with conventional local wound care to support healing of pressure ulcers. This article describes the characteristics of these modalities, their physiologic effects on the healing process, and the research to evaluate their efficacy.

Effects of electrical stimulation on wound healing in patients with diabetic ulcers.
Baker LL Chambers R DeMuth SK Villar F
Diabetes Care (1997 Mar) 20(3):405-12

OBJECTIVE: To evaluate the effects of two stimulation waveforms on healing rates in patients with diabetes and open ulcers. The hypothesis was that stimulus waveforms with minimal polar characteristics would provide significant healing for this patient sample. RESEARCH DESIGN AND METHODS: This was a prospective study that enrolled 80 patients with open ulcers. Patients received stimulation with either an asymmetric biphasic (A) or symmetric biphasic (B) square-wave pulse. Amplitudes were set to activate intact peripheral nerves in the skin. Two other groups received either very low levels of stimulation current (MC), or no electrical stimulation (C). When

combined these groups were referred to as the control group. Treatment was carried out daily until the wound healed, the patient withdrew from the study, or the physician changed the overall wound management program. Average healing rates were calculated from weekly measures of the wound perimeter and were used for statistical comparison through a one-way analysis of variance. RESULTS: Stimulation with the A protocol significantly increased the healing rate, enhancing healing by nearly 60% over the control rate of healing. Stimulation with the B protocol did not increase the healing rate when compared with control subjects. CONCLUSIONS: Electrical stimulation, given daily with a short pulsed, asymmetric biphasic waveform, was effective for enhancement of healing rates for patients with diabetes and open ulcers.

The benefit of electrical stimulation to enhance perfusion in persons with diabetes mellitus.

Peters EJ Armstrong DG Wunderlich RP Bosma J Stacpoole-Shea S Lavery LA
J Foot Ankle Surg (1998 Sep-Oct) 37(5):396-400; discussion 447-8

The purpose of this study was to evaluate the effect of galvanic electrical stimulation on vascular perfusion in diabetic patients. Nineteen subjects with diabetes were enrolled. Eleven subjects (57.9%) were diagnosed with impaired peripheral perfusion based upon their initial transcutaneous oximetry values (< 40 mm Hg). The subjects were studied over a 2-day period. On the 1st day, one foot was electrically stimulated for four 60-minute periods by an external electrical stimulation device. Vascular perfusion of both feet was assessed before and after the sessions of electrical stimulation. On the 2nd day, no electrical stimulation was applied and noninvasive vascular measurements were repeated. For the 1st hour, transcutaneous oxygen pressure was measured continuously during stimulation at the lateral aspect of the leg. Subsequently, perfusion between the periods of stimulation was measured on the dorsum of the foot with both transcutaneous oximetry and laser Doppler flowmetry after each stimulation period. In the group with impaired peripheral perfusion, a significant rise in tissue oxygenation as compared to the control measurements was measured during the first 5 minutes of stimulation ($p < .040$). For those without vascular disease (TcpO2 > 40 mm Hg) however, there was not a significant increase compared to baseline ($p = .280$). After the periods of stimulation, the stimulated feet did not show any higher perfusion levels than the control feet. Patterns in perfusion during the day, as measured by laser Doppler flowmetry, were similar in the tested feet and in the controls. These data suggest that external subsensory electrical stimulation induces a transient rise in skin perfusion in persons with diabetes and impaired peripheral perfusion.

Treatment of chronic wounds by means of electric and electromagnetic fields. Part 2. Value of FES parameters for pressure sore treatment.

Stefanovska A Vodovnik L Benko H Turk R
Med Biol Eng Comput (1993 May) 31(3):213-20

Subjects with spinal cord injury are often distressed by pressure sores, which usually appear after prolonged pressure (wheelchair, bed) across the soft tissue which has already lost sensibility and has diminished microcirculation. The healing ability and its dynamics depend on the state of the subject's overall health. Consequently, evaluation of a particular treatment requires careful consideration of as many as possible of the parameters relevant to healing and an adequate criterion for assessing the state of the pressure sore. Bearing in mind these two circumstances, the results of a multicentre clinical study are analysed. The aim of the study

was to test two hypotheses: first that healing is faster when sores are also treated by electric currents (ECs) (in addition to conventional treatment); and secondly that there exist differences in the efficiency of the treatment if direct or low-frequency pulsed currents (FES parameters) are applied. The data analysed show that pressure sores are likely to heal twice as fast when treated with low-frequency pulsed currents. EC seems to improve the healing rate in cases where the natural healing mechanisms of the body are not sufficient (chronic wounds, older subjects).

Reduction of seating pressure using FES in patients with spinal cord injury. A preliminary report.

Ferguson AC Keating JF Delargy MA Andrews BJ
Paraplegia (1992 Jul) 30(7):474-8

The aim of this study was to investigate the use of functional electrical stimulation (FES) as a means of pressure sore prevention in seated spinal cord injured (SCI) subjects. Nine SCI subjects took part in tests in which electrical stimulation was applied to the quadriceps with the lower legs restrained. Ischial pressures were measured during periods of quiet sitting and FES application. A strain gauged lever arm was used to measure the knee moment during quadriceps stimulation. The average pressure drop at the right and left buttocks was 44 mmHg and 27 mmHg respectively. In general the greatest reductions occurred in subjects with larger knee moments; however, there was no direct relationship between the pressure reduction obtained and the quadriceps strength. This form of FES may be useful as a prophylactic aid in the management of pressure sores in SCI subjects.

Chronic dermal ulcer healing enhanced with monophasic pulsed electrical stimulation [see comments]

Feedar JA Kloth LC Gentzkow GD
Phys Ther (1991 Sep) 71(9):639-49

The purposes of this randomized, double-blind, multicenter study were to compare healing of chronic dermal ulcers treated with pulsed electrical stimulation with healing of similar wounds treated with sham electrical stimulation and to evaluate patient tolerance to the therapeutic protocol. Forty-seven patients, aged 29 to 91 years, with 50 stage II, III, and IV ulcers were randomly assigned to either a treatment group (n = 26) or a control (sham treatment) group (n = 24). Treated wounds received 30 minutes of pulsed cathodal electrical stimulation twice daily at a pulse frequency of 128 pulses per second (pps) and a peak amplitude of 29.2 mA if the wound contained necrotic tissue or any drainage that was not serosanguinous. A saline-moistened nontreatment electrode was applied 30.5 cm (12 in) cephalad from the wound. This protocol was continued for 3 days after the wound was debrided or exhibited serosanguinous drainage. Thereafter, the polarity of the treatment electrode on the wound was changed every 3 days until the wound progressed to a stage II classification. The pulse frequency was then reduced to 64 pps, and the treatment electrode polarity was changed daily until the wound was healed. Patients in the control group were treated with the same protocol, except they received sham electrical stimulation. After 4 weeks, wounds in the treatment and control groups were 44% and 67% of their initial size, respectively. The healing rates per week for the treatment and control groups were 14% and 8.25%, respectively. The results of this study indicate that

pulsed electrical stimulation has a beneficial effect on healing stage II, III, and IV chronic dermal ulcers.

Effect of electrical stimulation on foot skin perfusion in persons with or at risk for diabetic foot ulcers.

Gilcreast DM Stotts NA Froelicher ES Baker LL Moss KM
Wound Repair Regen (1998 Sep-Oct) 6(5):434-41

The failure of foot wounds to heal results in 54,000 people with diabetes having to undergo extremity amputations annually. Therefore, treatment is needed to speed healing in people with diabetes in order to reduce the need for amputation. This study tested the effect of high-voltage pulsed current on foot blood flow in human beings who are at risk for diabetic foot ulcers. Neuropathy, vascular disease, Wagner Class, glucose, gender, ethnicity, and age were measured. A sample of 132 subjects was tested using a repeated-measures design. A baseline transcutaneous oxygen level was obtained; stimulation was applied, and transcutaneous oxygen measurements were recorded at 30- and 60- minute time intervals. The grouped foot transcutaneous oxygen levels decreased ($F = 5.66$, $p =. 0039$) following electrical stimulation. Analysis of variance (Scheffe, $p <.05$) showed that initial transcutaneous oxygen was significantly higher than subsequent readings. However, oxygen response was distributed bimodally: 35 (27%) subjects showed increased transcutaneous oxygen (mean 14.8 mm Hg), and 97 (73%) experienced a decreased transcutaneous oxygen reading (mean 12.2 mm Hg). Logistic regression analysis did not explain these differences. Although this treatment appears to increase blood flow in a subset of patients, further study is needed to identify probable mechanisms for this response.

Biofeedback and functional electric stimulation in stroke Rehabilitation.

Cozean CD Pease WS Hubbell SL
Arch Phys Med Rehabil (1988 Jun) 69(6):401-5

The study examined the efficacy of functional electric stimulation (FES) and biofeedback (BFB) treatment of gait dysfunction in patients with hemiplegia after stroke. These two therapeutic modalities were tested alone and in combination in a prospective, controlled, randomized trial. The authors hypothesized that in concurrent use, these two modalities would complement one another. Thirty-six hemiplegic patients undergoing rehabilitation after stroke were accepted for study and randomized into four groups to receive either control, FES, BFB, or combined therapies. Each patient received 30 minutes of treatment three times per week for six weeks, in addition to their general rehabilitation program. Quantitative gait analysis was performed biweekly on each subject during the experimental therapy and for four weeks afterward. Thirty-two subjects completed the study. Combined therapy with BFB and FES resulted in improvements in both knee and ankle minimum flexion angles during swing phase that were statistically significant with $p = 0.05$ and $p = 0.02$, respectively. Velocity of gait, cycle time, and symmetry of stance phases also improved. The length of time elapsed since the stroke did not prove to be a significant factor.

Reduction of seating pressure using FES in patients with spinal cord injury. A preliminary report.

Ferguson AC Keating JF Delargy MA Andrews BJ
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The aim of this study was to investigate the use of functional electrical stimulation (FES) as a means of pressure sore prevention in seated spinal cord injured (SCI) subjects. Nine SCI subjects took part in tests in which electrical stimulation was applied to the quadriceps with the lower legs restrained. Ischial pressures were measured during periods of quiet sitting and FES application. A strain gauged lever arm was used to measure the knee moment during quadriceps stimulation. The average pressure drop at the right and left buttocks was 44 mmHg and 27 mmHg respectively. In general the greatest reductions occurred in subjects with larger knee moments; however, there was no direct relationship between the pressure reduction obtained and the quadriceps strength. This form of FES may be useful as a prophylactic aid in the management of pressure sores in SCI subjects.

Relative changes in blood flow with functional electrical stimulation during exercise of the paralyzed lower limbs.

Phillips W Burkett LN Munro R Davis M Pomeroy K
Paraplegia (1995 Feb) 33(2):90-3

Eight spinal cord injured (SCI) patients performed three sets of exercise with two conditions, 60% and 80% of VO2peak, with an arm crank ergometer. Functional neuromuscular stimulation was used to induce static leg contractions in two of the above sets of exercise. The three exercise sets were performed with no functional neuromuscular stimulation (NOS); with functional neuromuscular stimulation at 40 milliamperes; and with functional neuromuscular stimulation at 80 milliamperes (HIS). The lower limb blood flow was estimated by a photoelectric plethysmograph. Results showed that the lower limb blood flow was consistently reduced across both functional neuromuscular stimulation levels (17.4% from NOS to LOS; 13.8% from LOS to HIS; and 28.8% from NOS to HIS), and work loads (15.3% from rest to 60% VO2peak; 38.0% from 60% VO2peak to 80% VO2peak; and 47.5% from rest to 80% VO2peak). Rate-pressure product was decreased by 8.3% between NOS and HIS at 60% VO2peak (15.7 +/- 3.4 to 14.4 +/- 3.8), by 6.8% between NOS and HIS at 80% VO2peak (18.9 +/- 53 to 17.6 +/- 4.8), and by 12.4% between LOS and HIS at 80% VO2peak (20.1 +/- 6.7 to 17.6 +/- 4.8). These data indicate that in SCI (a) functional neuromuscular stimulation-induced contractions of the lower limb muscles can increase blood flow and thus reduce venous blood pooling in the paralyzed muscles, and (b) such improvements are associated with a reduced rate pressure product.(ABSTRACT TRUNCATED AT 250 WORDS)

Promotion of wound healing with electrical stimulation.

Kloth LC McCulloch JM
Adv Wound Care (1996 Sep-Oct) 9(5):42-5

Clinicians involved in the conservative care of chronic wounds have many treatment interventions from which to choose, including debridement/irrigation, dressings, pressure-relieving devices, hyperbaric or topically applied oxygen, whirlpool/pulsed lavage, ultrasound, topical antibiotics, and cytokine growth factors. All except the last two interventions are physical treatments that create a wound-tissue environment conducive to healing. Unfortunately, many chronic wounds heal very slowly, do

not heal, or worsen despite the best efforts of caregivers to promote tissue repair. An intervention commonly used to treat chronic wounds, especially by physical therapists, is electrical stimulation (ES). The rationale for use of this method is based on the fact that the human body has an endogenous bioelectric system that enhances healing of bone fractures and soft-tissue wounds. When the body's endogenous bioelectric system fails and cannot contribute to wound repair processes, therapeutic levels of electrical current may be delivered into the wound tissue from an external source. The external current may serve to mimic the failed natural bioelectric currents so that wound healing can proceed. Certain chemotaxic factors found in wound substrates contribute to tissue repair processes by attracting cells into the wound environment. Neutrophil, macrophage, fibroblast, and epidermal cells involved in wound repair carry either a positive or negative charge. When these cells are needed to contribute to autolysis, granulation tissue formation, anti-inflammatory activities, or epidermal resurfacing, ES may facilitate galvanotaxic attraction of these cells into the wound tissue and thereby accelerate healing.

Electrical nerve stimulation improves healing of diabetic ulcers.

Lundeberg TC Eriksson SV Malm M
Ann Plast Surg (1992 Oct) 29(4):328-31

A controlled study of the effects of electrical nerve stimulation (ENS) was performed in conjunction with a standard treatment for healing chronic diabetic ulcers on 64 patients divided randomly into two groups. All patients received standard treatment (paste-impregnated bandage and a self-adhesive elastic bandage) plus placebo ENS or ENS (alternating constant current; frequency, 80 Hz; pulse width, 1 msec; intensity-evoking strong paresthesias) for 20 minutes twice daily for 12 weeks. Comparison of percentages of healed ulcer area and the number of healed ulcers was made after 2, 4, 6, 8, and 12 weeks. There were significant differences ($p < 0.05$) in both ulcer area and healed ulcers in the ENS group compared with the placebo group after 12 weeks of treatment. The results of the present study support the use of ENS in diabetic ulcers. ENS is easy to apply and can be used by the patient at home following instructions from a medical doctor or a therapist experienced in electrical stimulation and the treatment of ulcers. Additional studies are needed to identify the mechanisms involved in the promotion of ulcer healing with electrical stimulation and to determine the stimulus variables that most efficaciously accelerate tissue repair.

Effects of electrical stimulation on wound healing in patients with diabetic ulcers.

Baker LL Chambers R DeMuth SK Villar F
Diabetes Care (1997 Mar) 20(3):405-12

OBJECTIVE: To evaluate the effects of two stimulation waveforms on healing rates in patients with diabetes and open ulcers. The hypothesis was that stimulus waveforms with minimal polar characteristics would provide significant healing for this patient sample. RESEARCH DESIGN AND METHODS: This was a prospective study that enrolled 80 patients with open ulcers. Patients received stimulation with either an asymmetric biphasic (A) or symmetric biphasic (B) square-wave pulse. Amplitudes were set to activate intact peripheral nerves in the skin. Two other groups received either very low levels of stimulation current (MC), or no electrical stimulation (C). When

combined these groups were referred to as the control group. Treatment was carried out daily until the wound healed, the patient withdrew from the study, or the physician changed the overall wound management program. Average healing rates were calculated from weekly measures of the wound perimeter and were used for statistical comparison through a one-way analysis of variance. RESULTS: Stimulation with the A protocol significantly increased the healing rate, enhancing healing by nearly 60% over the control rate of healing. Stimulation with the B protocol did not increase the healing rate when compared with control subjects. CONCLUSIONS: Electrical stimulation, given daily with a short pulsed, asymmetric biphasic waveform, was effective for enhancement of healing rates for patients with diabetes and open ulcers.

Electrical stimulation to heal dermal wounds.

Gentzkow GD
J Dermatol Surg Oncol (1993 Aug) 19(8):753-8

BACKGROUND. Numerous human and animal efficacy studies have demonstrated that electrical stimulation of the correct charge, density and total energy causes dramatically improved healing of dermal wounds. The investigations of biological actions (in vitro, animal, and human) demonstrate several effects that go a long way to explaining why electrical stimulation works. OBJECTIVE. To discuss recent research and advances in electrical stimulation of wound healing. RESULTS. Based on the latest scientific understanding of the wound healing process, one would expect a beneficial outcome from a therapy what decreases edema, debrides necrotic tissue, attracts neutrophils and macrophages, stimulates receptor sites for growth factors, stimulates growth of fibroblasts and granulation tissue, increases blood flow, stimulates neurite growth, induces epidermal cell migration, prevents post-ischemic oxygen radical-mediated damage, inhibits bacteria, and reduces numbers of mast cells. CONCLUSION. Taken together, the efficacy studies and the "mechanism of action" studies provide compelling, scientific evidence that electrical stimulation is safe and effective for promoting the healing of dermal wounds.

Alteration in alpha- and beta-adrenoceptor profile of rabbit knee joint blood vessels due to acute inflammation.

Najafipour H.
Exp Physiol. 2000 May;85(3):267-73.
Department of Physiology, Medical faculty, Kerman University of Medical Sciences and Health Services, Bulvd. 22 Bahman, Kerman, Iran.

Experiments were performed to investigate the nature of - and -adrenoceptors in blood vessels supplying the posterior capsule of the acutely inflamed rabbit knee joint, and results were compared to findings from previous experiments on the normal joint, to assess any alteration which may occur in the adrenoceptor profile due to the inflammation process. Electrical stimulation of the posterior articular nerve resulted in vasoconstriction which was reversed to vasodilatation by phentolamine and yohimbine. The dose-response curves to close intra-arterial injection of -adrenoceptor agonists showed a rank-order potency of: adrenaline = phenylephrine = clonidine. The adrenaline dose-response curve was shifted to the right by administration of antagonists with a rank-order potency of: phentolamine = yohimbine = prazosin. At this stage of the experiments there was an equal response of 1- and 2-adrenoceptors in blood vessels of the acutely inflamed rabbit knee joint. In another group of animals the neurally mediated vasodilatation, which appeared after administration of phentolamine, was completely blocked by propranolol, and was reduced by about 50 % by atenolol.

The dose-response curves to close intra-arterial injection of -adrenoceptor agonists showed a rank-order potency of: isoprenaline > salbutamol = dobutamine. The isoprenaline dose-response curve was shifted to the right by administration of antagonists with a rank-order potency of: propranolol > atenolol. These experiments also showed an almost equal response of 1- and 2-adrenoceptors in blood vessels of the acutely inflamed rabbit knee joint. Overall, compared to previous experiments on the normal joint in which 2- and 1-adrenoceptor responses predominated, acute inflammation resulted in a shift from 2- towards 1- and from 1- towards 2-adrenoceptor responses.

Sympathetically induced paradoxical increases of the cutaneous blood flow in chronically inflamed rats.

Tsujii Y, Koeda T, Sato J, Suzuki S, Kumazawa T.
J Auton Nerv Syst. 1996 Jul 5;59(3):103-12.
Department of Neural Regulation, Nagoya University, Japan.

In adjuvant arthritic (AA) rats, an abnormal responsiveness of nociceptors (C-fibre polymodal receptors) to sympathetic activities, i.e., alpha 2-adrenoceptor mediated activation of C-fibre polymodal receptors (CPRs), has been observed. The present investigations were undertaken to determine if a similar plastic change would occur in the cutaneous vascular system in the rat chronic inflammation model. The vascular responses were measured by a laser-Doppler flowmeter in the hindpaw skin of the AA rats after electrical stimulation of lumbar sympathetic trunk (sympathetic stimulation). In control non-arthritic rats, the sympathetic stimulation caused decrease in blood flow of the skin (SkBF) in all animals tested (n = 7). On the other hand, the sympathetic stimulation in the AA rats caused both increase (n = 15) as well as decrease (n = 11) in SkBF. In contrast to the abnormal responsiveness of CPRs, the intra-arterial injection of noradrenaline caused the expected decrease in SkBF in all animals tested, and in no instances increases in SkBF were observed. To determine whether activation of nitric oxide (NO), which is known to be a potent endogenous vasodilatation substance, was involved in the vasodilating effect to sympathetic stimulation, an inhibitor of NO synthase, NG-monomethyl-L-arginine (L-NMMA), was applied systemically. L-NMMA significantly increased baseline blood pressure in the control and the AA rats, but it did not significantly alter the SkBF in the control or the AA rats after the sympathetic stimulation, suggesting that NO is not a mediator in the vasoactive responses. The results of the current studies showed for the first time that electrical stimulation of the lumbar sympathetic trunk causes vasodilatation in the skin of the AA rats. This abnormal responsiveness of regional SkBF after sympathetic stimulation was not mediated by adrenergic or NO system.

Papers on Wound Healing

Increased Blood Flow to the effected Treatment Area and Wound Healing while using electrical stimulation.

Effects of aging on neurogenic vasodilator responses evoked by transcutaneous electrical nerve stimulation: relevance to wound healing.

Khalil Z, Merhi M
J Gerontol A Biol Sci Med Sci. 2000 Jun; 55(6):B257-63.
National Ageing Research Institute, University of Melbourne, Victoria, Australia.

We have previously shown an age-related decline in the modulation of skin vascular reactivity by sensory nerves that correlates with a decline in wound repair efficacy. This study was designed to examine the possibility that improving the functional ability of aged sensory nerves using noninvasive transcutaneous electrical nerve stimulation (TENS) could also accelerate tissue repair. TENS of the sciatic nerve, combined with measuring blood flow responses in the rat hind-footpad using laser Doppler flowmetry, was used to establish the vascular effects. Following TENS (using parameters 20V, 5 Hz for 1 min), similar increases in vascular responses were obtained in both young (13.2+/-0.9 cm2) and old rats (11.6+/-2.3 cm2). In contrast, capsaicin-pretreated rats showed markedly diminished responses. Sympathetic fibers did not appear to modulate these sensory nerve responses. In the second part, a thermal wound was induced (using a CO2 laser) in the interscapular region of old rats (under anesthesia). In the active treatment group, TENS was applied twice daily for the initial 5 days, and the sham group received inactive TENS. Using the healing endpoint as the time when full wound contraction occurred, the active group required 14.7+/-0.2 days for complete healing, a significant improvement over the sham group (21.8+/-0.3 days). We contend that low-frequency TENS can improve the vascular response of old rats. In addition, wound healing in aged rats can be accelerated by peripheral activation of sensory nerves at low-frequency electrical stimulation parameters.

Epidural spinal cord electrical stimulation in diabetic critical lower limb ischemia.

Petrakis IE, Sciacca V
Title Abbreviation: J Diabetes Complications.
1999 Sep-Dec; Volume Issue: 13(5-6):293-9.
First Department of General Surgery, Policlinico Umberto I, University of Rome, La Sapienza, Rome, Italy.

Spinal cord stimulation (SCS) has been suggested to improve microcirculatory blood flow to relieve ischemic pain and to reduce amputation rate in patients with peripheral arterial occlusive disease (PAOD). The aim of this study was to evaluate the specific prognostic parameters in the prediction of successful SCS, in diabetic patients, performing a retrospective data analysis. To perform this evaluation, 64 diabetic patients (39 men, 25 women; mean age, 69 years) classified as Fontaine's stage III and IV, with PAOD, were treated with SCS for rest pain and trophic lesions with dry gangrene, after failed conservative or surgical treatment. In clinical controls, pedal transcutaneous oxygen tension (TcPO(2)), ankle/brachial blood pressure index (ABI), and toe pressure Doppler measurements were utilized to select and follow-up the patients. After 58 months of follow-up (range, 20-128 months), pain relief

greater than 75% and limb salvage were achieved in 38 diabetic patients. A partial success was obtained in nine patients with pain relief greater than 50% and limb salvage for at least 6 months. The method failed in 17 patients or the device was removed due to technical problems, and the limb was amputated in these patients. TcPO(2) was assessed on the dorsum of the foot. Clinical improvement and SCS success were associated with increase of TcPO(2), before and after implantation. Limb salvage was achieved in the patients who had significant TcPO(2) increase within the 2 weeks of the testing period, independently of the stage of the disease. A TcPO(2) increase of more than 50% in the first 2 months after implantation was predictive of success, and was related to the presence of adequate paresthesias in the painful area during the trial period. TcPO(2) significantly increased after long-term follow-up in all patients with limb salvage (from 22.1 to 43.1 mm Hg in the rest pain patients, from 15.8 to 36.4 mm Hg in those with trophic lesions of less than 3 cm(2), and from 12.1 to 28.1 in those with trophic lesions of greater than 3 cm(2), ($p < 0.01$). ABI did not changed under stimulation. In diabetic patients with PAOD, the SCS increases the skin blood flow, is associated with significant pain relief, and could be proven an excellent alternative therapy, improving the life quality. Significant TcPO(2) increase within the 2-week test period, is a predictive index of therapy success and should be considered before the final decision in terms of cost effectiveness, before the permanent implantation.

Effects of transcutaneous nerve stimulation on the microcirculation in chronic leg ulcers.

Cosmo P, Svensson H, Bornmyr S, Wikstrom SO
Scand J Plast Reconstr Surg Hand Surg. 2000 Mar; 34(1):61-4.
Department of Plastic and Reconstructive Surgery, Malmo University Hospital, Sweden.

The purpose of this study was to find out to what extent transcutaneous electrical nerve stimulation (TENS) affects the blood flow in and around chronic lower leg ulcers, as measured with a new technique, laser Doppler imaging (LDI). Fifteen patients, mean age 73 years (range 38-85) with chronic leg ulcers of various causes participated in the study. The duration of the ulcers ranged from 3 months to 16 years. Low-frequency (2 Hz; 10-45 mA) TENS was given for 60 minutes. The changes in blood flow were measured every 5 minutes by LDI. After 60 minutes, mean blood flow had increased in the ulcer by 35%, and in the intact skin surrounding the ulcer by 15%. Even 15 minutes after the TENS had finished there was still a mean blood flow increase of 29% in the ulcer and 9% in the skin. The present results show that TENS has a stimulating effect on local blood circulation in and around chronic ulcers.

Effect of transcutaneous nerve stimulation on microcirculation in intact skin and blister wounds in healthy volunteers.

Wikstrom SO, Svedman P, Svensson H, Tanweer AS
Scand J Plast Reconstr Surg Hand Surg. 1999 Jun; 33(2):195-201.
Department of Plastic and Reconstructive Surgery, University Hospital MAS, Malmo, Sweden.

Healthy non-smoking volunteers participated in two experimental studies in which the circulatory changes induced by transcutaneous nerve stimulation (TENS) were quantified by two different methods. In experimental series 1 (intact skin), nine volunteers were given TENS on the left lower leg for 60 minutes on three occasions at different frequencies each time (2 Hz, 100 Hz, and sham). Changes in blood flow were assessed by laser Doppler imaging

technique every five minutes. The mean blood flow increased by 40% during low frequency TENS and by 12% during high frequency TENS. There was no change in mean blood flow during sham stimulation. In experimental series 2 (blister wound), the circulatory changes induced by TENS were studied by intravital video microscopy and computerised image analysis in standard blister wounds on the lower leg. The microcirculatory blood flow, measured as red blood cell velocity (RBC-V) in 5-14 individual capillaries in each wound, was assessed before and during 45 minutes of TENS (2 Hz and 100 Hz). Mean RBC-V increased by 23% during low frequency TENS (n = 6) and by 17% during high frequency TENS (n = 8). The results show that: laser Doppler imaging and intravital video microscopy techniques can be used to study events at the microcirculatory level; the blister wound is an interesting new standard wound for use in clinical studies; and TENS stimulates the peripheral circulation.

Prognostic factors in the prediction of chronic wound healing by electrical stimulation.

Cukjati D, Robnik-Sikonja M, Rebersek S, Kononenko I, Miklavcic D.
Med Biol Eng Comput. 2001 Sep;39(5):542-50.
Faculty of Electrical Engineering, University of Ljubljana, Slovenia.

The aim of the study is to determine the effects of wound, patient and treatment attributes on the wound healing rate and to propose a system for wound healing rate prediction. Predicting the wound healing rate from the initial wound, patient and treatment data collected in a database of 300 chronic wounds is not possible. After considering weekly follow-ups, it was determined that the best prognostic factors are weekly follow-ups of the wound healing process, which alone were found to predict accurately the wound healing rate after a minimum follow-up period of four weeks (at least five measurements of wound area). After combining the follow-ups with wound, patient and treatment attributes, the minimum follow-up period was reduced to two weeks (at least three measurements of wound area). After a follow-up period of two weeks, it was possible to predict the wound healing rate of an independent test set of chronic wounds with a relative squared error of 0.347, and after three weeks, with a relative squared error of 0.181 (using regression trees with linear equations in its leaves). Regression trees with a relative squared error close to 0 produce better prediction than with an error closer to 1. Results show that the type of treatment is just one of many prognostic factors. Arranged in order of decreasing prediction capability, prognostic factors are: wound size, patient's age, elapsed time from wound appearance to the beginning of the treatment, width-to-length ratio, location and type of treatment. The data collected support former findings that the biphasic- and direct-current stimulation contributes to faster healing of chronic wounds. The model of wound healing dynamics aids the prediction of chronic wound healing rate, and hence helps with the formulation of appropriate treatment decisions.

Choosing an adjunctive therapy for the treatment of chronic wounds.
Houghton PE, Campbell KE.

Ostomy Wound Manage. 1999 Aug;45(8):43-52; quiz 53-4.
St. Joseph's Health Center, School of Physiotherapy, University of Western Ontario, London, Canada.

Adjunctive therapies such as ultrasound, laser, ultraviolet light, superficial heating, pulsed electromagnetic fields, and electrical stimulation have all been indicated in the treatment of chronic wounds. The purpose of this article is to outline the issues a healthcare professional must consider when

choosing the best adjunctive therapy for a chronic wound. It summarizes the effects of therapeutic modalities on the wound healing process, analyzes the clinical research evidence, discusses practical considerations, and reviews indications, contraindications, precautions, and safety considerations. Finally, an algorithm is presented to help guide the clinician in selecting a modality. In summary, research evidence exists in the literature that suggests these adjunctive therapies can directly stimulate new tissue growth, augment wound tissue strength, improve local circulation and oxygenation, reduce edema, and/or inhibit bacterial growth. Electrical stimulation and ultrasound are the only therapeutic modalities that currently have sufficient clinical research evidence to support their use in the treatment of chronic wounds. Practical issues such as cost, time and training required, and patient and therapist safety concerns, will ultimately influence the selection of these modalities.

Effect of electrical stimulation on chronic wound healing: a meta-analysis.
Gardner SE, Frantz RA, Schmidt FL.

Wound Repair Regen. 1999 Nov-Dec;7(6):495-503.
Colleges of Nursing, The University of Iowa, Iowa City, IA 52242-7066, USA.

The purpose of this meta-analysis was to quantify the effect of electrical stimulation on chronic wound healing. Fifteen studies, which included 24 electrical stimulation samples and 15 control samples, were analyzed. The average rate of healing per week was calculated for the electrical stimulation and control samples. Ninety-five percentage confidence intervals were also calculated. The samples were then grouped by type of electrical stimulation device and chronic wound and reanalyzed. Rate of healing per week was 22% for electrical stimulation samples and 9% for control samples. The net effect of electrical stimulation was 13% per week, an increase of 144% over the control rate. The 95% confidence intervals of the electrical stimulation (18-26%) and control samples (3.8-14%) did not overlap. Electrical stimulation was most effective on pressure ulcers (net effect = 13%). Findings regarding the relative effectiveness of different types of electrical stimulation device were inconclusive. Although electrical stimulation produces a substantial improvement in the healing of chronic wounds, further research is needed to identify which electrical stimulation devices are most effective and which wounds respond best to this treatment.

A comparative study of the effect of ultrasound and electrostimulation on wound healing in rats.

Taskan I, Ozyazgan I, Tercan M, Kardas HY, Balkanli S, Saraymen R, Zorlu U
Plast Reconstr Surg. 1997 Sep;100(4):966-72.
Physical Therapy and Rehabilitation Center, Medical Faculty of Inonu University, Istanbul, Turkey.

A comparative study has been carried out to investigate the effects of electrical stimulation and ultrasound on wound healing. Eighty-four female rats were divided into four groups depending on the treatment received. The first group was given electrical stimulation of 300 microA direct current, 30 minutes daily, starting with negative polarity and then changed after 3 days of treatment. Group 2 received sham electrostimulation treatment. The third group received 0.1 W/cm2 pulsed ultrasound using the moving applicator technique for 5 minutes a day. Group 4 received sham ultrasound treatment. A total of 7 days of treatment was given to all groups. Histopathologic and biochemical analyses on the fourth and seventh days and wound breaking

strength on the twenty-fifth day were performed for all groups. By accelerating the inflammatory phase, electrical stimulation had progressed the proliferative phase of wound healing earlier than ultrasound had done. Both electrical stimulation and ultrasound have positive effects on proliferative phases, but electrical stimulation was superior to ultrasound at the maturation phase. There was no difference between the two experimental groups on the mast cell reduction effect. Although ultrasound treatment may seem to be efficient in terms of time, when the effects of electrical stimulation and ultrasound on wound healing with the methods employed in our study are considered, it is concluded that electrical stimulation is a means of treatment superior to ultrasound in wound healing.

Effects of electrical stimulation on wound healing in patients with diabetic ulcers.

Baker LL, Chambers R, DeMuth SK, Villar F.
Diabetes Care. 1997 Mar;20(3):405-12.
Department of Biokinesiology and Physical Therapy, University of Southern California, Los Angeles 90033,

OBJECTIVE: To evaluate the effects of two stimulation waveforms on healing rates in patients with diabetes and open ulcers. The hypothesis was that stimulus waveforms with minimal polar characteristics would provide significant healing for this patient sample. RESEARCH DESIGN AND METHODS: This was a prospective study that enrolled 80 patients with open ulcers. Patients received stimulation with either an asymmetric biphasic (A) or symmetric biphasic (B) square-wave pulse. Amplitudes were set to activate intact peripheral nerves in the skin. Two other groups received either very low levels of stimulation current (MC), or no electrical stimulation (C). When combined these groups were referred to as the control group. Treatment was carried out daily until the wound healed, the patient withdrew from the study, or the physician changed the overall wound management program. Average healing rates were calculated from weekly measures of the wound perimeter and were used for statistical comparison through a one-way analysis of variance. RESULTS: Stimulation with the A protocol significantly increased the healing rate, enhancing healing by nearly 60% over the control rate of healing. Stimulation with the B protocol did not increase the healing rate when compared with control subjects. CONCLUSIONS: Electrical stimulation, given daily with a short pulsed, asymmetric biphasic waveform, was effective for enhancement of healing rates for patients with diabetes and open ulcers.

Promotion of wound healing with electrical stimulation.

Kloth LC, McCulloch JM.
Adv Wound Care. 1996 Sep-Oct;9(5):42-5.
Program of Physical Therapy, Marquette University, Milwaukee, Wis, USA.

Clinicians involved in the conservative care of chronic wounds have many treatment interventions from which to choose, including debridement/irrigation, dressings, pressure-relieving devices, hyperbaric or topically applied oxygen, whirlpool/pulsed lavage, ultrasound, topical antibiotics, and cytokine growth factors. All except the last two interventions are physical treatments that create a wound-tissue environment conducive to healing. Unfortunately, many chronic wounds heal very slowly, do not heal, or worsen despite the best efforts of caregivers to promote tissue repair. An intervention commonly used to treat chronic wounds, especially by physical therapists, is electrical stimulation (ES). The rationale for use of

this method is based on the fact that the human body has an endogenous bioelectric system that enhances healing of bone fractures and soft-tissue wounds. When the body's endogenous bioelectric system fails and cannot contribute to wound repair processes, therapeutic levels of electrical current may be delivered into the wound tissue from an external source. The external current may serve to mimic the failed natural bioelectric currents so that wound healing can proceed. Certain chemotaxic factors found in wound substrates contribute to tissue repair processes by attracting cells into the wound environment. Neutrophil, macrophage, fibroblast, and epidermal cells involved in wound repair carry either a positive or negative charge. When these cells are needed to contribute to autolysis, granulation tissue formation, anti-inflammatory activities, or epidermal resurfacing, ES may facilitate galvanotaxic attraction of these cells into the wound tissue and thereby accelerate healing.

Physical modalities in wound management: UVC, therapeutic heating and electrical stimulation.

Kloth LC.
Ostomy Wound Manage. 1995 Jun;41(5):18-20, 22-4, 26-7.

In spite of efforts to create an optimum wound environment for healing, there are times that a wound may not heal, may heal very slowly, or may worsen. In these cases, a series of treatments with an appropriate physical agent can be added to the patient's care plan to augment tissue reparative processes. Three modalities that have received support in the literature for use in wound healing are ultraviolet "C" radiation (UVC), therapeutic heating, and electrical stimulation. Treatment goals for UVC are hyperplasia and enhanced re-epithelialization or desquamation of the leading edge of periulcer epidermal cells, granulation tissue formation, sloughing of necrotic tissue, and bactericidal effects. Treatment goals for therapeutic heating are increased blood perfusion with subsequent increased delivery of oxygen to the tissues (avoiding the dessication of wound tissues). The treatment goal for electrical stimulation is to attract negatively or positively charged cells into the wound area, such as neutrophils, macrophages, epidermal cells and fibroblasts that in turn will contribute to wound healing processes by way of their individual cellular activities.

Experimental wound healing with electrical stimulation.

Reger SI, Hyodo A, Negami S, Kambic HE, Sahgal V
Title Abbreviation: Artif Organs.
1999 May; 23(5):460-2.
Department of Physical Medicine and Rehabilitation, The Cleveland Clinic Foundation, Ohio 44195, USA.

The effect of alternating current (AC) and direct current (DC) stimulation was studied on experimental pressure ulcer healing in a new monoplegic pig model. The study was conducted in 30 healthy young Hanford minipigs. The rate of wound healing, histology, vascularization, collagen formation, microbiology, perfusion, and the mechanical strength of the healed wounds were studied. Normal pigskin was compared to denervated control and denervated AC and DC stimulated healed skin. Hind limb denervation was by right unilateral extradural rhizotomies from the L2 to S1 nerve roots. Reproducible uniformly controlled Stage III or higher tissue ulcers were created. When compared to the control wounds, both the AC and DC stimulated wounds showed reduced healing time and increased perfusion in the early phases of healing. DC

stimulation reduced the wound area more rapidly than AC, but AC stimulation reduced the wound volume more rapidly than DC. The electrical stimulation did not reduce the strength of the healing wounds below those of the nonstimulated controls. The applied current appears to orient new collagen formation even in the absence of neural influences.

Electric muscle stimulation for pressure sore prevention: tissue shape variation.

Levine SP Kett RL Cederna PS Brooks SV
Arch Phys Med Rehabil (1990 Mar) 71(3):210-5

This study measured changes in tissue shape and deformation at the seating interface produced by electric muscle stimulation (EMS) of the gluteus maximus. The purpose of the study was to investigate the application of EMS for pressure sore prevention. Limitations of pressure measurements for analysis of load distribution are discussed and a rationale developed for using tissue shape and deformation to further characterize the seating interface. Ultrasonic imaging of the seating interface is described under three conditions: buttocks suspended, external load applied with no EMS, and external load applied with bilateral EMS of the buttocks. Results show that low level stimulation of the gluteus maximus produces substantial changes in the shape of the loaded buttocks and an external contour more nearly shaped like the suspended buttocks. It is concluded that EMS produces buttock tissue undulation and shape reconfiguration which may assist in preventing pressure sores over the seating surface.

Adjuvant therapy for ulcer care.

Frantz RA
Clin Geriatr Med (1997 Aug) 13(3):553-64

Adjuvant therapies, specifically electrotherapy, hyperbaric oxygen, ultrasound, and hydrotherapy, are considered increasingly for use with conventional local wound care to support healing of pressure ulcers. This article describes the characteristics of these modalities, their physiologic effects on the healing process, and the research to evaluate their efficacy.

Effects of electrical stimulation on wound healing in patients with diabetic ulcers.
Baker LL Chambers R DeMuth SK Villar F
Diabetes Care (1997 Mar) 20(3):405-12

OBJECTIVE: To evaluate the effects of two stimulation waveforms on healing rates in patients with diabetes and open ulcers. The hypothesis was that stimulus waveforms with minimal polar characteristics would provide significant healing for this patient sample. RESEARCH DESIGN AND METHODS: This was a prospective study that enrolled 80 patients with open ulcers. Patients received stimulation with either an asymmetric biphasic (A) or symmetric biphasic (B) square-wave pulse. Amplitudes were set to activate intact peripheral nerves in the skin. Two other groups received either very low levels of stimulation current (MC), or no electrical stimulation (C). When

combined these groups were referred to as the control group. Treatment was carried out daily until the wound healed, the patient withdrew from the study, or the physician changed the overall wound management program. Average healing rates were calculated from weekly measures of the wound perimeter and were used for statistical comparison through a one-way analysis of variance. RESULTS: Stimulation with the A protocol significantly increased the healing rate, enhancing healing by nearly 60% over the control rate of healing. Stimulation with the B protocol did not increase the healing rate when compared with control subjects. CONCLUSIONS: Electrical stimulation, given daily with a short pulsed, asymmetric biphasic waveform, was effective for enhancement of healing rates for patients with diabetes and open ulcers.

The benefit of electrical stimulation to enhance perfusion in persons with diabetes mellitus.

Peters EJ Armstrong DG Wunderlich RP Bosma J Stacpoole-Shea S Lavery LA
J Foot Ankle Surg (1998 Sep-Oct) 37(5):396-400; discussion 447-8

The purpose of this study was to evaluate the effect of galvanic electrical stimulation on vascular perfusion in diabetic patients. Nineteen subjects with diabetes were enrolled. Eleven subjects (57.9%) were diagnosed with impaired peripheral perfusion based upon their initial transcutaneous oximetry values (< 40 mm Hg). The subjects were studied over a 2-day period. On the 1st day, one foot was electrically stimulated for four 60-minute periods by an external electrical stimulation device. Vascular perfusion of both feet was assessed before and after the sessions of electrical stimulation. On the 2nd day, no electrical stimulation was applied and noninvasive vascular measurements were repeated. For the 1st hour, transcutaneous oxygen pressure was measured continuously during stimulation at the lateral aspect of the leg. Subsequently, perfusion between the periods of stimulation was measured on the dorsum of the foot with both transcutaneous oximetry and laser Doppler flowmetry after each stimulation period. In the group with impaired peripheral perfusion, a significant rise in tissue oxygenation as compared to the control measurements was measured during the first 5 minutes of stimulation ($p < .040$). For those without vascular disease (TcpO2 > 40 mm Hg) however, there was not a significant increase compared to baseline ($p = .280$). After the periods of stimulation, the stimulated feet did not show any higher perfusion levels than the control feet. Patterns in perfusion during the day, as measured by laser Doppler flowmetry, were similar in the tested feet and in the controls. These data suggest that external subsensory electrical stimulation induces a transient rise in skin perfusion in persons with diabetes and impaired peripheral perfusion.

Treatment of chronic wounds by means of electric and electromagnetic fields. Part 2. Value of FES parameters for pressure sore treatment.

Stefanovska A Vodovnik L Benko H Turk R
Med Biol Eng Comput (1993 May) 31(3):213-20

Subjects with spinal cord injury are often distressed by pressure sores, which usually appear after prolonged pressure (wheelchair, bed) across the soft tissue which has already lost sensibility and has diminished microcirculation. The healing ability and its dynamics depend on the state of the subject's overall health. Consequently, evaluation of a particular treatment requires careful consideration of as many as possible of the parameters relevant to healing and an adequate criterion for assessing the state of the pressure sore. Bearing in mind these two circumstances, the results of a multicentre clinical study are analysed. The aim of the study

was to test two hypotheses: first that healing is faster when sores are also treated by electric currents (ECs) (in addition to conventional treatment); and secondly that there exist differences in the efficiency of the treatment if direct or low-frequency pulsed currents (FES parameters) are applied. The data analysed show that pressure sores are likely to heal twice as fast when treated with low-frequency pulsed currents. EC seems to improve the healing rate in cases where the natural healing mechanisms of the body are not sufficient (chronic wounds, older subjects).

Reduction of seating pressure using FES in patients with spinal cord injury. A preliminary report.

Ferguson AC Keating JF Delargy MA Andrews BJ
Paraplegia (1992 Jul) 30(7):474-8

The aim of this study was to investigate the use of functional electrical stimulation (FES) as a means of pressure sore prevention in seated spinal cord injured (SCI) subjects. Nine SCI subjects took part in tests in which electrical stimulation was applied to the quadriceps with the lower legs restrained. Ischial pressures were measured during periods of quiet sitting and FES application. A strain gauged lever arm was used to measure the knee moment during quadriceps stimulation. The average pressure drop at the right and left buttocks was 44 mmHg and 27 mmHg respectively. In general the greatest reductions occurred in subjects with larger knee moments; however, there was no direct relationship between the pressure reduction obtained and the quadriceps strength. This form of FES may be useful as a prophylactic aid in the management of pressure sores in SCI subjects.

Chronic dermal ulcer healing enhanced with monophasic pulsed electrical stimulation [see comments]

Feedar JA Kloth LC Gentzkow GD
Phys Ther (1991 Sep) 71(9):639-49

The purposes of this randomized, double-blind, multicenter study were to compare healing of chronic dermal ulcers treated with pulsed electrical stimulation with healing of similar wounds treated with sham electrical stimulation and to evaluate patient tolerance to the therapeutic protocol. Forty-seven patients, aged 29 to 91 years, with 50 stage II, III, and IV ulcers were randomly assigned to either a treatment group (n = 26) or a control (sham treatment) group (n = 24). Treated wounds received 30 minutes of pulsed cathodal electrical stimulation twice daily at a pulse frequency of 128 pulses per second (pps) and a peak amplitude of 29.2 mA if the wound contained necrotic tissue or any drainage that was not serosanguinous. A saline-moistened nontreatment electrode was applied 30.5 cm (12 in) cephalad from the wound. This protocol was continued for 3 days after the wound was debrided or exhibited serosanguinous drainage. Thereafter, the polarity of the treatment electrode on the wound was changed every 3 days until the wound progressed to a stage II classification. The pulse frequency was then reduced to 64 pps, and the treatment electrode polarity was changed daily until the wound was healed. Patients in the control group were treated with the same protocol, except they received sham electrical stimulation. After 4 weeks, wounds in the treatment and control groups were 44% and 67% of their initial size, respectively. The healing rates per week for the treatment and control groups were 14% and 8.25%, respectively. The results of this study indicate that

pulsed electrical stimulation has a beneficial effect on healing stage II, III, and IV chronic dermal ulcers.

Effect of electrical stimulation on foot skin perfusion in persons with or at risk for diabetic foot ulcers.

Gilcreast DM Stotts NA Froelicher ES Baker LL Moss KM
Wound Repair Regen (1998 Sep-Oct) 6(5):434-41

The failure of foot wounds to heal results in 54,000 people with diabetes having to undergo extremity amputations annually. Therefore, treatment is needed to speed healing in people with diabetes in order to reduce the need for amputation. This study tested the effect of high-voltage pulsed current on foot blood flow in human beings who are at risk for diabetic foot ulcers. Neuropathy, vascular disease, Wagner Class, glucose, gender, ethnicity, and age were measured. A sample of 132 subjects was tested using a repeated-measures design. A baseline transcutaneous oxygen level was obtained; stimulation was applied, and transcutaneous oxygen measurements were recorded at 30- and 60- minute time intervals. The grouped foot transcutaneous oxygen levels decreased ($F = 5.66$, $p =. 0039$) following electrical stimulation. Analysis of variance (Scheffe, $p <.05$) showed that initial transcutaneous oxygen was significantly higher than subsequent readings. However, oxygen response was distributed bimodally: 35 (27%) subjects showed increased transcutaneous oxygen (mean 14.8 mm Hg), and 97 (73%) experienced a decreased transcutaneous oxygen reading (mean 12.2 mm Hg). Logistic regression analysis did not explain these differences. Although this treatment appears to increase blood flow in a subset of patients, further study is needed to identify probable mechanisms for this response.

Biofeedback and functional electric stimulation in stroke Rehabilitation.

Cozean CD Pease WS Hubbell SL
Arch Phys Med Rehabil (1988 Jun) 69(6):401-5

The study examined the efficacy of functional electric stimulation (FES) and biofeedback (BFB) treatment of gait dysfunction in patients with hemiplegia after stroke. These two therapeutic modalities were tested alone and in combination in a prospective, controlled, randomized trial. The authors hypothesized that in concurrent use, these two modalities would complement one another. Thirty-six hemiplegic patients undergoing rehabilitation after stroke were accepted for study and randomized into four groups to receive either control, FES, BFB, or combined therapies. Each patient received 30 minutes of treatment three times per week for six weeks, in addition to their general rehabilitation program. Quantitative gait analysis was performed biweekly on each subject during the experimental therapy and for four weeks afterward. Thirty-two subjects completed the study. Combined therapy with BFB and FES resulted in improvements in both knee and ankle minimum flexion angles during swing phase that were statistically significant with $p = 0.05$ and $p = 0.02$, respectively. Velocity of gait, cycle time, and symmetry of stance phases also improved. The length of time elapsed since the stroke did not prove to be a significant factor.

Reduction of seating pressure using FES in patients with spinal cord injury. A preliminary report.

Ferguson AC Keating JF Delargy MA Andrews BJ
Paraplegia (1992 Jul) 30(7):474-8

The aim of this study was to investigate the use of functional electrical stimulation (FES) as a means of pressure sore prevention in seated spinal cord injured (SCI) subjects. Nine SCI subjects took part in tests in which electrical stimulation was applied to the quadriceps with the lower legs restrained. Ischial pressures were measured during periods of quiet sitting and FES application. A strain gauged lever arm was used to measure the knee moment during quadriceps stimulation. The average pressure drop at the right and left buttocks was 44 mmHg and 27 mmHg respectively. In general the greatest reductions occurred in subjects with larger knee moments; however, there was no direct relationship between the pressure reduction obtained and the quadriceps strength. This form of FES may be useful as a prophylactic aid in the management of pressure sores in SCI subjects.

Relative changes in blood flow with functional electrical stimulation during exercise of the paralyzed lower limbs.

Phillips W Burkett LN Munro R Davis M Pomeroy K
Paraplegia (1995 Feb) 33(2):90-3

Eight spinal cord injured (SCI) patients performed three sets of exercise with two conditions, 60% and 80% of VO2peak, with an arm crank ergometer. Functional neuromuscular stimulation was used to induce static leg contractions in two of the above sets of exercise. The three exercise sets were performed with no functional neuromuscular stimulation (NOS); with functional neuromuscular stimulation at 40 milliamperes; and with functional neuromuscular stimulation at 80 milliamperes (HIS). The lower limb blood flow was estimated by a photoelectric plethysmograph. Results showed that the lower limb blood flow was consistently reduced across both functional neuromuscular stimulation levels (17.4% from NOS to LOS; 13.8% from LOS to HIS; and 28.8% from NOS to HIS), and work loads (15.3% from rest to 60% VO2peak; 38.0% from 60% VO2peak to 80% VO2peak; and 47.5% from rest to 80% VO2peak). Rate-pressure product was decreased by 8.3% between NOS and HIS at 60% VO2peak (15.7 +/- 3.4 to 14.4 +/- 3.8), by 6.8% between NOS and HIS at 80% VO2peak (18.9 +/- 53 to 17.6 +/- 4.8), and by 12.4% between LOS and HIS at 80% VO2peak (20.1 +/- 6.7 to 17.6 +/- 4.8). These data indicate that in SCI (a) functional neuromuscular stimulation-induced contractions of the lower limb muscles can increase blood flow and thus reduce venous blood pooling in the paralyzed muscles, and (b) such improvements are associated with a reduced rate pressure product.(ABSTRACT TRUNCATED AT 250 WORDS)

Promotion of wound healing with electrical stimulation.

Kloth LC McCulloch JM
Adv Wound Care (1996 Sep-Oct) 9(5):42-5

Clinicians involved in the conservative care of chronic wounds have many treatment interventions from which to choose, including debridement/irrigation, dressings, pressure-relieving devices, hyperbaric or topically applied oxygen, whirlpool/pulsed lavage, ultrasound, topical antibiotics, and cytokine growth factors. All except the last two interventions are physical treatments that create a wound-tissue environment conducive to healing. Unfortunately, many chronic wounds heal very slowly, do

not heal, or worsen despite the best efforts of caregivers to promote tissue repair. An intervention commonly used to treat chronic wounds, especially by physical therapists, is electrical stimulation (ES). The rationale for use of this method is based on the fact that the human body has an endogenous bioelectric system that enhances healing of bone fractures and soft-tissue wounds. When the body's endogenous bioelectric system fails and cannot contribute to wound repair processes, therapeutic levels of electrical current may be delivered into the wound tissue from an external source. The external current may serve to mimic the failed natural bioelectric currents so that wound healing can proceed. Certain chemotaxic factors found in wound substrates contribute to tissue repair processes by attracting cells into the wound environment. Neutrophil, macrophage, fibroblast, and epidermal cells involved in wound repair carry either a positive or negative charge. When these cells are needed to contribute to autolysis, granulation tissue formation, anti-inflammatory activities, or epidermal resurfacing, ES may facilitate galvanotaxic attraction of these cells into the wound tissue and thereby accelerate healing.

Electrical nerve stimulation improves healing of diabetic ulcers.

Lundeberg TC Eriksson SV Malm M
Ann Plast Surg (1992 Oct) 29(4):328-31

A controlled study of the effects of electrical nerve stimulation (ENS) was performed in conjunction with a standard treatment for healing chronic diabetic ulcers on 64 patients divided randomly into two groups. All patients received standard treatment (paste-impregnated bandage and a self-adhesive elastic bandage) plus placebo ENS or ENS (alternating constant current; frequency, 80 Hz; pulse width, 1 msec; intensity-evoking strong paresthesias) for 20 minutes twice daily for 12 weeks. Comparison of percentages of healed ulcer area and the number of healed ulcers was made after 2, 4, 6, 8, and 12 weeks. There were significant differences ($p < 0.05$) in both ulcer area and healed ulcers in the ENS group compared with the placebo group after 12 weeks of treatment. The results of the present study support the use of ENS in diabetic ulcers. ENS is easy to apply and can be used by the patient at home following instructions from a medical doctor or a therapist experienced in electrical stimulation and the treatment of ulcers. Additional studies are needed to identify the mechanisms involved in the promotion of ulcer healing with electrical stimulation and to determine the stimulus variables that most efficaciously accelerate tissue repair.

Effects of electrical stimulation on wound healing in patients with diabetic ulcers.

Baker LL Chambers R DeMuth SK Villar F
Diabetes Care (1997 Mar) 20(3):405-12

OBJECTIVE: To evaluate the effects of two stimulation waveforms on healing rates in patients with diabetes and open ulcers. The hypothesis was that stimulus waveforms with minimal polar characteristics would provide significant healing for this patient sample. RESEARCH DESIGN AND METHODS: This was a prospective study that enrolled 80 patients with open ulcers. Patients received stimulation with either an asymmetric biphasic (A) or symmetric biphasic (B) square-wave pulse. Amplitudes were set to activate intact peripheral nerves in the skin. Two other groups received either very low levels of stimulation current (MC), or no electrical stimulation (C). When

combined these groups were referred to as the control group. Treatment was carried out daily until the wound healed, the patient withdrew from the study, or the physician changed the overall wound management program. Average healing rates were calculated from weekly measures of the wound perimeter and were used for statistical comparison through a one-way analysis of variance. RESULTS: Stimulation with the A protocol significantly increased the healing rate, enhancing healing by nearly 60% over the control rate of healing. Stimulation with the B protocol did not increase the healing rate when compared with control subjects. CONCLUSIONS: Electrical stimulation, given daily with a short pulsed, asymmetric biphasic waveform, was effective for enhancement of healing rates for patients with diabetes and open ulcers.

Electrical stimulation to heal dermal wounds.

Gentzkow GD
J Dermatol Surg Oncol (1993 Aug) 19(8):753-8

BACKGROUND. Numerous human and animal efficacy studies have demonstrated that electrical stimulation of the correct charge, density and total energy causes dramatically improved healing of dermal wounds. The investigations of biological actions (in vitro, animal, and human) demonstrate several effects that go a long way to explaining why electrical stimulation works. OBJECTIVE. To discuss recent research and advances in electrical stimulation of wound healing. RESULTS. Based on the latest scientific understanding of the wound healing process, one would expect a beneficial outcome from a therapy what decreases edema, debrides necrotic tissue, attracts neutrophils and macrophages, stimulates receptor sites for growth factors, stimulates growth of fibroblasts and granulation tissue, increases blood flow, stimulates neurite growth, induces epidermal cell migration, prevents post-ischemic oxygen radical-mediated damage, inhibits bacteria, and reduces numbers of mast cells. CONCLUSION. Taken together, the efficacy studies and the "mechanism of action" studies provide compelling, scientific evidence that electrical stimulation is safe and effective for promoting the healing of dermal wounds.

Alteration in alpha- and beta-adrenoceptor profile of rabbit knee joint blood vessels due to acute inflammation.

Najafipour H.
Exp Physiol. 2000 May;85(3):267-73.
Department of Physiology, Medical faculty, Kerman University of Medical Sciences and Health Services, Bulvd. 22 Bahman, Kerman, Iran.

Experiments were performed to investigate the nature of - and -adrenoceptors in blood vessels supplying the posterior capsule of the acutely inflamed rabbit knee joint, and results were compared to findings from previous experiments on the normal joint, to assess any alteration which may occur in the adrenoceptor profile due to the inflammation process. Electrical stimulation of the posterior articular nerve resulted in vasoconstriction which was reversed to vasodilatation by phentolamine and yohimbine. The dose-response curves to close intra-arterial injection of -adrenoceptor agonists showed a rank-order potency of: adrenaline = phenylephrine = clonidine. The adrenaline dose-response curve was shifted to the right by administration of antagonists with a rank-order potency of: phentolamine = yohimbine = prazosin. At this stage of the experiments there was an equal response of 1- and 2-adrenoceptors in blood vessels of the acutely inflamed rabbit knee joint. In another group of animals the neurally mediated vasodilatation, which appeared after administration of phentolamine, was completely blocked by propranolol, and was reduced by about 50 % by atenolol.

The dose-response curves to close intra-arterial injection of -adrenoceptor agonists showed a rank-order potency of: isoprenaline > salbutamol = dobutamine. The isoprenaline dose-response curve was shifted to the right by administration of antagonists with a rank-order potency of: propranolol > atenolol. These experiments also showed an almost equal response of 1- and 2-adrenoceptors in blood vessels of the acutely inflamed rabbit knee joint. Overall, compared to previous experiments on the normal joint in which 2- and 1-adrenoceptor responses predominated, acute inflammation resulted in a shift from 2- towards 1- and from 1- towards 2-adrenoceptor responses.

Sympathetically induced paradoxical increases of the cutaneous blood flow in chronically inflamed rats.

Tsujii Y, Koeda T, Sato J, Suzuki S, Kumazawa T.
J Auton Nerv Syst. 1996 Jul 5;59(3):103-12.
Department of Neural Regulation, Nagoya University, Japan.

In adjuvant arthritic (AA) rats, an abnormal responsiveness of nociceptors (C-fibre polymodal receptors) to sympathetic activities, i.e., alpha 2-adrenoceptor mediated activation of C-fibre polymodal receptors (CPRs), has been observed. The present investigations were undertaken to determine if a similar plastic change would occur in the cutaneous vascular system in the rat chronic inflammation model. The vascular responses were measured by a laser-Doppler flowmeter in the hindpaw skin of the AA rats after electrical stimulation of lumbar sympathetic trunk (sympathetic stimulation). In control non-arthritic rats, the sympathetic stimulation caused decrease in blood flow of the skin (SkBF) in all animals tested (n = 7). On the other hand, the sympathetic stimulation in the AA rats caused both increase (n = 15) as well as decrease (n = 11) in SkBF. In contrast to the abnormal responsiveness of CPRs, the intra-arterial injection of noradrenaline caused the expected decrease in SkBF in all animals tested, and in no instances increases in SkBF were observed. To determine whether activation of nitric oxide (NO), which is known to be a potent endogenous vasodilatation substance, was involved in the vasodilating effect to sympathetic stimulation, an inhibitor of NO synthase, NG-monomethyl-L-arginine (L-NMMA), was applied systemically. L-NMMA significantly increased baseline blood pressure in the control and the AA rats, but it did not significantly alter the SkBF in the control or the AA rats after the sympathetic stimulation, suggesting that NO is not a mediator in the vasoactive responses. The results of the current studies showed for the first time that electrical stimulation of the lumbar sympathetic trunk causes vasodilatation in the skin of the AA rats. This abnormal responsiveness of regional SkBF after sympathetic stimulation was not mediated by adrenergic or NO system.

Papers on Wound Healing

Increased Blood Flow to the effected Treatment Area and Wound Healing while using electrical stimulation.

Effects of aging on neurogenic vasodilator responses evoked by transcutaneous electrical nerve stimulation: relevance to wound healing.

Khalil Z, Merhi M
J Gerontol A Biol Sci Med Sci. 2000 Jun; 55(6):B257-63.
National Ageing Research Institute, University of Melbourne, Victoria, Australia.

We have previously shown an age-related decline in the modulation of skin vascular reactivity by sensory nerves that correlates with a decline in wound repair efficacy. This study was designed to examine the possibility that improving the functional ability of aged sensory nerves using noninvasive transcutaneous electrical nerve stimulation (TENS) could also accelerate tissue repair. TENS of the sciatic nerve, combined with measuring blood flow responses in the rat hind-footpad using laser Doppler flowmetry, was used to establish the vascular effects. Following TENS (using parameters 20V, 5 Hz for 1 min), similar increases in vascular responses were obtained in both young (13.2+/-0.9 cm2) and old rats (11.6+/-2.3 cm2). In contrast, capsaicin-pretreated rats showed markedly diminished responses. Sympathetic fibers did not appear to modulate these sensory nerve responses. In the second part, a thermal wound was induced (using a CO2 laser) in the interscapular region of old rats (under anesthesia). In the active treatment group, TENS was applied twice daily for the initial 5 days, and the sham group received inactive TENS. Using the healing endpoint as the time when full wound contraction occurred, the active group required 14.7+/-0.2 days for complete healing, a significant improvement over the sham group (21.8+/-0.3 days). We contend that low-frequency TENS can improve the vascular response of old rats. In addition, wound healing in aged rats can be accelerated by peripheral activation of sensory nerves at low-frequency electrical stimulation parameters.

Epidural spinal cord electrical stimulation in diabetic critical lower limb ischemia.

Petrakis IE, Sciacca V
Title Abbreviation: J Diabetes Complications.
1999 Sep-Dec; Volume Issue: 13(5-6):293-9.
First Department of General Surgery, Policlinico Umberto I, University of Rome, La Sapienza, Rome, Italy.

Spinal cord stimulation (SCS) has been suggested to improve microcirculatory blood flow to relieve ischemic pain and to reduce amputation rate in patients with peripheral arterial occlusive disease (PAOD). The aim of this study was to evaluate the specific prognostic parameters in the prediction of successful SCS, in diabetic patients, performing a retrospective data analysis. To perform this evaluation, 64 diabetic patients (39 men, 25 women; mean age, 69 years) classified as Fontaine's stage III and IV, with PAOD, were treated with SCS for rest pain and trophic lesions with dry gangrene, after failed conservative or surgical treatment. In clinical controls, pedal transcutaneous oxygen tension (TcPO(2)), ankle/brachial blood pressure index (ABI), and toe pressure Doppler measurements were utilized to select and follow-up the patients. After 58 months of follow-up (range, 20-128 months), pain relief

greater than 75% and limb salvage were achieved in 38 diabetic patients. A partial success was obtained in nine patients with pain relief greater than 50% and limb salvage for at least 6 months. The method failed in 17 patients or the device was removed due to technical problems, and the limb was amputated in these patients. TcPO(2) was assessed on the dorsum of the foot. Clinical improvement and SCS success were associated with increase of TcPO(2), before and after implantation. Limb salvage was achieved in the patients who had significant TcPO(2) increase within the 2 weeks of the testing period, independently of the stage of the disease. A TcPO(2) increase of more than 50% in the first 2 months after implantation was predictive of success, and was related to the presence of adequate paresthesias in the painful area during the trial period. TcPO(2) significantly increased after long-term follow-up in all patients with limb salvage (from 22.1 to 43.1 mm Hg in the rest pain patients, from 15.8 to 36.4 mm Hg in those with trophic lesions of less than 3 cm(2), and from 12.1 to 28.1 in those with trophic lesions of greater than 3 cm(2), ($p < 0.01$). ABI did not changed under stimulation. In diabetic patients with PAOD, the SCS increases the skin blood flow, is associated with significant pain relief, and could be proven an excellent alternative therapy, improving the life quality. Significant TcPO(2) increase within the 2-week test period, is a predictive index of therapy success and should be considered before the final decision in terms of cost effectiveness, before the permanent implantation.

Effects of transcutaneous nerve stimulation on the microcirculation in chronic leg ulcers.

Cosmo P, Svensson H, Bornmyr S, Wikstrom SO
Scand J Plast Reconstr Surg Hand Surg. 2000 Mar; 34(1):61-4.
Department of Plastic and Reconstructive Surgery, Malmo University Hospital, Sweden.

The purpose of this study was to find out to what extent transcutaneous electrical nerve stimulation (TENS) affects the blood flow in and around chronic lower leg ulcers, as measured with a new technique, laser Doppler imaging (LDI). Fifteen patients, mean age 73 years (range 38-85) with chronic leg ulcers of various causes participated in the study. The duration of the ulcers ranged from 3 months to 16 years. Low-frequency (2 Hz; 10-45 mA) TENS was given for 60 minutes. The changes in blood flow were measured every 5 minutes by LDI. After 60 minutes, mean blood flow had increased in the ulcer by 35%, and in the intact skin surrounding the ulcer by 15%. Even 15 minutes after the TENS had finished there was still a mean blood flow increase of 29% in the ulcer and 9% in the skin. The present results show that TENS has a stimulating effect on local blood circulation in and around chronic ulcers.

Effect of transcutaneous nerve stimulation on microcirculation in intact skin and blister wounds in healthy volunteers.

Wikstrom SO, Svedman P, Svensson H, Tanweer AS
Scand J Plast Reconstr Surg Hand Surg. 1999 Jun; 33(2):195-201.
Department of Plastic and Reconstructive Surgery, University Hospital MAS, Malmo, Sweden.

Healthy non-smoking volunteers participated in two experimental studies in which the circulatory changes induced by transcutaneous nerve stimulation (TENS) were quantified by two different methods. In experimental series 1 (intact skin), nine volunteers were given TENS on the left lower leg for 60 minutes on three occasions at different frequencies each time (2 Hz, 100 Hz, and sham). Changes in blood flow were assessed by laser Doppler imaging

technique every five minutes. The mean blood flow increased by 40% during low frequency TENS and by 12% during high frequency TENS. There was no change in mean blood flow during sham stimulation. In experimental series 2 (blister wound), the circulatory changes induced by TENS were studied by intravital video microscopy and computerised image analysis in standard blister wounds on the lower leg. The microcirculatory blood flow, measured as red blood cell velocity (RBC-V) in 5-14 individual capillaries in each wound, was assessed before and during 45 minutes of TENS (2 Hz and 100 Hz). Mean RBC-V increased by 23% during low frequency TENS (n = 6) and by 17% during high frequency TENS (n = 8). The results show that: laser Doppler imaging and intravital video microscopy techniques can be used to study events at the microcirculatory level; the blister wound is an interesting new standard wound for use in clinical studies; and TENS stimulates the peripheral circulation.

Prognostic factors in the prediction of chronic wound healing by electrical stimulation.

Cukjati D, Robnik-Sikonja M, Rebersek S, Kononenko I, Miklavcic D.
Med Biol Eng Comput. 2001 Sep;39(5):542-50.
Faculty of Electrical Engineering, University of Ljubljana, Slovenia.

The aim of the study is to determine the effects of wound, patient and treatment attributes on the wound healing rate and to propose a system for wound healing rate prediction. Predicting the wound healing rate from the initial wound, patient and treatment data collected in a database of 300 chronic wounds is not possible. After considering weekly follow-ups, it was determined that the best prognostic factors are weekly follow-ups of the wound healing process, which alone were found to predict accurately the wound healing rate after a minimum follow-up period of four weeks (at least five measurements of wound area). After combining the follow-ups with wound, patient and treatment attributes, the minimum follow-up period was reduced to two weeks (at least three measurements of wound area). After a follow-up period of two weeks, it was possible to predict the wound healing rate of an independent test set of chronic wounds with a relative squared error of 0.347, and after three weeks, with a relative squared error of 0.181 (using regression trees with linear equations in its leaves). Regression trees with a relative squared error close to 0 produce better prediction than with an error closer to 1. Results show that the type of treatment is just one of many prognostic factors. Arranged in order of decreasing prediction capability, prognostic factors are: wound size, patient's age, elapsed time from wound appearance to the beginning of the treatment, width-to-length ratio, location and type of treatment. The data collected support former findings that the biphasic- and direct-current stimulation contributes to faster healing of chronic wounds. The model of wound healing dynamics aids the prediction of chronic wound healing rate, and hence helps with the formulation of appropriate treatment decisions.

Choosing an adjunctive therapy for the treatment of chronic wounds.
Houghton PE, Campbell KE.

Ostomy Wound Manage. 1999 Aug;45(8):43-52; quiz 53-4.
St. Joseph's Health Center, School of Physiotherapy, University of Western Ontario, London, Canada.

Adjunctive therapies such as ultrasound, laser, ultraviolet light, superficial heating, pulsed electromagnetic fields, and electrical stimulation have all been indicated in the treatment of chronic wounds. The purpose of this article is to outline the issues a healthcare professional must consider when

choosing the best adjunctive therapy for a chronic wound. It summarizes the effects of therapeutic modalities on the wound healing process, analyzes the clinical research evidence, discusses practical considerations, and reviews indications, contraindications, precautions, and safety considerations. Finally, an algorithm is presented to help guide the clinician in selecting a modality. In summary, research evidence exists in the literature that suggests these adjunctive therapies can directly stimulate new tissue growth, augment wound tissue strength, improve local circulation and oxygenation, reduce edema, and/or inhibit bacterial growth. Electrical stimulation and ultrasound are the only therapeutic modalities that currently have sufficient clinical research evidence to support their use in the treatment of chronic wounds. Practical issues such as cost, time and training required, and patient and therapist safety concerns, will ultimately influence the selection of these modalities.

Effect of electrical stimulation on chronic wound healing: a meta-analysis.
Gardner SE, Frantz RA, Schmidt FL.

Wound Repair Regen. 1999 Nov-Dec;7(6):495-503.
Colleges of Nursing, The University of Iowa, Iowa City, IA 52242-7066, USA.

The purpose of this meta-analysis was to quantify the effect of electrical stimulation on chronic wound healing. Fifteen studies, which included 24 electrical stimulation samples and 15 control samples, were analyzed. The average rate of healing per week was calculated for the electrical stimulation and control samples. Ninety-five percentage confidence intervals were also calculated. The samples were then grouped by type of electrical stimulation device and chronic wound and reanalyzed. Rate of healing per week was 22% for electrical stimulation samples and 9% for control samples. The net effect of electrical stimulation was 13% per week, an increase of 144% over the control rate. The 95% confidence intervals of the electrical stimulation (18-26%) and control samples (3.8-14%) did not overlap. Electrical stimulation was most effective on pressure ulcers (net effect = 13%). Findings regarding the relative effectiveness of different types of electrical stimulation device were inconclusive. Although electrical stimulation produces a substantial improvement in the healing of chronic wounds, further research is needed to identify which electrical stimulation devices are most effective and which wounds respond best to this treatment.

A comparative study of the effect of ultrasound and electrostimulation on wound healing in rats.

Taskan I, Ozyazgan I, Tercan M, Kardas HY, Balkanli S, Saraymen R, Zorlu U
Plast Reconstr Surg. 1997 Sep;100(4):966-72.
Physical Therapy and Rehabilitation Center, Medical Faculty of Inonu University, Istanbul, Turkey.

A comparative study has been carried out to investigate the effects of electrical stimulation and ultrasound on wound healing. Eighty-four female rats were divided into four groups depending on the treatment received. The first group was given electrical stimulation of 300 microA direct current, 30 minutes daily, starting with negative polarity and then changed after 3 days of treatment. Group 2 received sham electrostimulation treatment. The third group received 0.1 W/cm2 pulsed ultrasound using the moving applicator technique for 5 minutes a day. Group 4 received sham ultrasound treatment. A total of 7 days of treatment was given to all groups. Histopathologic and biochemical analyses on the fourth and seventh days and wound breaking

strength on the twenty-fifth day were performed for all groups. By accelerating the inflammatory phase, electrical stimulation had progressed the proliferative phase of wound healing earlier than ultrasound had done. Both electrical stimulation and ultrasound have positive effects on proliferative phases, but electrical stimulation was superior to ultrasound at the maturation phase. There was no difference between the two experimental groups on the mast cell reduction effect. Although ultrasound treatment may seem to be efficient in terms of time, when the effects of electrical stimulation and ultrasound on wound healing with the methods employed in our study are considered, it is concluded that electrical stimulation is a means of treatment superior to ultrasound in wound healing.

Effects of electrical stimulation on wound healing in patients with diabetic ulcers.

Baker LL, Chambers R, DeMuth SK, Villar F.
Diabetes Care. 1997 Mar;20(3):405-12.
Department of Biokinesiology and Physical Therapy, University of Southern California, Los Angeles 90033,

OBJECTIVE: To evaluate the effects of two stimulation waveforms on healing rates in patients with diabetes and open ulcers. The hypothesis was that stimulus waveforms with minimal polar characteristics would provide significant healing for this patient sample. RESEARCH DESIGN AND METHODS: This was a prospective study that enrolled 80 patients with open ulcers. Patients received stimulation with either an asymmetric biphasic (A) or symmetric biphasic (B) square-wave pulse. Amplitudes were set to activate intact peripheral nerves in the skin. Two other groups received either very low levels of stimulation current (MC), or no electrical stimulation (C). When combined these groups were referred to as the control group. Treatment was carried out daily until the wound healed, the patient withdrew from the study, or the physician changed the overall wound management program. Average healing rates were calculated from weekly measures of the wound perimeter and were used for statistical comparison through a one-way analysis of variance. RESULTS: Stimulation with the A protocol significantly increased the healing rate, enhancing healing by nearly 60% over the control rate of healing. Stimulation with the B protocol did not increase the healing rate when compared with control subjects. CONCLUSIONS: Electrical stimulation, given daily with a short pulsed, asymmetric biphasic waveform, was effective for enhancement of healing rates for patients with diabetes and open ulcers.

Promotion of wound healing with electrical stimulation.

Kloth LC, McCulloch JM.
Adv Wound Care. 1996 Sep-Oct;9(5):42-5.
Program of Physical Therapy, Marquette University, Milwaukee, Wis, USA.

Clinicians involved in the conservative care of chronic wounds have many treatment interventions from which to choose, including debridement/irrigation, dressings, pressure-relieving devices, hyperbaric or topically applied oxygen, whirlpool/pulsed lavage, ultrasound, topical antibiotics, and cytokine growth factors. All except the last two interventions are physical treatments that create a wound-tissue environment conducive to healing. Unfortunately, many chronic wounds heal very slowly, do not heal, or worsen despite the best efforts of caregivers to promote tissue repair. An intervention commonly used to treat chronic wounds, especially by physical therapists, is electrical stimulation (ES). The rationale for use of

this method is based on the fact that the human body has an endogenous bioelectric system that enhances healing of bone fractures and soft-tissue wounds. When the body's endogenous bioelectric system fails and cannot contribute to wound repair processes, therapeutic levels of electrical current may be delivered into the wound tissue from an external source. The external current may serve to mimic the failed natural bioelectric currents so that wound healing can proceed. Certain chemotaxic factors found in wound substrates contribute to tissue repair processes by attracting cells into the wound environment. Neutrophil, macrophage, fibroblast, and epidermal cells involved in wound repair carry either a positive or negative charge. When these cells are needed to contribute to autolysis, granulation tissue formation, anti-inflammatory activities, or epidermal resurfacing, ES may facilitate galvanotaxic attraction of these cells into the wound tissue and thereby accelerate healing.

Physical modalities in wound management: UVC, therapeutic heating and electrical stimulation.

Kloth LC.
Ostomy Wound Manage. 1995 Jun;41(5):18-20, 22-4, 26-7.

In spite of efforts to create an optimum wound environment for healing, there are times that a wound may not heal, may heal very slowly, or may worsen. In these cases, a series of treatments with an appropriate physical agent can be added to the patient's care plan to augment tissue reparative processes. Three modalities that have received support in the literature for use in wound healing are ultraviolet "C" radiation (UVC), therapeutic heating, and electrical stimulation. Treatment goals for UVC are hyperplasia and enhanced re-epithelialization or desquamation of the leading edge of periulcer epidermal cells, granulation tissue formation, sloughing of necrotic tissue, and bactericidal effects. Treatment goals for therapeutic heating are increased blood perfusion with subsequent increased delivery of oxygen to the tissues (avoiding the dessication of wound tissues). The treatment goal for electrical stimulation is to attract negatively or positively charged cells into the wound area, such as neutrophils, macrophages, epidermal cells and fibroblasts that in turn will contribute to wound healing processes by way of their individual cellular activities.

Experimental wound healing with electrical stimulation.

Reger SI, Hyodo A, Negami S, Kambic HE, Sahgal V
Title Abbreviation: Artif Organs.
1999 May; 23(5):460-2.
Department of Physical Medicine and Rehabilitation, The Cleveland Clinic Foundation, Ohio 44195, USA.

The effect of alternating current (AC) and direct current (DC) stimulation was studied on experimental pressure ulcer healing in a new monoplegic pig model. The study was conducted in 30 healthy young Hanford minipigs. The rate of wound healing, histology, vascularization, collagen formation, microbiology, perfusion, and the mechanical strength of the healed wounds were studied. Normal pigskin was compared to denervated control and denervated AC and DC stimulated healed skin. Hind limb denervation was by right unilateral extradural rhizotomies from the L2 to S1 nerve roots. Reproducible uniformly controlled Stage III or higher tissue ulcers were created. When compared to the control wounds, both the AC and DC stimulated wounds showed reduced healing time and increased perfusion in the early phases of healing. DC

stimulation reduced the wound area more rapidly than AC, but AC stimulation reduced the wound volume more rapidly than DC. The electrical stimulation did not reduce the strength of the healing wounds below those of the nonstimulated controls. The applied current appears to orient new collagen formation even in the absence of neural influences.

Electric muscle stimulation for pressure sore prevention: tissue shape variation.

Levine SP Kett RL Cederna PS Brooks SV
Arch Phys Med Rehabil (1990 Mar) 71(3):210-5

This study measured changes in tissue shape and deformation at the seating interface produced by electric muscle stimulation (EMS) of the gluteus maximus. The purpose of the study was to investigate the application of EMS for pressure sore prevention. Limitations of pressure measurements for analysis of load distribution are discussed and a rationale developed for using tissue shape and deformation to further characterize the seating interface. Ultrasonic imaging of the seating interface is described under three conditions: buttocks suspended, external load applied with no EMS, and external load applied with bilateral EMS of the buttocks. Results show that low level stimulation of the gluteus maximus produces substantial changes in the shape of the loaded buttocks and an external contour more nearly shaped like the suspended buttocks. It is concluded that EMS produces buttock tissue undulation and shape reconfiguration which may assist in preventing pressure sores over the seating surface.

Adjuvant therapy for ulcer care.

Frantz RA
Clin Geriatr Med (1997 Aug) 13(3):553-64

Adjuvant therapies, specifically electrotherapy, hyperbaric oxygen, ultrasound, and hydrotherapy, are considered increasingly for use with conventional local wound care to support healing of pressure ulcers. This article describes the characteristics of these modalities, their physiologic effects on the healing process, and the research to evaluate their efficacy.

Effects of electrical stimulation on wound healing in patients with diabetic ulcers.
Baker LL Chambers R DeMuth SK Villar F
Diabetes Care (1997 Mar) 20(3):405-12

OBJECTIVE: To evaluate the effects of two stimulation waveforms on healing rates in patients with diabetes and open ulcers. The hypothesis was that stimulus waveforms with minimal polar characteristics would provide significant healing for this patient sample. RESEARCH DESIGN AND METHODS: This was a prospective study that enrolled 80 patients with open ulcers. Patients received stimulation with either an asymmetric biphasic (A) or symmetric biphasic (B) square-wave pulse. Amplitudes were set to activate intact peripheral nerves in the skin. Two other groups received either very low levels of stimulation current (MC), or no electrical stimulation (C). When

combined these groups were referred to as the control group. Treatment was carried out daily until the wound healed, the patient withdrew from the study, or the physician changed the overall wound management program. Average healing rates were calculated from weekly measures of the wound perimeter and were used for statistical comparison through a one-way analysis of variance. RESULTS: Stimulation with the A protocol significantly increased the healing rate, enhancing healing by nearly 60% over the control rate of healing. Stimulation with the B protocol did not increase the healing rate when compared with control subjects. CONCLUSIONS: Electrical stimulation, given daily with a short pulsed, asymmetric biphasic waveform, was effective for enhancement of healing rates for patients with diabetes and open ulcers.

The benefit of electrical stimulation to enhance perfusion in persons with diabetes mellitus.

Peters EJ Armstrong DG Wunderlich RP Bosma J Stacpoole-Shea S Lavery LA
J Foot Ankle Surg (1998 Sep-Oct) 37(5):396-400; discussion 447-8

The purpose of this study was to evaluate the effect of galvanic electrical stimulation on vascular perfusion in diabetic patients. Nineteen subjects with diabetes were enrolled. Eleven subjects (57.9%) were diagnosed with impaired peripheral perfusion based upon their initial transcutaneous oximetry values (< 40 mm Hg). The subjects were studied over a 2-day period. On the 1st day, one foot was electrically stimulated for four 60-minute periods by an external electrical stimulation device. Vascular perfusion of both feet was assessed before and after the sessions of electrical stimulation. On the 2nd day, no electrical stimulation was applied and noninvasive vascular measurements were repeated. For the 1st hour, transcutaneous oxygen pressure was measured continuously during stimulation at the lateral aspect of the leg. Subsequently, perfusion between the periods of stimulation was measured on the dorsum of the foot with both transcutaneous oximetry and laser Doppler flowmetry after each stimulation period. In the group with impaired peripheral perfusion, a significant rise in tissue oxygenation as compared to the control measurements was measured during the first 5 minutes of stimulation ($p < .040$). For those without vascular disease (TcpO2 > 40 mm Hg) however, there was not a significant increase compared to baseline ($p = .280$). After the periods of stimulation, the stimulated feet did not show any higher perfusion levels than the control feet. Patterns in perfusion during the day, as measured by laser Doppler flowmetry, were similar in the tested feet and in the controls. These data suggest that external subsensory electrical stimulation induces a transient rise in skin perfusion in persons with diabetes and impaired peripheral perfusion.

Treatment of chronic wounds by means of electric and electromagnetic fields. Part 2. Value of FES parameters for pressure sore treatment.

Stefanovska A Vodovnik L Benko H Turk R
Med Biol Eng Comput (1993 May) 31(3):213-20

Subjects with spinal cord injury are often distressed by pressure sores, which usually appear after prolonged pressure (wheelchair, bed) across the soft tissue which has already lost sensibility and has diminished microcirculation. The healing ability and its dynamics depend on the state of the subject's overall health. Consequently, evaluation of a particular treatment requires careful consideration of as many as possible of the parameters relevant to healing and an adequate criterion for assessing the state of the pressure sore. Bearing in mind these two circumstances, the results of a multicentre clinical study are analysed. The aim of the study

was to test two hypotheses: first that healing is faster when sores are also treated by electric currents (ECs) (in addition to conventional treatment); and secondly that there exist differences in the efficiency of the treatment if direct or low-frequency pulsed currents (FES parameters) are applied. The data analysed show that pressure sores are likely to heal twice as fast when treated with low-frequency pulsed currents. EC seems to improve the healing rate in cases where the natural healing mechanisms of the body are not sufficient (chronic wounds, older subjects).

Reduction of seating pressure using FES in patients with spinal cord injury. A preliminary report.

Ferguson AC Keating JF Delargy MA Andrews BJ
Paraplegia (1992 Jul) 30(7):474-8

The aim of this study was to investigate the use of functional electrical stimulation (FES) as a means of pressure sore prevention in seated spinal cord injured (SCI) subjects. Nine SCI subjects took part in tests in which electrical stimulation was applied to the quadriceps with the lower legs restrained. Ischial pressures were measured during periods of quiet sitting and FES application. A strain gauged lever arm was used to measure the knee moment during quadriceps stimulation. The average pressure drop at the right and left buttocks was 44 mmHg and 27 mmHg respectively. In general the greatest reductions occurred in subjects with larger knee moments; however, there was no direct relationship between the pressure reduction obtained and the quadriceps strength. This form of FES may be useful as a prophylactic aid in the management of pressure sores in SCI subjects.

Chronic dermal ulcer healing enhanced with monophasic pulsed electrical stimulation [see comments]

Feedar JA Kloth LC Gentzkow GD
Phys Ther (1991 Sep) 71(9):639-49

The purposes of this randomized, double-blind, multicenter study were to compare healing of chronic dermal ulcers treated with pulsed electrical stimulation with healing of similar wounds treated with sham electrical stimulation and to evaluate patient tolerance to the therapeutic protocol. Forty-seven patients, aged 29 to 91 years, with 50 stage II, III, and IV ulcers were randomly assigned to either a treatment group (n = 26) or a control (sham treatment) group (n = 24). Treated wounds received 30 minutes of pulsed cathodal electrical stimulation twice daily at a pulse frequency of 128 pulses per second (pps) and a peak amplitude of 29.2 mA if the wound contained necrotic tissue or any drainage that was not serosanguinous. A saline-moistened nontreatment electrode was applied 30.5 cm (12 in) cephalad from the wound. This protocol was continued for 3 days after the wound was debrided or exhibited serosanguinous drainage. Thereafter, the polarity of the treatment electrode on the wound was changed every 3 days until the wound progressed to a stage II classification. The pulse frequency was then reduced to 64 pps, and the treatment electrode polarity was changed daily until the wound was healed. Patients in the control group were treated with the same protocol, except they received sham electrical stimulation. After 4 weeks, wounds in the treatment and control groups were 44% and 67% of their initial size, respectively. The healing rates per week for the treatment and control groups were 14% and 8.25%, respectively. The results of this study indicate that

pulsed electrical stimulation has a beneficial effect on healing stage II, III, and IV chronic dermal ulcers.

Effect of electrical stimulation on foot skin perfusion in persons with or at risk for diabetic foot ulcers.

Gilcreast DM Stotts NA Froelicher ES Baker LL Moss KM
Wound Repair Regen (1998 Sep-Oct) 6(5):434-41

The failure of foot wounds to heal results in 54,000 people with diabetes having to undergo extremity amputations annually. Therefore, treatment is needed to speed healing in people with diabetes in order to reduce the need for amputation. This study tested the effect of high-voltage pulsed current on foot blood flow in human beings who are at risk for diabetic foot ulcers. Neuropathy, vascular disease, Wagner Class, glucose, gender, ethnicity, and age were measured. A sample of 132 subjects was tested using a repeated-measures design. A baseline transcutaneous oxygen level was obtained; stimulation was applied, and transcutaneous oxygen measurements were recorded at 30- and 60- minute time intervals. The grouped foot transcutaneous oxygen levels decreased ($F = 5.66$, $p =. 0039$) following electrical stimulation. Analysis of variance (Scheffe, $p <.05$) showed that initial transcutaneous oxygen was significantly higher than subsequent readings. However, oxygen response was distributed bimodally: 35 (27%) subjects showed increased transcutaneous oxygen (mean 14.8 mm Hg), and 97 (73%) experienced a decreased transcutaneous oxygen reading (mean 12.2 mm Hg). Logistic regression analysis did not explain these differences. Although this treatment appears to increase blood flow in a subset of patients, further study is needed to identify probable mechanisms for this response.

Biofeedback and functional electric stimulation in stroke Rehabilitation.

Cozean CD Pease WS Hubbell SL
Arch Phys Med Rehabil (1988 Jun) 69(6):401-5

The study examined the efficacy of functional electric stimulation (FES) and biofeedback (BFB) treatment of gait dysfunction in patients with hemiplegia after stroke. These two therapeutic modalities were tested alone and in combination in a prospective, controlled, randomized trial. The authors hypothesized that in concurrent use, these two modalities would complement one another. Thirty-six hemiplegic patients undergoing rehabilitation after stroke were accepted for study and randomized into four groups to receive either control, FES, BFB, or combined therapies. Each patient received 30 minutes of treatment three times per week for six weeks, in addition to their general rehabilitation program. Quantitative gait analysis was performed biweekly on each subject during the experimental therapy and for four weeks afterward. Thirty-two subjects completed the study. Combined therapy with BFB and FES resulted in improvements in both knee and ankle minimum flexion angles during swing phase that were statistically significant with $p = 0.05$ and $p = 0.02$, respectively. Velocity of gait, cycle time, and symmetry of stance phases also improved. The length of time elapsed since the stroke did not prove to be a significant factor.

Reduction of seating pressure using FES in patients with spinal cord injury. A preliminary report.

Ferguson AC Keating JF Delargy MA Andrews BJ
Paraplegia (1992 Jul) 30(7):474-8

The aim of this study was to investigate the use of functional electrical stimulation (FES) as a means of pressure sore prevention in seated spinal cord injured (SCI) subjects. Nine SCI subjects took part in tests in which electrical stimulation was applied to the quadriceps with the lower legs restrained. Ischial pressures were measured during periods of quiet sitting and FES application. A strain gauged lever arm was used to measure the knee moment during quadriceps stimulation. The average pressure drop at the right and left buttocks was 44 mmHg and 27 mmHg respectively. In general the greatest reductions occurred in subjects with larger knee moments; however, there was no direct relationship between the pressure reduction obtained and the quadriceps strength. This form of FES may be useful as a prophylactic aid in the management of pressure sores in SCI subjects.

Relative changes in blood flow with functional electrical stimulation during exercise of the paralyzed lower limbs.

Phillips W Burkett LN Munro R Davis M Pomeroy K
Paraplegia (1995 Feb) 33(2):90-3

Eight spinal cord injured (SCI) patients performed three sets of exercise with two conditions, 60% and 80% of VO2peak, with an arm crank ergometer. Functional neuromuscular stimulation was used to induce static leg contractions in two of the above sets of exercise. The three exercise sets were performed with no functional neuromuscular stimulation (NOS); with functional neuromuscular stimulation at 40 milliamperes; and with functional neuromuscular stimulation at 80 milliamperes (HIS). The lower limb blood flow was estimated by a photoelectric plethysmograph. Results showed that the lower limb blood flow was consistently reduced across both functional neuromuscular stimulation levels (17.4% from NOS to LOS; 13.8% from LOS to HIS; and 28.8% from NOS to HIS), and work loads (15.3% from rest to 60% VO2peak; 38.0% from 60% VO2peak to 80% VO2peak; and 47.5% from rest to 80% VO2peak). Rate-pressure product was decreased by 8.3% between NOS and HIS at 60% VO2peak (15.7 +/- 3.4 to 14.4 +/- 3.8), by 6.8% between NOS and HIS at 80% VO2peak (18.9 +/- 53 to 17.6 +/- 4.8), and by 12.4% between LOS and HIS at 80% VO2peak (20.1 +/- 6.7 to 17.6 +/- 4.8). These data indicate that in SCI (a) functional neuromuscular stimulation-induced contractions of the lower limb muscles can increase blood flow and thus reduce venous blood pooling in the paralyzed muscles, and (b) such improvements are associated with a reduced rate pressure product.(ABSTRACT TRUNCATED AT 250 WORDS)

Promotion of wound healing with electrical stimulation.

Kloth LC McCulloch JM
Adv Wound Care (1996 Sep-Oct) 9(5):42-5

Clinicians involved in the conservative care of chronic wounds have many treatment interventions from which to choose, including debridement/irrigation, dressings, pressure-relieving devices, hyperbaric or topically applied oxygen, whirlpool/pulsed lavage, ultrasound, topical antibiotics, and cytokine growth factors. All except the last two interventions are physical treatments that create a wound-tissue environment conducive to healing. Unfortunately, many chronic wounds heal very slowly, do

not heal, or worsen despite the best efforts of caregivers to promote tissue repair. An intervention commonly used to treat chronic wounds, especially by physical therapists, is electrical stimulation (ES). The rationale for use of this method is based on the fact that the human body has an endogenous bioelectric system that enhances healing of bone fractures and soft-tissue wounds. When the body's endogenous bioelectric system fails and cannot contribute to wound repair processes, therapeutic levels of electrical current may be delivered into the wound tissue from an external source. The external current may serve to mimic the failed natural bioelectric currents so that wound healing can proceed. Certain chemotaxic factors found in wound substrates contribute to tissue repair processes by attracting cells into the wound environment. Neutrophil, macrophage, fibroblast, and epidermal cells involved in wound repair carry either a positive or negative charge. When these cells are needed to contribute to autolysis, granulation tissue formation, anti-inflammatory activities, or epidermal resurfacing, ES may facilitate galvanotaxic attraction of these cells into the wound tissue and thereby accelerate healing.

Electrical nerve stimulation improves healing of diabetic ulcers.

Lundeberg TC Eriksson SV Malm M
Ann Plast Surg (1992 Oct) 29(4):328-31

A controlled study of the effects of electrical nerve stimulation (ENS) was performed in conjunction with a standard treatment for healing chronic diabetic ulcers on 64 patients divided randomly into two groups. All patients received standard treatment (paste-impregnated bandage and a self-adhesive elastic bandage) plus placebo ENS or ENS (alternating constant current; frequency, 80 Hz; pulse width, 1 msec; intensity-evoking strong paresthesias) for 20 minutes twice daily for 12 weeks. Comparison of percentages of healed ulcer area and the number of healed ulcers was made after 2, 4, 6, 8, and 12 weeks. There were significant differences ($p < 0.05$) in both ulcer area and healed ulcers in the ENS group compared with the placebo group after 12 weeks of treatment. The results of the present study support the use of ENS in diabetic ulcers. ENS is easy to apply and can be used by the patient at home following instructions from a medical doctor or a therapist experienced in electrical stimulation and the treatment of ulcers. Additional studies are needed to identify the mechanisms involved in the promotion of ulcer healing with electrical stimulation and to determine the stimulus variables that most efficaciously accelerate tissue repair.

Effects of electrical stimulation on wound healing in patients with diabetic ulcers.

Baker LL Chambers R DeMuth SK Villar F
Diabetes Care (1997 Mar) 20(3):405-12

OBJECTIVE: To evaluate the effects of two stimulation waveforms on healing rates in patients with diabetes and open ulcers. The hypothesis was that stimulus waveforms with minimal polar characteristics would provide significant healing for this patient sample. RESEARCH DESIGN AND METHODS: This was a prospective study that enrolled 80 patients with open ulcers. Patients received stimulation with either an asymmetric biphasic (A) or symmetric biphasic (B) square-wave pulse. Amplitudes were set to activate intact peripheral nerves in the skin. Two other groups received either very low levels of stimulation current (MC), or no electrical stimulation (C). When

combined these groups were referred to as the control group. Treatment was carried out daily until the wound healed, the patient withdrew from the study, or the physician changed the overall wound management program. Average healing rates were calculated from weekly measures of the wound perimeter and were used for statistical comparison through a one-way analysis of variance. RESULTS: Stimulation with the A protocol significantly increased the healing rate, enhancing healing by nearly 60% over the control rate of healing. Stimulation with the B protocol did not increase the healing rate when compared with control subjects. CONCLUSIONS: Electrical stimulation, given daily with a short pulsed, asymmetric biphasic waveform, was effective for enhancement of healing rates for patients with diabetes and open ulcers.

Electrical stimulation to heal dermal wounds.

Gentzkow GD
J Dermatol Surg Oncol (1993 Aug) 19(8):753-8

BACKGROUND. Numerous human and animal efficacy studies have demonstrated that electrical stimulation of the correct charge, density and total energy causes dramatically improved healing of dermal wounds. The investigations of biological actions (in vitro, animal, and human) demonstrate several effects that go a long way to explaining why electrical stimulation works. OBJECTIVE. To discuss recent research and advances in electrical stimulation of wound healing. RESULTS. Based on the latest scientific understanding of the wound healing process, one would expect a beneficial outcome from a therapy what decreases edema, debrides necrotic tissue, attracts neutrophils and macrophages, stimulates receptor sites for growth factors, stimulates growth of fibroblasts and granulation tissue, increases blood flow, stimulates neurite growth, induces epidermal cell migration, prevents post-ischemic oxygen radical-mediated damage, inhibits bacteria, and reduces numbers of mast cells. CONCLUSION. Taken together, the efficacy studies and the "mechanism of action" studies provide compelling, scientific evidence that electrical stimulation is safe and effective for promoting the healing of dermal wounds.

Alteration in alpha- and beta-adrenoceptor profile of rabbit knee joint blood vessels due to acute inflammation.

Najafipour H.
Exp Physiol. 2000 May;85(3):267-73.
Department of Physiology, Medical faculty, Kerman University of Medical Sciences and Health Services, Bulvd. 22 Bahman, Kerman, Iran.

Experiments were performed to investigate the nature of - and -adrenoceptors in blood vessels supplying the posterior capsule of the acutely inflamed rabbit knee joint, and results were compared to findings from previous experiments on the normal joint, to assess any alteration which may occur in the adrenoceptor profile due to the inflammation process. Electrical stimulation of the posterior articular nerve resulted in vasoconstriction which was reversed to vasodilatation by phentolamine and yohimbine. The dose-response curves to close intra-arterial injection of -adrenoceptor agonists showed a rank-order potency of: adrenaline = phenylephrine = clonidine. The adrenaline dose-response curve was shifted to the right by administration of antagonists with a rank-order potency of: phentolamine = yohimbine = prazosin. At this stage of the experiments there was an equal response of 1- and 2-adrenoceptors in blood vessels of the acutely inflamed rabbit knee joint. In another group of animals the neurally mediated vasodilatation, which appeared after administration of phentolamine, was completely blocked by propranolol, and was reduced by about 50 % by atenolol.

The dose-response curves to close intra-arterial injection of -adrenoceptor agonists showed a rank-order potency of: isoprenaline > salbutamol = dobutamine. The isoprenaline dose-response curve was shifted to the right by administration of antagonists with a rank-order potency of: propranolol > atenolol. These experiments also showed an almost equal response of 1- and 2-adrenoceptors in blood vessels of the acutely inflamed rabbit knee joint. Overall, compared to previous experiments on the normal joint in which 2- and 1-adrenoceptor responses predominated, acute inflammation resulted in a shift from 2- towards 1- and from 1- towards 2-adrenoceptor responses.

Sympathetically induced paradoxical increases of the cutaneous blood flow in chronically inflamed rats.

Tsujii Y, Koeda T, Sato J, Suzuki S, Kumazawa T.
J Auton Nerv Syst. 1996 Jul 5;59(3):103-12.
Department of Neural Regulation, Nagoya University, Japan.

In adjuvant arthritic (AA) rats, an abnormal responsiveness of nociceptors (C-fibre polymodal receptors) to sympathetic activities, i.e., alpha 2-adrenoceptor mediated activation of C-fibre polymodal receptors (CPRs), has been observed. The present investigations were undertaken to determine if a similar plastic change would occur in the cutaneous vascular system in the rat chronic inflammation model. The vascular responses were measured by a laser-Doppler flowmeter in the hindpaw skin of the AA rats after electrical stimulation of lumbar sympathetic trunk (sympathetic stimulation). In control non-arthritic rats, the sympathetic stimulation caused decrease in blood flow of the skin (SkBF) in all animals tested (n = 7). On the other hand, the sympathetic stimulation in the AA rats caused both increase (n = 15) as well as decrease (n = 11) in SkBF. In contrast to the abnormal responsiveness of CPRs, the intra-arterial injection of noradrenaline caused the expected decrease in SkBF in all animals tested, and in no instances increases in SkBF were observed. To determine whether activation of nitric oxide (NO), which is known to be a potent endogenous vasodilatation substance, was involved in the vasodilating effect to sympathetic stimulation, an inhibitor of NO synthase, NG-monomethyl-L-arginine (L-NMMA), was applied systemically. L-NMMA significantly increased baseline blood pressure in the control and the AA rats, but it did not significantly alter the SkBF in the control or the AA rats after the sympathetic stimulation, suggesting that NO is not a mediator in the vasoactive responses. The results of the current studies showed for the first time that electrical stimulation of the lumbar sympathetic trunk causes vasodilatation in the skin of the AA rats. This abnormal responsiveness of regional SkBF after sympathetic stimulation was not mediated by adrenergic or NO system.

Papers on Wound Healing

Increased Blood Flow to the effected Treatment Area and Wound Healing while using electrical stimulation.

Effects of aging on neurogenic vasodilator responses evoked by transcutaneous electrical nerve stimulation: relevance to wound healing.

Khalil Z, Merhi M
J Gerontol A Biol Sci Med Sci. 2000 Jun; 55(6):B257-63.
National Ageing Research Institute, University of Melbourne, Victoria, Australia.

We have previously shown an age-related decline in the modulation of skin vascular reactivity by sensory nerves that correlates with a decline in wound repair efficacy. This study was designed to examine the possibility that improving the functional ability of aged sensory nerves using noninvasive transcutaneous electrical nerve stimulation (TENS) could also accelerate tissue repair. TENS of the sciatic nerve, combined with measuring blood flow responses in the rat hind-footpad using laser Doppler flowmetry, was used to establish the vascular effects. Following TENS (using parameters 20V, 5 Hz for 1 min), similar increases in vascular responses were obtained in both young (13.2+/-0.9 cm2) and old rats (11.6+/-2.3 cm2). In contrast, capsaicin-pretreated rats showed markedly diminished responses. Sympathetic fibers did not appear to modulate these sensory nerve responses. In the second part, a thermal wound was induced (using a CO2 laser) in the interscapular region of old rats (under anesthesia). In the active treatment group, TENS was applied twice daily for the initial 5 days, and the sham group received inactive TENS. Using the healing endpoint as the time when full wound contraction occurred, the active group required 14.7+/-0.2 days for complete healing, a significant improvement over the sham group (21.8+/-0.3 days). We contend that low-frequency TENS can improve the vascular response of old rats. In addition, wound healing in aged rats can be accelerated by peripheral activation of sensory nerves at low-frequency electrical stimulation parameters.

Epidural spinal cord electrical stimulation in diabetic critical lower limb ischemia.

Petrakis IE, Sciacca V
Title Abbreviation: J Diabetes Complications.
1999 Sep-Dec; Volume Issue: 13(5-6):293-9.
First Department of General Surgery, Policlinico Umberto I, University of Rome, La Sapienza, Rome, Italy.

Spinal cord stimulation (SCS) has been suggested to improve microcirculatory blood flow to relieve ischemic pain and to reduce amputation rate in patients with peripheral arterial occlusive disease (PAOD). The aim of this study was to evaluate the specific prognostic parameters in the prediction of successful SCS, in diabetic patients, performing a retrospective data analysis. To perform this evaluation, 64 diabetic patients (39 men, 25 women; mean age, 69 years) classified as Fontaine's stage III and IV, with PAOD, were treated with SCS for rest pain and trophic lesions with dry gangrene, after failed conservative or surgical treatment. In clinical controls, pedal transcutaneous oxygen tension (TcPO(2)), ankle/brachial blood pressure index (ABI), and toe pressure Doppler measurements were utilized to select and follow-up the patients. After 58 months of follow-up (range, 20-128 months), pain relief

greater than 75% and limb salvage were achieved in 38 diabetic patients. A partial success was obtained in nine patients with pain relief greater than 50% and limb salvage for at least 6 months. The method failed in 17 patients or the device was removed due to technical problems, and the limb was amputated in these patients. TcPO(2) was assessed on the dorsum of the foot. Clinical improvement and SCS success were associated with increase of TcPO(2), before and after implantation. Limb salvage was achieved in the patients who had significant TcPO(2) increase within the 2 weeks of the testing period, independently of the stage of the disease. A TcPO(2) increase of more than 50% in the first 2 months after implantation was predictive of success, and was related to the presence of adequate paresthesias in the painful area during the trial period. TcPO(2) significantly increased after long-term follow-up in all patients with limb salvage (from 22.1 to 43.1 mm Hg in the rest pain patients, from 15.8 to 36.4 mm Hg in those with trophic lesions of less than 3 cm(2), and from 12.1 to 28.1 in those with trophic lesions of greater than 3 cm(2), ($p < 0.01$). ABI did not changed under stimulation. In diabetic patients with PAOD, the SCS increases the skin blood flow, is associated with significant pain relief, and could be proven an excellent alternative therapy, improving the life quality. Significant TcPO(2) increase within the 2-week test period, is a predictive index of therapy success and should be considered before the final decision in terms of cost effectiveness, before the permanent implantation.

Effects of transcutaneous nerve stimulation on the microcirculation in chronic leg ulcers.

Cosmo P, Svensson H, Bornmyr S, Wikstrom SO
Scand J Plast Reconstr Surg Hand Surg. 2000 Mar; 34(1):61-4.
Department of Plastic and Reconstructive Surgery, Malmo University Hospital, Sweden.

The purpose of this study was to find out to what extent transcutaneous electrical nerve stimulation (TENS) affects the blood flow in and around chronic lower leg ulcers, as measured with a new technique, laser Doppler imaging (LDI). Fifteen patients, mean age 73 years (range 38-85) with chronic leg ulcers of various causes participated in the study. The duration of the ulcers ranged from 3 months to 16 years. Low-frequency (2 Hz; 10-45 mA) TENS was given for 60 minutes. The changes in blood flow were measured every 5 minutes by LDI. After 60 minutes, mean blood flow had increased in the ulcer by 35%, and in the intact skin surrounding the ulcer by 15%. Even 15 minutes after the TENS had finished there was still a mean blood flow increase of 29% in the ulcer and 9% in the skin. The present results show that TENS has a stimulating effect on local blood circulation in and around chronic ulcers.

Effect of transcutaneous nerve stimulation on microcirculation in intact skin and blister wounds in healthy volunteers.

Wikstrom SO, Svedman P, Svensson H, Tanweer AS
Scand J Plast Reconstr Surg Hand Surg. 1999 Jun; 33(2):195-201.
Department of Plastic and Reconstructive Surgery, University Hospital MAS, Malmo, Sweden.

Healthy non-smoking volunteers participated in two experimental studies in which the circulatory changes induced by transcutaneous nerve stimulation (TENS) were quantified by two different methods. In experimental series 1 (intact skin), nine volunteers were given TENS on the left lower leg for 60 minutes on three occasions at different frequencies each time (2 Hz, 100 Hz, and sham). Changes in blood flow were assessed by laser Doppler imaging

technique every five minutes. The mean blood flow increased by 40% during low frequency TENS and by 12% during high frequency TENS. There was no change in mean blood flow during sham stimulation. In experimental series 2 (blister wound), the circulatory changes induced by TENS were studied by intravital video microscopy and computerised image analysis in standard blister wounds on the lower leg. The microcirculatory blood flow, measured as red blood cell velocity (RBC-V) in 5-14 individual capillaries in each wound, was assessed before and during 45 minutes of TENS (2 Hz and 100 Hz). Mean RBC-V increased by 23% during low frequency TENS (n = 6) and by 17% during high frequency TENS (n = 8). The results show that: laser Doppler imaging and intravital video microscopy techniques can be used to study events at the microcirculatory level; the blister wound is an interesting new standard wound for use in clinical studies; and TENS stimulates the peripheral circulation.

Prognostic factors in the prediction of chronic wound healing by electrical stimulation.

Cukjati D, Robnik-Sikonja M, Rebersek S, Kononenko I, Miklavcic D.
Med Biol Eng Comput. 2001 Sep;39(5):542-50.
Faculty of Electrical Engineering, University of Ljubljana, Slovenia.

The aim of the study is to determine the effects of wound, patient and treatment attributes on the wound healing rate and to propose a system for wound healing rate prediction. Predicting the wound healing rate from the initial wound, patient and treatment data collected in a database of 300 chronic wounds is not possible. After considering weekly follow-ups, it was determined that the best prognostic factors are weekly follow-ups of the wound healing process, which alone were found to predict accurately the wound healing rate after a minimum follow-up period of four weeks (at least five measurements of wound area). After combining the follow-ups with wound, patient and treatment attributes, the minimum follow-up period was reduced to two weeks (at least three measurements of wound area). After a follow-up period of two weeks, it was possible to predict the wound healing rate of an independent test set of chronic wounds with a relative squared error of 0.347, and after three weeks, with a relative squared error of 0.181 (using regression trees with linear equations in its leaves). Regression trees with a relative squared error close to 0 produce better prediction than with an error closer to 1. Results show that the type of treatment is just one of many prognostic factors. Arranged in order of decreasing prediction capability, prognostic factors are: wound size, patient's age, elapsed time from wound appearance to the beginning of the treatment, width-to-length ratio, location and type of treatment. The data collected support former findings that the biphasic- and direct-current stimulation contributes to faster healing of chronic wounds. The model of wound healing dynamics aids the prediction of chronic wound healing rate, and hence helps with the formulation of appropriate treatment decisions.

Choosing an adjunctive therapy for the treatment of chronic wounds.
Houghton PE, Campbell KE.

Ostomy Wound Manage. 1999 Aug;45(8):43-52; quiz 53-4.
St. Joseph's Health Center, School of Physiotherapy, University of Western Ontario, London, Canada.

Adjunctive therapies such as ultrasound, laser, ultraviolet light, superficial heating, pulsed electromagnetic fields, and electrical stimulation have all been indicated in the treatment of chronic wounds. The purpose of this article is to outline the issues a healthcare professional must consider when

choosing the best adjunctive therapy for a chronic wound. It summarizes the effects of therapeutic modalities on the wound healing process, analyzes the clinical research evidence, discusses practical considerations, and reviews indications, contraindications, precautions, and safety considerations. Finally, an algorithm is presented to help guide the clinician in selecting a modality. In summary, research evidence exists in the literature that suggests these adjunctive therapies can directly stimulate new tissue growth, augment wound tissue strength, improve local circulation and oxygenation, reduce edema, and/or inhibit bacterial growth. Electrical stimulation and ultrasound are the only therapeutic modalities that currently have sufficient clinical research evidence to support their use in the treatment of chronic wounds. Practical issues such as cost, time and training required, and patient and therapist safety concerns, will ultimately influence the selection of these modalities.

Effect of electrical stimulation on chronic wound healing: a meta-analysis.
Gardner SE, Frantz RA, Schmidt FL.

Wound Repair Regen. 1999 Nov-Dec;7(6):495-503.
Colleges of Nursing, The University of Iowa, Iowa City, IA 52242-7066, USA.

The purpose of this meta-analysis was to quantify the effect of electrical stimulation on chronic wound healing. Fifteen studies, which included 24 electrical stimulation samples and 15 control samples, were analyzed. The average rate of healing per week was calculated for the electrical stimulation and control samples. Ninety-five percentage confidence intervals were also calculated. The samples were then grouped by type of electrical stimulation device and chronic wound and reanalyzed. Rate of healing per week was 22% for electrical stimulation samples and 9% for control samples. The net effect of electrical stimulation was 13% per week, an increase of 144% over the control rate. The 95% confidence intervals of the electrical stimulation (18-26%) and control samples (3.8-14%) did not overlap. Electrical stimulation was most effective on pressure ulcers (net effect = 13%). Findings regarding the relative effectiveness of different types of electrical stimulation device were inconclusive. Although electrical stimulation produces a substantial improvement in the healing of chronic wounds, further research is needed to identify which electrical stimulation devices are most effective and which wounds respond best to this treatment.

A comparative study of the effect of ultrasound and electrostimulation on wound healing in rats.

Taskan I, Ozyazgan I, Tercan M, Kardas HY, Balkanli S, Saraymen R, Zorlu U
Plast Reconstr Surg. 1997 Sep;100(4):966-72.
Physical Therapy and Rehabilitation Center, Medical Faculty of Inonu University, Istanbul, Turkey.

A comparative study has been carried out to investigate the effects of electrical stimulation and ultrasound on wound healing. Eighty-four female rats were divided into four groups depending on the treatment received. The first group was given electrical stimulation of 300 microA direct current, 30 minutes daily, starting with negative polarity and then changed after 3 days of treatment. Group 2 received sham electrostimulation treatment. The third group received 0.1 W/cm2 pulsed ultrasound using the moving applicator technique for 5 minutes a day. Group 4 received sham ultrasound treatment. A total of 7 days of treatment was given to all groups. Histopathologic and biochemical analyses on the fourth and seventh days and wound breaking

strength on the twenty-fifth day were performed for all groups. By accelerating the inflammatory phase, electrical stimulation had progressed the proliferative phase of wound healing earlier than ultrasound had done. Both electrical stimulation and ultrasound have positive effects on proliferative phases, but electrical stimulation was superior to ultrasound at the maturation phase. There was no difference between the two experimental groups on the mast cell reduction effect. Although ultrasound treatment may seem to be efficient in terms of time, when the effects of electrical stimulation and ultrasound on wound healing with the methods employed in our study are considered, it is concluded that electrical stimulation is a means of treatment superior to ultrasound in wound healing.

Effects of electrical stimulation on wound healing in patients with diabetic ulcers.

Baker LL, Chambers R, DeMuth SK, Villar F.
Diabetes Care. 1997 Mar;20(3):405-12.
Department of Biokinesiology and Physical Therapy, University of Southern California, Los Angeles 90033,

OBJECTIVE: To evaluate the effects of two stimulation waveforms on healing rates in patients with diabetes and open ulcers. The hypothesis was that stimulus waveforms with minimal polar characteristics would provide significant healing for this patient sample. RESEARCH DESIGN AND METHODS: This was a prospective study that enrolled 80 patients with open ulcers. Patients received stimulation with either an asymmetric biphasic (A) or symmetric biphasic (B) square-wave pulse. Amplitudes were set to activate intact peripheral nerves in the skin. Two other groups received either very low levels of stimulation current (MC), or no electrical stimulation (C). When combined these groups were referred to as the control group. Treatment was carried out daily until the wound healed, the patient withdrew from the study, or the physician changed the overall wound management program. Average healing rates were calculated from weekly measures of the wound perimeter and were used for statistical comparison through a one-way analysis of variance. RESULTS: Stimulation with the A protocol significantly increased the healing rate, enhancing healing by nearly 60% over the control rate of healing. Stimulation with the B protocol did not increase the healing rate when compared with control subjects. CONCLUSIONS: Electrical stimulation, given daily with a short pulsed, asymmetric biphasic waveform, was effective for enhancement of healing rates for patients with diabetes and open ulcers.

Promotion of wound healing with electrical stimulation.

Kloth LC, McCulloch JM.
Adv Wound Care. 1996 Sep-Oct;9(5):42-5.
Program of Physical Therapy, Marquette University, Milwaukee, Wis, USA.

Clinicians involved in the conservative care of chronic wounds have many treatment interventions from which to choose, including debridement/irrigation, dressings, pressure-relieving devices, hyperbaric or topically applied oxygen, whirlpool/pulsed lavage, ultrasound, topical antibiotics, and cytokine growth factors. All except the last two interventions are physical treatments that create a wound-tissue environment conducive to healing. Unfortunately, many chronic wounds heal very slowly, do not heal, or worsen despite the best efforts of caregivers to promote tissue repair. An intervention commonly used to treat chronic wounds, especially by physical therapists, is electrical stimulation (ES). The rationale for use of

this method is based on the fact that the human body has an endogenous bioelectric system that enhances healing of bone fractures and soft-tissue wounds. When the body's endogenous bioelectric system fails and cannot contribute to wound repair processes, therapeutic levels of electrical current may be delivered into the wound tissue from an external source. The external current may serve to mimic the failed natural bioelectric currents so that wound healing can proceed. Certain chemotaxic factors found in wound substrates contribute to tissue repair processes by attracting cells into the wound environment. Neutrophil, macrophage, fibroblast, and epidermal cells involved in wound repair carry either a positive or negative charge. When these cells are needed to contribute to autolysis, granulation tissue formation, anti-inflammatory activities, or epidermal resurfacing, ES may facilitate galvanotaxic attraction of these cells into the wound tissue and thereby accelerate healing.

Physical modalities in wound management: UVC, therapeutic heating and electrical stimulation.

Kloth LC.
Ostomy Wound Manage. 1995 Jun;41(5):18-20, 22-4, 26-7.

In spite of efforts to create an optimum wound environment for healing, there are times that a wound may not heal, may heal very slowly, or may worsen. In these cases, a series of treatments with an appropriate physical agent can be added to the patient's care plan to augment tissue reparative processes. Three modalities that have received support in the literature for use in wound healing are ultraviolet "C" radiation (UVC), therapeutic heating, and electrical stimulation. Treatment goals for UVC are hyperplasia and enhanced re-epithelialization or desquamation of the leading edge of periulcer epidermal cells, granulation tissue formation, sloughing of necrotic tissue, and bactericidal effects. Treatment goals for therapeutic heating are increased blood perfusion with subsequent increased delivery of oxygen to the tissues (avoiding the dessication of wound tissues). The treatment goal for electrical stimulation is to attract negatively or positively charged cells into the wound area, such as neutrophils, macrophages, epidermal cells and fibroblasts that in turn will contribute to wound healing processes by way of their individual cellular activities.

Experimental wound healing with electrical stimulation.

Reger SI, Hyodo A, Negami S, Kambic HE, Sahgal V
Title Abbreviation: Artif Organs.
1999 May; 23(5):460-2.
Department of Physical Medicine and Rehabilitation, The Cleveland Clinic Foundation, Ohio 44195, USA.

The effect of alternating current (AC) and direct current (DC) stimulation was studied on experimental pressure ulcer healing in a new monoplegic pig model. The study was conducted in 30 healthy young Hanford minipigs. The rate of wound healing, histology, vascularization, collagen formation, microbiology, perfusion, and the mechanical strength of the healed wounds were studied. Normal pigskin was compared to denervated control and denervated AC and DC stimulated healed skin. Hind limb denervation was by right unilateral extradural rhizotomies from the L2 to S1 nerve roots. Reproducible uniformly controlled Stage III or higher tissue ulcers were created. When compared to the control wounds, both the AC and DC stimulated wounds showed reduced healing time and increased perfusion in the early phases of healing. DC

stimulation reduced the wound area more rapidly than AC, but AC stimulation reduced the wound volume more rapidly than DC. The electrical stimulation did not reduce the strength of the healing wounds below those of the nonstimulated controls. The applied current appears to orient new collagen formation even in the absence of neural influences.

Electric muscle stimulation for pressure sore prevention: tissue shape variation.

Levine SP Kett RL Cederna PS Brooks SV
Arch Phys Med Rehabil (1990 Mar) 71(3):210-5

This study measured changes in tissue shape and deformation at the seating interface produced by electric muscle stimulation (EMS) of the gluteus maximus. The purpose of the study was to investigate the application of EMS for pressure sore prevention. Limitations of pressure measurements for analysis of load distribution are discussed and a rationale developed for using tissue shape and deformation to further characterize the seating interface. Ultrasonic imaging of the seating interface is described under three conditions: buttocks suspended, external load applied with no EMS, and external load applied with bilateral EMS of the buttocks. Results show that low level stimulation of the gluteus maximus produces substantial changes in the shape of the loaded buttocks and an external contour more nearly shaped like the suspended buttocks. It is concluded that EMS produces buttock tissue undulation and shape reconfiguration which may assist in preventing pressure sores over the seating surface.

Adjuvant therapy for ulcer care.

Frantz RA
Clin Geriatr Med (1997 Aug) 13(3):553-64

Adjuvant therapies, specifically electrotherapy, hyperbaric oxygen, ultrasound, and hydrotherapy, are considered increasingly for use with conventional local wound care to support healing of pressure ulcers. This article describes the characteristics of these modalities, their physiologic effects on the healing process, and the research to evaluate their efficacy.

Effects of electrical stimulation on wound healing in patients with diabetic ulcers.
Baker LL Chambers R DeMuth SK Villar F
Diabetes Care (1997 Mar) 20(3):405-12

OBJECTIVE: To evaluate the effects of two stimulation waveforms on healing rates in patients with diabetes and open ulcers. The hypothesis was that stimulus waveforms with minimal polar characteristics would provide significant healing for this patient sample. RESEARCH DESIGN AND METHODS: This was a prospective study that enrolled 80 patients with open ulcers. Patients received stimulation with either an asymmetric biphasic (A) or symmetric biphasic (B) square-wave pulse. Amplitudes were set to activate intact peripheral nerves in the skin. Two other groups received either very low levels of stimulation current (MC), or no electrical stimulation (C). When

combined these groups were referred to as the control group. Treatment was carried out daily until the wound healed, the patient withdrew from the study, or the physician changed the overall wound management program. Average healing rates were calculated from weekly measures of the wound perimeter and were used for statistical comparison through a one-way analysis of variance. RESULTS: Stimulation with the A protocol significantly increased the healing rate, enhancing healing by nearly 60% over the control rate of healing. Stimulation with the B protocol did not increase the healing rate when compared with control subjects. CONCLUSIONS: Electrical stimulation, given daily with a short pulsed, asymmetric biphasic waveform, was effective for enhancement of healing rates for patients with diabetes and open ulcers.

The benefit of electrical stimulation to enhance perfusion in persons with diabetes mellitus.

Peters EJ Armstrong DG Wunderlich RP Bosma J Stacpoole-Shea S Lavery LA
J Foot Ankle Surg (1998 Sep-Oct) 37(5):396-400; discussion 447-8

The purpose of this study was to evaluate the effect of galvanic electrical stimulation on vascular perfusion in diabetic patients. Nineteen subjects with diabetes were enrolled. Eleven subjects (57.9%) were diagnosed with impaired peripheral perfusion based upon their initial transcutaneous oximetry values (< 40 mm Hg). The subjects were studied over a 2-day period. On the 1st day, one foot was electrically stimulated for four 60-minute periods by an external electrical stimulation device. Vascular perfusion of both feet was assessed before and after the sessions of electrical stimulation. On the 2nd day, no electrical stimulation was applied and noninvasive vascular measurements were repeated. For the 1st hour, transcutaneous oxygen pressure was measured continuously during stimulation at the lateral aspect of the leg. Subsequently, perfusion between the periods of stimulation was measured on the dorsum of the foot with both transcutaneous oximetry and laser Doppler flowmetry after each stimulation period. In the group with impaired peripheral perfusion, a significant rise in tissue oxygenation as compared to the control measurements was measured during the first 5 minutes of stimulation ($p < .040$). For those without vascular disease (TcpO2 > 40 mm Hg) however, there was not a significant increase compared to baseline ($p = .280$). After the periods of stimulation, the stimulated feet did not show any higher perfusion levels than the control feet. Patterns in perfusion during the day, as measured by laser Doppler flowmetry, were similar in the tested feet and in the controls. These data suggest that external subsensory electrical stimulation induces a transient rise in skin perfusion in persons with diabetes and impaired peripheral perfusion.

Treatment of chronic wounds by means of electric and electromagnetic fields. Part 2. Value of FES parameters for pressure sore treatment.

Stefanovska A Vodovnik L Benko H Turk R
Med Biol Eng Comput (1993 May) 31(3):213-20

Subjects with spinal cord injury are often distressed by pressure sores, which usually appear after prolonged pressure (wheelchair, bed) across the soft tissue which has already lost sensibility and has diminished microcirculation. The healing ability and its dynamics depend on the state of the subject's overall health. Consequently, evaluation of a particular treatment requires careful consideration of as many as possible of the parameters relevant to healing and an adequate criterion for assessing the state of the pressure sore. Bearing in mind these two circumstances, the results of a multicentre clinical study are analysed. The aim of the study

was to test two hypotheses: first that healing is faster when sores are also treated by electric currents (ECs) (in addition to conventional treatment); and secondly that there exist differences in the efficiency of the treatment if direct or low-frequency pulsed currents (FES parameters) are applied. The data analysed show that pressure sores are likely to heal twice as fast when treated with low-frequency pulsed currents. EC seems to improve the healing rate in cases where the natural healing mechanisms of the body are not sufficient (chronic wounds, older subjects).

Reduction of seating pressure using FES in patients with spinal cord injury. A preliminary report.

Ferguson AC Keating JF Delargy MA Andrews BJ
Paraplegia (1992 Jul) 30(7):474-8

The aim of this study was to investigate the use of functional electrical stimulation (FES) as a means of pressure sore prevention in seated spinal cord injured (SCI) subjects. Nine SCI subjects took part in tests in which electrical stimulation was applied to the quadriceps with the lower legs restrained. Ischial pressures were measured during periods of quiet sitting and FES application. A strain gauged lever arm was used to measure the knee moment during quadriceps stimulation. The average pressure drop at the right and left buttocks was 44 mmHg and 27 mmHg respectively. In general the greatest reductions occurred in subjects with larger knee moments; however, there was no direct relationship between the pressure reduction obtained and the quadriceps strength. This form of FES may be useful as a prophylactic aid in the management of pressure sores in SCI subjects.

Chronic dermal ulcer healing enhanced with monophasic pulsed electrical stimulation [see comments]

Feedar JA Kloth LC Gentzkow GD
Phys Ther (1991 Sep) 71(9):639-49

The purposes of this randomized, double-blind, multicenter study were to compare healing of chronic dermal ulcers treated with pulsed electrical stimulation with healing of similar wounds treated with sham electrical stimulation and to evaluate patient tolerance to the therapeutic protocol. Forty-seven patients, aged 29 to 91 years, with 50 stage II, III, and IV ulcers were randomly assigned to either a treatment group (n = 26) or a control (sham treatment) group (n = 24). Treated wounds received 30 minutes of pulsed cathodal electrical stimulation twice daily at a pulse frequency of 128 pulses per second (pps) and a peak amplitude of 29.2 mA if the wound contained necrotic tissue or any drainage that was not serosanguinous. A saline-moistened nontreatment electrode was applied 30.5 cm (12 in) cephalad from the wound. This protocol was continued for 3 days after the wound was debrided or exhibited serosanguinous drainage. Thereafter, the polarity of the treatment electrode on the wound was changed every 3 days until the wound progressed to a stage II classification. The pulse frequency was then reduced to 64 pps, and the treatment electrode polarity was changed daily until the wound was healed. Patients in the control group were treated with the same protocol, except they received sham electrical stimulation. After 4 weeks, wounds in the treatment and control groups were 44% and 67% of their initial size, respectively. The healing rates per week for the treatment and control groups were 14% and 8.25%, respectively. The results of this study indicate that

pulsed electrical stimulation has a beneficial effect on healing stage II, III, and IV chronic dermal ulcers.

Effect of electrical stimulation on foot skin perfusion in persons with or at risk for diabetic foot ulcers.

Gilcreast DM Stotts NA Froelicher ES Baker LL Moss KM
Wound Repair Regen (1998 Sep-Oct) 6(5):434-41

The failure of foot wounds to heal results in 54,000 people with diabetes having to undergo extremity amputations annually. Therefore, treatment is needed to speed healing in people with diabetes in order to reduce the need for amputation. This study tested the effect of high-voltage pulsed current on foot blood flow in human beings who are at risk for diabetic foot ulcers. Neuropathy, vascular disease, Wagner Class, glucose, gender, ethnicity, and age were measured. A sample of 132 subjects was tested using a repeated-measures design. A baseline transcutaneous oxygen level was obtained; stimulation was applied, and transcutaneous oxygen measurements were recorded at 30- and 60- minute time intervals. The grouped foot transcutaneous oxygen levels decreased ($F = 5.66$, $p =. 0039$) following electrical stimulation. Analysis of variance (Scheffe, $p <.05$) showed that initial transcutaneous oxygen was significantly higher than subsequent readings. However, oxygen response was distributed bimodally: 35 (27%) subjects showed increased transcutaneous oxygen (mean 14.8 mm Hg), and 97 (73%) experienced a decreased transcutaneous oxygen reading (mean 12.2 mm Hg). Logistic regression analysis did not explain these differences. Although this treatment appears to increase blood flow in a subset of patients, further study is needed to identify probable mechanisms for this response.

Biofeedback and functional electric stimulation in stroke Rehabilitation.

Cozean CD Pease WS Hubbell SL
Arch Phys Med Rehabil (1988 Jun) 69(6):401-5

The study examined the efficacy of functional electric stimulation (FES) and biofeedback (BFB) treatment of gait dysfunction in patients with hemiplegia after stroke. These two therapeutic modalities were tested alone and in combination in a prospective, controlled, randomized trial. The authors hypothesized that in concurrent use, these two modalities would complement one another. Thirty-six hemiplegic patients undergoing rehabilitation after stroke were accepted for study and randomized into four groups to receive either control, FES, BFB, or combined therapies. Each patient received 30 minutes of treatment three times per week for six weeks, in addition to their general rehabilitation program. Quantitative gait analysis was performed biweekly on each subject during the experimental therapy and for four weeks afterward. Thirty-two subjects completed the study. Combined therapy with BFB and FES resulted in improvements in both knee and ankle minimum flexion angles during swing phase that were statistically significant with $p = 0.05$ and $p = 0.02$, respectively. Velocity of gait, cycle time, and symmetry of stance phases also improved. The length of time elapsed since the stroke did not prove to be a significant factor.

Reduction of seating pressure using FES in patients with spinal cord injury. A preliminary report.

Ferguson AC Keating JF Delargy MA Andrews BJ
Paraplegia (1992 Jul) 30(7):474-8

The aim of this study was to investigate the use of functional electrical stimulation (FES) as a means of pressure sore prevention in seated spinal cord injured (SCI) subjects. Nine SCI subjects took part in tests in which electrical stimulation was applied to the quadriceps with the lower legs restrained. Ischial pressures were measured during periods of quiet sitting and FES application. A strain gauged lever arm was used to measure the knee moment during quadriceps stimulation. The average pressure drop at the right and left buttocks was 44 mmHg and 27 mmHg respectively. In general the greatest reductions occurred in subjects with larger knee moments; however, there was no direct relationship between the pressure reduction obtained and the quadriceps strength. This form of FES may be useful as a prophylactic aid in the management of pressure sores in SCI subjects.

Relative changes in blood flow with functional electrical stimulation during exercise of the paralyzed lower limbs.

Phillips W Burkett LN Munro R Davis M Pomeroy K
Paraplegia (1995 Feb) 33(2):90-3

Eight spinal cord injured (SCI) patients performed three sets of exercise with two conditions, 60% and 80% of VO2peak, with an arm crank ergometer. Functional neuromuscular stimulation was used to induce static leg contractions in two of the above sets of exercise. The three exercise sets were performed with no functional neuromuscular stimulation (NOS); with functional neuromuscular stimulation at 40 milliamperes; and with functional neuromuscular stimulation at 80 milliamperes (HIS). The lower limb blood flow was estimated by a photoelectric plethysmograph. Results showed that the lower limb blood flow was consistently reduced across both functional neuromuscular stimulation levels (17.4% from NOS to LOS; 13.8% from LOS to HIS; and 28.8% from NOS to HIS), and work loads (15.3% from rest to 60% VO2peak; 38.0% from 60% VO2peak to 80% VO2peak; and 47.5% from rest to 80% VO2peak). Rate-pressure product was decreased by 8.3% between NOS and HIS at 60% VO2peak (15.7 +/- 3.4 to 14.4 +/- 3.8), by 6.8% between NOS and HIS at 80% VO2peak (18.9 +/- 53 to 17.6 +/- 4.8), and by 12.4% between LOS and HIS at 80% VO2peak (20.1 +/- 6.7 to 17.6 +/- 4.8). These data indicate that in SCI (a) functional neuromuscular stimulation-induced contractions of the lower limb muscles can increase blood flow and thus reduce venous blood pooling in the paralyzed muscles, and (b) such improvements are associated with a reduced rate pressure product.(ABSTRACT TRUNCATED AT 250 WORDS)

Promotion of wound healing with electrical stimulation.

Kloth LC McCulloch JM
Adv Wound Care (1996 Sep-Oct) 9(5):42-5

Clinicians involved in the conservative care of chronic wounds have many treatment interventions from which to choose, including debridement/irrigation, dressings, pressure-relieving devices, hyperbaric or topically applied oxygen, whirlpool/pulsed lavage, ultrasound, topical antibiotics, and cytokine growth factors. All except the last two interventions are physical treatments that create a wound-tissue environment conducive to healing. Unfortunately, many chronic wounds heal very slowly, do

not heal, or worsen despite the best efforts of caregivers to promote tissue repair. An intervention commonly used to treat chronic wounds, especially by physical therapists, is electrical stimulation (ES). The rationale for use of this method is based on the fact that the human body has an endogenous bioelectric system that enhances healing of bone fractures and soft-tissue wounds. When the body's endogenous bioelectric system fails and cannot contribute to wound repair processes, therapeutic levels of electrical current may be delivered into the wound tissue from an external source. The external current may serve to mimic the failed natural bioelectric currents so that wound healing can proceed. Certain chemotaxic factors found in wound substrates contribute to tissue repair processes by attracting cells into the wound environment. Neutrophil, macrophage, fibroblast, and epidermal cells involved in wound repair carry either a positive or negative charge. When these cells are needed to contribute to autolysis, granulation tissue formation, anti-inflammatory activities, or epidermal resurfacing, ES may facilitate galvanotaxic attraction of these cells into the wound tissue and thereby accelerate healing.

Electrical nerve stimulation improves healing of diabetic ulcers.

Lundeberg TC Eriksson SV Malm M
Ann Plast Surg (1992 Oct) 29(4):328-31

A controlled study of the effects of electrical nerve stimulation (ENS) was performed in conjunction with a standard treatment for healing chronic diabetic ulcers on 64 patients divided randomly into two groups. All patients received standard treatment (paste-impregnated bandage and a self-adhesive elastic bandage) plus placebo ENS or ENS (alternating constant current; frequency, 80 Hz; pulse width, 1 msec; intensity-evoking strong paresthesias) for 20 minutes twice daily for 12 weeks. Comparison of percentages of healed ulcer area and the number of healed ulcers was made after 2, 4, 6, 8, and 12 weeks. There were significant differences ($p < 0.05$) in both ulcer area and healed ulcers in the ENS group compared with the placebo group after 12 weeks of treatment. The results of the present study support the use of ENS in diabetic ulcers. ENS is easy to apply and can be used by the patient at home following instructions from a medical doctor or a therapist experienced in electrical stimulation and the treatment of ulcers. Additional studies are needed to identify the mechanisms involved in the promotion of ulcer healing with electrical stimulation and to determine the stimulus variables that most efficaciously accelerate tissue repair.

Effects of electrical stimulation on wound healing in patients with diabetic ulcers.

Baker LL Chambers R DeMuth SK Villar F
Diabetes Care (1997 Mar) 20(3):405-12

OBJECTIVE: To evaluate the effects of two stimulation waveforms on healing rates in patients with diabetes and open ulcers. The hypothesis was that stimulus waveforms with minimal polar characteristics would provide significant healing for this patient sample. RESEARCH DESIGN AND METHODS: This was a prospective study that enrolled 80 patients with open ulcers. Patients received stimulation with either an asymmetric biphasic (A) or symmetric biphasic (B) square-wave pulse. Amplitudes were set to activate intact peripheral nerves in the skin. Two other groups received either very low levels of stimulation current (MC), or no electrical stimulation (C). When

combined these groups were referred to as the control group. Treatment was carried out daily until the wound healed, the patient withdrew from the study, or the physician changed the overall wound management program. Average healing rates were calculated from weekly measures of the wound perimeter and were used for statistical comparison through a one-way analysis of variance. RESULTS: Stimulation with the A protocol significantly increased the healing rate, enhancing healing by nearly 60% over the control rate of healing. Stimulation with the B protocol did not increase the healing rate when compared with control subjects. CONCLUSIONS: Electrical stimulation, given daily with a short pulsed, asymmetric biphasic waveform, was effective for enhancement of healing rates for patients with diabetes and open ulcers.

Electrical stimulation to heal dermal wounds.

Gentzkow GD
J Dermatol Surg Oncol (1993 Aug) 19(8):753-8

BACKGROUND. Numerous human and animal efficacy studies have demonstrated that electrical stimulation of the correct charge, density and total energy causes dramatically improved healing of dermal wounds. The investigations of biological actions (in vitro, animal, and human) demonstrate several effects that go a long way to explaining why electrical stimulation works. OBJECTIVE. To discuss recent research and advances in electrical stimulation of wound healing. RESULTS. Based on the latest scientific understanding of the wound healing process, one would expect a beneficial outcome from a therapy what decreases edema, debrides necrotic tissue, attracts neutrophils and macrophages, stimulates receptor sites for growth factors, stimulates growth of fibroblasts and granulation tissue, increases blood flow, stimulates neurite growth, induces epidermal cell migration, prevents post-ischemic oxygen radical-mediated damage, inhibits bacteria, and reduces numbers of mast cells. CONCLUSION. Taken together, the efficacy studies and the "mechanism of action" studies provide compelling, scientific evidence that electrical stimulation is safe and effective for promoting the healing of dermal wounds.

Alteration in alpha- and beta-adrenoceptor profile of rabbit knee joint blood vessels due to acute inflammation.

Najafipour H.
Exp Physiol. 2000 May;85(3):267-73.
Department of Physiology, Medical faculty, Kerman University of Medical Sciences and Health Services, Bulvd. 22 Bahman, Kerman, Iran.

Experiments were performed to investigate the nature of - and -adrenoceptors in blood vessels supplying the posterior capsule of the acutely inflamed rabbit knee joint, and results were compared to findings from previous experiments on the normal joint, to assess any alteration which may occur in the adrenoceptor profile due to the inflammation process. Electrical stimulation of the posterior articular nerve resulted in vasoconstriction which was reversed to vasodilatation by phentolamine and yohimbine. The dose-response curves to close intra-arterial injection of -adrenoceptor agonists showed a rank-order potency of: adrenaline = phenylephrine = clonidine. The adrenaline dose-response curve was shifted to the right by administration of antagonists with a rank-order potency of: phentolamine = yohimbine = prazosin. At this stage of the experiments there was an equal response of 1- and 2-adrenoceptors in blood vessels of the acutely inflamed rabbit knee joint. In another group of animals the neurally mediated vasodilatation, which appeared after administration of phentolamine, was completely blocked by propranolol, and was reduced by about 50 % by atenolol.

The dose-response curves to close intra-arterial injection of -adrenoceptor agonists showed a rank-order potency of: isoprenaline > salbutamol = dobutamine. The isoprenaline dose-response curve was shifted to the right by administration of antagonists with a rank-order potency of: propranolol > atenolol. These experiments also showed an almost equal response of 1- and 2-adrenoceptors in blood vessels of the acutely inflamed rabbit knee joint. Overall, compared to previous experiments on the normal joint in which 2- and 1-adrenoceptor responses predominated, acute inflammation resulted in a shift from 2- towards 1- and from 1- towards 2-adrenoceptor responses.

Sympathetically induced paradoxical increases of the cutaneous blood flow in chronically inflamed rats.

Tsujii Y, Koeda T, Sato J, Suzuki S, Kumazawa T.
J Auton Nerv Syst. 1996 Jul 5;59(3):103-12.
Department of Neural Regulation, Nagoya University, Japan.

In adjuvant arthritic (AA) rats, an abnormal responsiveness of nociceptors (C-fibre polymodal receptors) to sympathetic activities, i.e., alpha 2-adrenoceptor mediated activation of C-fibre polymodal receptors (CPRs), has been observed. The present investigations were undertaken to determine if a similar plastic change would occur in the cutaneous vascular system in the rat chronic inflammation model. The vascular responses were measured by a laser-Doppler flowmeter in the hindpaw skin of the AA rats after electrical stimulation of lumbar sympathetic trunk (sympathetic stimulation). In control non-arthritic rats, the sympathetic stimulation caused decrease in blood flow of the skin (SkBF) in all animals tested (n = 7). On the other hand, the sympathetic stimulation in the AA rats caused both increase (n = 15) as well as decrease (n = 11) in SkBF. In contrast to the abnormal responsiveness of CPRs, the intra-arterial injection of noradrenaline caused the expected decrease in SkBF in all animals tested, and in no instances increases in SkBF were observed. To determine whether activation of nitric oxide (NO), which is known to be a potent endogenous vasodilatation substance, was involved in the vasodilating effect to sympathetic stimulation, an inhibitor of NO synthase, NG-monomethyl-L-arginine (L-NMMA), was applied systemically. L-NMMA significantly increased baseline blood pressure in the control and the AA rats, but it did not significantly alter the SkBF in the control or the AA rats after the sympathetic stimulation, suggesting that NO is not a mediator in the vasoactive responses. The results of the current studies showed for the first time that electrical stimulation of the lumbar sympathetic trunk causes vasodilatation in the skin of the AA rats. This abnormal responsiveness of regional SkBF after sympathetic stimulation was not mediated by adrenergic or NO system.

Papers on Wound Healing

Increased Blood Flow to the effected Treatment Area and Wound Healing while using electrical stimulation.

Effects of aging on neurogenic vasodilator responses evoked by transcutaneous electrical nerve stimulation: relevance to wound healing.

Khalil Z, Merhi M
J Gerontol A Biol Sci Med Sci. 2000 Jun; 55(6):B257-63.
National Ageing Research Institute, University of Melbourne, Victoria, Australia.

We have previously shown an age-related decline in the modulation of skin vascular reactivity by sensory nerves that correlates with a decline in wound repair efficacy. This study was designed to examine the possibility that improving the functional ability of aged sensory nerves using noninvasive transcutaneous electrical nerve stimulation (TENS) could also accelerate tissue repair. TENS of the sciatic nerve, combined with measuring blood flow responses in the rat hind-footpad using laser Doppler flowmetry, was used to establish the vascular effects. Following TENS (using parameters 20V, 5 Hz for 1 min), similar increases in vascular responses were obtained in both young (13.2+/-0.9 cm2) and old rats (11.6+/-2.3 cm2). In contrast, capsaicin-pretreated rats showed markedly diminished responses. Sympathetic fibers did not appear to modulate these sensory nerve responses. In the second part, a thermal wound was induced (using a CO2 laser) in the interscapular region of old rats (under anesthesia). In the active treatment group, TENS was applied twice daily for the initial 5 days, and the sham group received inactive TENS. Using the healing endpoint as the time when full wound contraction occurred, the active group required 14.7+/-0.2 days for complete healing, a significant improvement over the sham group (21.8+/-0.3 days). We contend that low-frequency TENS can improve the vascular response of old rats. In addition, wound healing in aged rats can be accelerated by peripheral activation of sensory nerves at low-frequency electrical stimulation parameters.

Epidural spinal cord electrical stimulation in diabetic critical lower limb ischemia.

Petrakis IE, Sciacca V
Title Abbreviation: J Diabetes Complications.
1999 Sep-Dec; Volume Issue: 13(5-6):293-9.
First Department of General Surgery, Policlinico Umberto I, University of Rome, La Sapienza, Rome, Italy.

Spinal cord stimulation (SCS) has been suggested to improve microcirculatory blood flow to relieve ischemic pain and to reduce amputation rate in patients with peripheral arterial occlusive disease (PAOD). The aim of this study was to evaluate the specific prognostic parameters in the prediction of successful SCS, in diabetic patients, performing a retrospective data analysis. To perform this evaluation, 64 diabetic patients (39 men, 25 women; mean age, 69 years) classified as Fontaine's stage III and IV, with PAOD, were treated with SCS for rest pain and trophic lesions with dry gangrene, after failed conservative or surgical treatment. In clinical controls, pedal transcutaneous oxygen tension (TcPO(2)), ankle/brachial blood pressure index (ABI), and toe pressure Doppler measurements were utilized to select and follow-up the patients. After 58 months of follow-up (range, 20-128 months), pain relief

greater than 75% and limb salvage were achieved in 38 diabetic patients. A partial success was obtained in nine patients with pain relief greater than 50% and limb salvage for at least 6 months. The method failed in 17 patients or the device was removed due to technical problems, and the limb was amputated in these patients. TcPO(2) was assessed on the dorsum of the foot. Clinical improvement and SCS success were associated with increase of TcPO(2), before and after implantation. Limb salvage was achieved in the patients who had significant TcPO(2) increase within the 2 weeks of the testing period, independently of the stage of the disease. A TcPO(2) increase of more than 50% in the first 2 months after implantation was predictive of success, and was related to the presence of adequate paresthesias in the painful area during the trial period. TcPO(2) significantly increased after long-term follow-up in all patients with limb salvage (from 22.1 to 43.1 mm Hg in the rest pain patients, from 15.8 to 36.4 mm Hg in those with trophic lesions of less than 3 cm(2), and from 12.1 to 28.1 in those with trophic lesions of greater than 3 cm(2), ($p < 0.01$). ABI did not changed under stimulation. In diabetic patients with PAOD, the SCS increases the skin blood flow, is associated with significant pain relief, and could be proven an excellent alternative therapy, improving the life quality. Significant TcPO(2) increase within the 2-week test period, is a predictive index of therapy success and should be considered before the final decision in terms of cost effectiveness, before the permanent implantation.

Effects of transcutaneous nerve stimulation on the microcirculation in chronic leg ulcers.

Cosmo P, Svensson H, Bornmyr S, Wikstrom SO
Scand J Plast Reconstr Surg Hand Surg. 2000 Mar; 34(1):61-4.
Department of Plastic and Reconstructive Surgery, Malmo University Hospital, Sweden.

The purpose of this study was to find out to what extent transcutaneous electrical nerve stimulation (TENS) affects the blood flow in and around chronic lower leg ulcers, as measured with a new technique, laser Doppler imaging (LDI). Fifteen patients, mean age 73 years (range 38-85) with chronic leg ulcers of various causes participated in the study. The duration of the ulcers ranged from 3 months to 16 years. Low-frequency (2 Hz; 10-45 mA) TENS was given for 60 minutes. The changes in blood flow were measured every 5 minutes by LDI. After 60 minutes, mean blood flow had increased in the ulcer by 35%, and in the intact skin surrounding the ulcer by 15%. Even 15 minutes after the TENS had finished there was still a mean blood flow increase of 29% in the ulcer and 9% in the skin. The present results show that TENS has a stimulating effect on local blood circulation in and around chronic ulcers.

Effect of transcutaneous nerve stimulation on microcirculation in intact skin and blister wounds in healthy volunteers.

Wikstrom SO, Svedman P, Svensson H, Tanweer AS
Scand J Plast Reconstr Surg Hand Surg. 1999 Jun; 33(2):195-201.
Department of Plastic and Reconstructive Surgery, University Hospital MAS, Malmo, Sweden.

Healthy non-smoking volunteers participated in two experimental studies in which the circulatory changes induced by transcutaneous nerve stimulation (TENS) were quantified by two different methods. In experimental series 1 (intact skin), nine volunteers were given TENS on the left lower leg for 60 minutes on three occasions at different frequencies each time (2 Hz, 100 Hz, and sham). Changes in blood flow were assessed by laser Doppler imaging

technique every five minutes. The mean blood flow increased by 40% during low frequency TENS and by 12% during high frequency TENS. There was no change in mean blood flow during sham stimulation. In experimental series 2 (blister wound), the circulatory changes induced by TENS were studied by intravital video microscopy and computerised image analysis in standard blister wounds on the lower leg. The microcirculatory blood flow, measured as red blood cell velocity (RBC-V) in 5-14 individual capillaries in each wound, was assessed before and during 45 minutes of TENS (2 Hz and 100 Hz). Mean RBC-V increased by 23% during low frequency TENS (n = 6) and by 17% during high frequency TENS (n = 8). The results show that: laser Doppler imaging and intravital video microscopy techniques can be used to study events at the microcirculatory level; the blister wound is an interesting new standard wound for use in clinical studies; and TENS stimulates the peripheral circulation.

Prognostic factors in the prediction of chronic wound healing by electrical stimulation.

Cukjati D, Robnik-Sikonja M, Rebersek S, Kononenko I, Miklavcic D.
Med Biol Eng Comput. 2001 Sep;39(5):542-50.
Faculty of Electrical Engineering, University of Ljubljana, Slovenia.

The aim of the study is to determine the effects of wound, patient and treatment attributes on the wound healing rate and to propose a system for wound healing rate prediction. Predicting the wound healing rate from the initial wound, patient and treatment data collected in a database of 300 chronic wounds is not possible. After considering weekly follow-ups, it was determined that the best prognostic factors are weekly follow-ups of the wound healing process, which alone were found to predict accurately the wound healing rate after a minimum follow-up period of four weeks (at least five measurements of wound area). After combining the follow-ups with wound, patient and treatment attributes, the minimum follow-up period was reduced to two weeks (at least three measurements of wound area). After a follow-up period of two weeks, it was possible to predict the wound healing rate of an independent test set of chronic wounds with a relative squared error of 0.347, and after three weeks, with a relative squared error of 0.181 (using regression trees with linear equations in its leaves). Regression trees with a relative squared error close to 0 produce better prediction than with an error closer to 1. Results show that the type of treatment is just one of many prognostic factors. Arranged in order of decreasing prediction capability, prognostic factors are: wound size, patient's age, elapsed time from wound appearance to the beginning of the treatment, width-to-length ratio, location and type of treatment. The data collected support former findings that the biphasic- and direct-current stimulation contributes to faster healing of chronic wounds. The model of wound healing dynamics aids the prediction of chronic wound healing rate, and hence helps with the formulation of appropriate treatment decisions.

Choosing an adjunctive therapy for the treatment of chronic wounds.
Houghton PE, Campbell KE.

Ostomy Wound Manage. 1999 Aug;45(8):43-52; quiz 53-4.
St. Joseph's Health Center, School of Physiotherapy, University of Western Ontario, London, Canada.

Adjunctive therapies such as ultrasound, laser, ultraviolet light, superficial heating, pulsed electromagnetic fields, and electrical stimulation have all been indicated in the treatment of chronic wounds. The purpose of this article is to outline the issues a healthcare professional must consider when

choosing the best adjunctive therapy for a chronic wound. It summarizes the effects of therapeutic modalities on the wound healing process, analyzes the clinical research evidence, discusses practical considerations, and reviews indications, contraindications, precautions, and safety considerations. Finally, an algorithm is presented to help guide the clinician in selecting a modality. In summary, research evidence exists in the literature that suggests these adjunctive therapies can directly stimulate new tissue growth, augment wound tissue strength, improve local circulation and oxygenation, reduce edema, and/or inhibit bacterial growth. Electrical stimulation and ultrasound are the only therapeutic modalities that currently have sufficient clinical research evidence to support their use in the treatment of chronic wounds. Practical issues such as cost, time and training required, and patient and therapist safety concerns, will ultimately influence the selection of these modalities.

Effect of electrical stimulation on chronic wound healing: a meta-analysis.
Gardner SE, Frantz RA, Schmidt FL.

Wound Repair Regen. 1999 Nov-Dec;7(6):495-503.
Colleges of Nursing, The University of Iowa, Iowa City, IA 52242-7066, USA.

The purpose of this meta-analysis was to quantify the effect of electrical stimulation on chronic wound healing. Fifteen studies, which included 24 electrical stimulation samples and 15 control samples, were analyzed. The average rate of healing per week was calculated for the electrical stimulation and control samples. Ninety-five percentage confidence intervals were also calculated. The samples were then grouped by type of electrical stimulation device and chronic wound and reanalyzed. Rate of healing per week was 22% for electrical stimulation samples and 9% for control samples. The net effect of electrical stimulation was 13% per week, an increase of 144% over the control rate. The 95% confidence intervals of the electrical stimulation (18-26%) and control samples (3.8-14%) did not overlap. Electrical stimulation was most effective on pressure ulcers (net effect = 13%). Findings regarding the relative effectiveness of different types of electrical stimulation device were inconclusive. Although electrical stimulation produces a substantial improvement in the healing of chronic wounds, further research is needed to identify which electrical stimulation devices are most effective and which wounds respond best to this treatment.

A comparative study of the effect of ultrasound and electrostimulation on wound healing in rats.

Taskan I, Ozyazgan I, Tercan M, Kardas HY, Balkanli S, Saraymen R, Zorlu U
Plast Reconstr Surg. 1997 Sep;100(4):966-72.
Physical Therapy and Rehabilitation Center, Medical Faculty of Inonu University, Istanbul, Turkey.

A comparative study has been carried out to investigate the effects of electrical stimulation and ultrasound on wound healing. Eighty-four female rats were divided into four groups depending on the treatment received. The first group was given electrical stimulation of 300 microA direct current, 30 minutes daily, starting with negative polarity and then changed after 3 days of treatment. Group 2 received sham electrostimulation treatment. The third group received 0.1 W/cm2 pulsed ultrasound using the moving applicator technique for 5 minutes a day. Group 4 received sham ultrasound treatment. A total of 7 days of treatment was given to all groups. Histopathologic and biochemical analyses on the fourth and seventh days and wound breaking

strength on the twenty-fifth day were performed for all groups. By accelerating the inflammatory phase, electrical stimulation had progressed the proliferative phase of wound healing earlier than ultrasound had done. Both electrical stimulation and ultrasound have positive effects on proliferative phases, but electrical stimulation was superior to ultrasound at the maturation phase. There was no difference between the two experimental groups on the mast cell reduction effect. Although ultrasound treatment may seem to be efficient in terms of time, when the effects of electrical stimulation and ultrasound on wound healing with the methods employed in our study are considered, it is concluded that electrical stimulation is a means of treatment superior to ultrasound in wound healing.

Effects of electrical stimulation on wound healing in patients with diabetic ulcers.

Baker LL, Chambers R, DeMuth SK, Villar F.
Diabetes Care. 1997 Mar;20(3):405-12.
Department of Biokinesiology and Physical Therapy, University of Southern California, Los Angeles 90033,

OBJECTIVE: To evaluate the effects of two stimulation waveforms on healing rates in patients with diabetes and open ulcers. The hypothesis was that stimulus waveforms with minimal polar characteristics would provide significant healing for this patient sample. RESEARCH DESIGN AND METHODS: This was a prospective study that enrolled 80 patients with open ulcers. Patients received stimulation with either an asymmetric biphasic (A) or symmetric biphasic (B) square-wave pulse. Amplitudes were set to activate intact peripheral nerves in the skin. Two other groups received either very low levels of stimulation current (MC), or no electrical stimulation (C). When combined these groups were referred to as the control group. Treatment was carried out daily until the wound healed, the patient withdrew from the study, or the physician changed the overall wound management program. Average healing rates were calculated from weekly measures of the wound perimeter and were used for statistical comparison through a one-way analysis of variance. RESULTS: Stimulation with the A protocol significantly increased the healing rate, enhancing healing by nearly 60% over the control rate of healing. Stimulation with the B protocol did not increase the healing rate when compared with control subjects. CONCLUSIONS: Electrical stimulation, given daily with a short pulsed, asymmetric biphasic waveform, was effective for enhancement of healing rates for patients with diabetes and open ulcers.

Promotion of wound healing with electrical stimulation.

Kloth LC, McCulloch JM.
Adv Wound Care. 1996 Sep-Oct;9(5):42-5.
Program of Physical Therapy, Marquette University, Milwaukee, Wis, USA.

Clinicians involved in the conservative care of chronic wounds have many treatment interventions from which to choose, including debridement/irrigation, dressings, pressure-relieving devices, hyperbaric or topically applied oxygen, whirlpool/pulsed lavage, ultrasound, topical antibiotics, and cytokine growth factors. All except the last two interventions are physical treatments that create a wound-tissue environment conducive to healing. Unfortunately, many chronic wounds heal very slowly, do not heal, or worsen despite the best efforts of caregivers to promote tissue repair. An intervention commonly used to treat chronic wounds, especially by physical therapists, is electrical stimulation (ES). The rationale for use of

this method is based on the fact that the human body has an endogenous bioelectric system that enhances healing of bone fractures and soft-tissue wounds. When the body's endogenous bioelectric system fails and cannot contribute to wound repair processes, therapeutic levels of electrical current may be delivered into the wound tissue from an external source. The external current may serve to mimic the failed natural bioelectric currents so that wound healing can proceed. Certain chemotaxic factors found in wound substrates contribute to tissue repair processes by attracting cells into the wound environment. Neutrophil, macrophage, fibroblast, and epidermal cells involved in wound repair carry either a positive or negative charge. When these cells are needed to contribute to autolysis, granulation tissue formation, anti-inflammatory activities, or epidermal resurfacing, ES may facilitate galvanotaxic attraction of these cells into the wound tissue and thereby accelerate healing.

Physical modalities in wound management: UVC, therapeutic heating and electrical stimulation.

Kloth LC.
Ostomy Wound Manage. 1995 Jun;41(5):18-20, 22-4, 26-7.

In spite of efforts to create an optimum wound environment for healing, there are times that a wound may not heal, may heal very slowly, or may worsen. In these cases, a series of treatments with an appropriate physical agent can be added to the patient's care plan to augment tissue reparative processes. Three modalities that have received support in the literature for use in wound healing are ultraviolet "C" radiation (UVC), therapeutic heating, and electrical stimulation. Treatment goals for UVC are hyperplasia and enhanced re-epithelialization or desquamation of the leading edge of periulcer epidermal cells, granulation tissue formation, sloughing of necrotic tissue, and bactericidal effects. Treatment goals for therapeutic heating are increased blood perfusion with subsequent increased delivery of oxygen to the tissues (avoiding the dessication of wound tissues). The treatment goal for electrical stimulation is to attract negatively or positively charged cells into the wound area, such as neutrophils, macrophages, epidermal cells and fibroblasts that in turn will contribute to wound healing processes by way of their individual cellular activities.

Experimental wound healing with electrical stimulation.

Reger SI, Hyodo A, Negami S, Kambic HE, Sahgal V
Title Abbreviation: Artif Organs.
1999 May; 23(5):460-2.
Department of Physical Medicine and Rehabilitation, The Cleveland Clinic Foundation, Ohio 44195, USA.

The effect of alternating current (AC) and direct current (DC) stimulation was studied on experimental pressure ulcer healing in a new monoplegic pig model. The study was conducted in 30 healthy young Hanford minipigs. The rate of wound healing, histology, vascularization, collagen formation, microbiology, perfusion, and the mechanical strength of the healed wounds were studied. Normal pigskin was compared to denervated control and denervated AC and DC stimulated healed skin. Hind limb denervation was by right unilateral extradural rhizotomies from the L2 to S1 nerve roots. Reproducible uniformly controlled Stage III or higher tissue ulcers were created. When compared to the control wounds, both the AC and DC stimulated wounds showed reduced healing time and increased perfusion in the early phases of healing. DC

stimulation reduced the wound area more rapidly than AC, but AC stimulation reduced the wound volume more rapidly than DC. The electrical stimulation did not reduce the strength of the healing wounds below those of the nonstimulated controls. The applied current appears to orient new collagen formation even in the absence of neural influences.

Electric muscle stimulation for pressure sore prevention: tissue shape variation.

Levine SP Kett RL Cederna PS Brooks SV
Arch Phys Med Rehabil (1990 Mar) 71(3):210-5

This study measured changes in tissue shape and deformation at the seating interface produced by electric muscle stimulation (EMS) of the gluteus maximus. The purpose of the study was to investigate the application of EMS for pressure sore prevention. Limitations of pressure measurements for analysis of load distribution are discussed and a rationale developed for using tissue shape and deformation to further characterize the seating interface. Ultrasonic imaging of the seating interface is described under three conditions: buttocks suspended, external load applied with no EMS, and external load applied with bilateral EMS of the buttocks. Results show that low level stimulation of the gluteus maximus produces substantial changes in the shape of the loaded buttocks and an external contour more nearly shaped like the suspended buttocks. It is concluded that EMS produces buttock tissue undulation and shape reconfiguration which may assist in preventing pressure sores over the seating surface.

Adjuvant therapy for ulcer care.

Frantz RA
Clin Geriatr Med (1997 Aug) 13(3):553-64

Adjuvant therapies, specifically electrotherapy, hyperbaric oxygen, ultrasound, and hydrotherapy, are considered increasingly for use with conventional local wound care to support healing of pressure ulcers. This article describes the characteristics of these modalities, their physiologic effects on the healing process, and the research to evaluate their efficacy.

Effects of electrical stimulation on wound healing in patients with diabetic ulcers.
Baker LL Chambers R DeMuth SK Villar F
Diabetes Care (1997 Mar) 20(3):405-12

OBJECTIVE: To evaluate the effects of two stimulation waveforms on healing rates in patients with diabetes and open ulcers. The hypothesis was that stimulus waveforms with minimal polar characteristics would provide significant healing for this patient sample. RESEARCH DESIGN AND METHODS: This was a prospective study that enrolled 80 patients with open ulcers. Patients received stimulation with either an asymmetric biphasic (A) or symmetric biphasic (B) square-wave pulse. Amplitudes were set to activate intact peripheral nerves in the skin. Two other groups received either very low levels of stimulation current (MC), or no electrical stimulation (C). When

combined these groups were referred to as the control group. Treatment was carried out daily until the wound healed, the patient withdrew from the study, or the physician changed the overall wound management program. Average healing rates were calculated from weekly measures of the wound perimeter and were used for statistical comparison through a one-way analysis of variance. RESULTS: Stimulation with the A protocol significantly increased the healing rate, enhancing healing by nearly 60% over the control rate of healing. Stimulation with the B protocol did not increase the healing rate when compared with control subjects. CONCLUSIONS: Electrical stimulation, given daily with a short pulsed, asymmetric biphasic waveform, was effective for enhancement of healing rates for patients with diabetes and open ulcers.

The benefit of electrical stimulation to enhance perfusion in persons with diabetes mellitus.

Peters EJ Armstrong DG Wunderlich RP Bosma J Stacpoole-Shea S Lavery LA
J Foot Ankle Surg (1998 Sep-Oct) 37(5):396-400; discussion 447-8

The purpose of this study was to evaluate the effect of galvanic electrical stimulation on vascular perfusion in diabetic patients. Nineteen subjects with diabetes were enrolled. Eleven subjects (57.9%) were diagnosed with impaired peripheral perfusion based upon their initial transcutaneous oximetry values (< 40 mm Hg). The subjects were studied over a 2-day period. On the 1st day, one foot was electrically stimulated for four 60-minute periods by an external electrical stimulation device. Vascular perfusion of both feet was assessed before and after the sessions of electrical stimulation. On the 2nd day, no electrical stimulation was applied and noninvasive vascular measurements were repeated. For the 1st hour, transcutaneous oxygen pressure was measured continuously during stimulation at the lateral aspect of the leg. Subsequently, perfusion between the periods of stimulation was measured on the dorsum of the foot with both transcutaneous oximetry and laser Doppler flowmetry after each stimulation period. In the group with impaired peripheral perfusion, a significant rise in tissue oxygenation as compared to the control measurements was measured during the first 5 minutes of stimulation ($p < .040$). For those without vascular disease (TcpO2 > 40 mm Hg) however, there was not a significant increase compared to baseline ($p = .280$). After the periods of stimulation, the stimulated feet did not show any higher perfusion levels than the control feet. Patterns in perfusion during the day, as measured by laser Doppler flowmetry, were similar in the tested feet and in the controls. These data suggest that external subsensory electrical stimulation induces a transient rise in skin perfusion in persons with diabetes and impaired peripheral perfusion.

Treatment of chronic wounds by means of electric and electromagnetic fields. Part 2. Value of FES parameters for pressure sore treatment.

Stefanovska A Vodovnik L Benko H Turk R
Med Biol Eng Comput (1993 May) 31(3):213-20

Subjects with spinal cord injury are often distressed by pressure sores, which usually appear after prolonged pressure (wheelchair, bed) across the soft tissue which has already lost sensibility and has diminished microcirculation. The healing ability and its dynamics depend on the state of the subject's overall health. Consequently, evaluation of a particular treatment requires careful consideration of as many as possible of the parameters relevant to healing and an adequate criterion for assessing the state of the pressure sore. Bearing in mind these two circumstances, the results of a multicentre clinical study are analysed. The aim of the study

was to test two hypotheses: first that healing is faster when sores are also treated by electric currents (ECs) (in addition to conventional treatment); and secondly that there exist differences in the efficiency of the treatment if direct or low-frequency pulsed currents (FES parameters) are applied. The data analysed show that pressure sores are likely to heal twice as fast when treated with low-frequency pulsed currents. EC seems to improve the healing rate in cases where the natural healing mechanisms of the body are not sufficient (chronic wounds, older subjects).

Reduction of seating pressure using FES in patients with spinal cord injury. A preliminary report.

Ferguson AC Keating JF Delargy MA Andrews BJ
Paraplegia (1992 Jul) 30(7):474-8

The aim of this study was to investigate the use of functional electrical stimulation (FES) as a means of pressure sore prevention in seated spinal cord injured (SCI) subjects. Nine SCI subjects took part in tests in which electrical stimulation was applied to the quadriceps with the lower legs restrained. Ischial pressures were measured during periods of quiet sitting and FES application. A strain gauged lever arm was used to measure the knee moment during quadriceps stimulation. The average pressure drop at the right and left buttocks was 44 mmHg and 27 mmHg respectively. In general the greatest reductions occurred in subjects with larger knee moments; however, there was no direct relationship between the pressure reduction obtained and the quadriceps strength. This form of FES may be useful as a prophylactic aid in the management of pressure sores in SCI subjects.

Chronic dermal ulcer healing enhanced with monophasic pulsed electrical stimulation [see comments]

Feedar JA Kloth LC Gentzkow GD
Phys Ther (1991 Sep) 71(9):639-49

The purposes of this randomized, double-blind, multicenter study were to compare healing of chronic dermal ulcers treated with pulsed electrical stimulation with healing of similar wounds treated with sham electrical stimulation and to evaluate patient tolerance to the therapeutic protocol. Forty-seven patients, aged 29 to 91 years, with 50 stage II, III, and IV ulcers were randomly assigned to either a treatment group (n = 26) or a control (sham treatment) group (n = 24). Treated wounds received 30 minutes of pulsed cathodal electrical stimulation twice daily at a pulse frequency of 128 pulses per second (pps) and a peak amplitude of 29.2 mA if the wound contained necrotic tissue or any drainage that was not serosanguinous. A saline-moistened nontreatment electrode was applied 30.5 cm (12 in) cephalad from the wound. This protocol was continued for 3 days after the wound was debrided or exhibited serosanguinous drainage. Thereafter, the polarity of the treatment electrode on the wound was changed every 3 days until the wound progressed to a stage II classification. The pulse frequency was then reduced to 64 pps, and the treatment electrode polarity was changed daily until the wound was healed. Patients in the control group were treated with the same protocol, except they received sham electrical stimulation. After 4 weeks, wounds in the treatment and control groups were 44% and 67% of their initial size, respectively. The healing rates per week for the treatment and control groups were 14% and 8.25%, respectively. The results of this study indicate that

pulsed electrical stimulation has a beneficial effect on healing stage II, III, and IV chronic dermal ulcers.

Effect of electrical stimulation on foot skin perfusion in persons with or at risk for diabetic foot ulcers.

Gilcreast DM Stotts NA Froelicher ES Baker LL Moss KM
Wound Repair Regen (1998 Sep-Oct) 6(5):434-41

The failure of foot wounds to heal results in 54,000 people with diabetes having to undergo extremity amputations annually. Therefore, treatment is needed to speed healing in people with diabetes in order to reduce the need for amputation. This study tested the effect of high-voltage pulsed current on foot blood flow in human beings who are at risk for diabetic foot ulcers. Neuropathy, vascular disease, Wagner Class, glucose, gender, ethnicity, and age were measured. A sample of 132 subjects was tested using a repeated-measures design. A baseline transcutaneous oxygen level was obtained; stimulation was applied, and transcutaneous oxygen measurements were recorded at 30- and 60- minute time intervals. The grouped foot transcutaneous oxygen levels decreased ($F = 5.66$, $p =. 0039$) following electrical stimulation. Analysis of variance (Scheffe, $p <.05$) showed that initial transcutaneous oxygen was significantly higher than subsequent readings. However, oxygen response was distributed bimodally: 35 (27%) subjects showed increased transcutaneous oxygen (mean 14.8 mm Hg), and 97 (73%) experienced a decreased transcutaneous oxygen reading (mean 12.2 mm Hg). Logistic regression analysis did not explain these differences. Although this treatment appears to increase blood flow in a subset of patients, further study is needed to identify probable mechanisms for this response.

Biofeedback and functional electric stimulation in stroke Rehabilitation.

Cozean CD Pease WS Hubbell SL
Arch Phys Med Rehabil (1988 Jun) 69(6):401-5

The study examined the efficacy of functional electric stimulation (FES) and biofeedback (BFB) treatment of gait dysfunction in patients with hemiplegia after stroke. These two therapeutic modalities were tested alone and in combination in a prospective, controlled, randomized trial. The authors hypothesized that in concurrent use, these two modalities would complement one another. Thirty-six hemiplegic patients undergoing rehabilitation after stroke were accepted for study and randomized into four groups to receive either control, FES, BFB, or combined therapies. Each patient received 30 minutes of treatment three times per week for six weeks, in addition to their general rehabilitation program. Quantitative gait analysis was performed biweekly on each subject during the experimental therapy and for four weeks afterward. Thirty-two subjects completed the study. Combined therapy with BFB and FES resulted in improvements in both knee and ankle minimum flexion angles during swing phase that were statistically significant with $p = 0.05$ and $p = 0.02$, respectively. Velocity of gait, cycle time, and symmetry of stance phases also improved. The length of time elapsed since the stroke did not prove to be a significant factor.

Reduction of seating pressure using FES in patients with spinal cord injury. A preliminary report.

Ferguson AC Keating JF Delargy MA Andrews BJ
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The aim of this study was to investigate the use of functional electrical stimulation (FES) as a means of pressure sore prevention in seated spinal cord injured (SCI) subjects. Nine SCI subjects took part in tests in which electrical stimulation was applied to the quadriceps with the lower legs restrained. Ischial pressures were measured during periods of quiet sitting and FES application. A strain gauged lever arm was used to measure the knee moment during quadriceps stimulation. The average pressure drop at the right and left buttocks was 44 mmHg and 27 mmHg respectively. In general the greatest reductions occurred in subjects with larger knee moments; however, there was no direct relationship between the pressure reduction obtained and the quadriceps strength. This form of FES may be useful as a prophylactic aid in the management of pressure sores in SCI subjects.

Relative changes in blood flow with functional electrical stimulation during exercise of the paralyzed lower limbs.

Phillips W Burkett LN Munro R Davis M Pomeroy K
Paraplegia (1995 Feb) 33(2):90-3

Eight spinal cord injured (SCI) patients performed three sets of exercise with two conditions, 60% and 80% of VO2peak, with an arm crank ergometer. Functional neuromuscular stimulation was used to induce static leg contractions in two of the above sets of exercise. The three exercise sets were performed with no functional neuromuscular stimulation (NOS); with functional neuromuscular stimulation at 40 milliamperes; and with functional neuromuscular stimulation at 80 milliamperes (HIS). The lower limb blood flow was estimated by a photoelectric plethysmograph. Results showed that the lower limb blood flow was consistently reduced across both functional neuromuscular stimulation levels (17.4% from NOS to LOS; 13.8% from LOS to HIS; and 28.8% from NOS to HIS), and work loads (15.3% from rest to 60% VO2peak; 38.0% from 60% VO2peak to 80% VO2peak; and 47.5% from rest to 80% VO2peak). Rate-pressure product was decreased by 8.3% between NOS and HIS at 60% VO2peak (15.7 +/- 3.4 to 14.4 +/- 3.8), by 6.8% between NOS and HIS at 80% VO2peak (18.9 +/- 53 to 17.6 +/- 4.8), and by 12.4% between LOS and HIS at 80% VO2peak (20.1 +/- 6.7 to 17.6 +/- 4.8). These data indicate that in SCI (a) functional neuromuscular stimulation-induced contractions of the lower limb muscles can increase blood flow and thus reduce venous blood pooling in the paralyzed muscles, and (b) such improvements are associated with a reduced rate pressure product.(ABSTRACT TRUNCATED AT 250 WORDS)

Promotion of wound healing with electrical stimulation.

Kloth LC McCulloch JM
Adv Wound Care (1996 Sep-Oct) 9(5):42-5

Clinicians involved in the conservative care of chronic wounds have many treatment interventions from which to choose, including debridement/irrigation, dressings, pressure-relieving devices, hyperbaric or topically applied oxygen, whirlpool/pulsed lavage, ultrasound, topical antibiotics, and cytokine growth factors. All except the last two interventions are physical treatments that create a wound-tissue environment conducive to healing. Unfortunately, many chronic wounds heal very slowly, do

not heal, or worsen despite the best efforts of caregivers to promote tissue repair. An intervention commonly used to treat chronic wounds, especially by physical therapists, is electrical stimulation (ES). The rationale for use of this method is based on the fact that the human body has an endogenous bioelectric system that enhances healing of bone fractures and soft-tissue wounds. When the body's endogenous bioelectric system fails and cannot contribute to wound repair processes, therapeutic levels of electrical current may be delivered into the wound tissue from an external source. The external current may serve to mimic the failed natural bioelectric currents so that wound healing can proceed. Certain chemotaxic factors found in wound substrates contribute to tissue repair processes by attracting cells into the wound environment. Neutrophil, macrophage, fibroblast, and epidermal cells involved in wound repair carry either a positive or negative charge. When these cells are needed to contribute to autolysis, granulation tissue formation, anti-inflammatory activities, or epidermal resurfacing, ES may facilitate galvanotaxic attraction of these cells into the wound tissue and thereby accelerate healing.

Electrical nerve stimulation improves healing of diabetic ulcers.

Lundeberg TC Eriksson SV Malm M
Ann Plast Surg (1992 Oct) 29(4):328-31

A controlled study of the effects of electrical nerve stimulation (ENS) was performed in conjunction with a standard treatment for healing chronic diabetic ulcers on 64 patients divided randomly into two groups. All patients received standard treatment (paste-impregnated bandage and a self-adhesive elastic bandage) plus placebo ENS or ENS (alternating constant current; frequency, 80 Hz; pulse width, 1 msec; intensity-evoking strong paresthesias) for 20 minutes twice daily for 12 weeks. Comparison of percentages of healed ulcer area and the number of healed ulcers was made after 2, 4, 6, 8, and 12 weeks. There were significant differences ($p < 0.05$) in both ulcer area and healed ulcers in the ENS group compared with the placebo group after 12 weeks of treatment. The results of the present study support the use of ENS in diabetic ulcers. ENS is easy to apply and can be used by the patient at home following instructions from a medical doctor or a therapist experienced in electrical stimulation and the treatment of ulcers. Additional studies are needed to identify the mechanisms involved in the promotion of ulcer healing with electrical stimulation and to determine the stimulus variables that most efficaciously accelerate tissue repair.

Effects of electrical stimulation on wound healing in patients with diabetic ulcers.

Baker LL Chambers R DeMuth SK Villar F
Diabetes Care (1997 Mar) 20(3):405-12

OBJECTIVE: To evaluate the effects of two stimulation waveforms on healing rates in patients with diabetes and open ulcers. The hypothesis was that stimulus waveforms with minimal polar characteristics would provide significant healing for this patient sample. RESEARCH DESIGN AND METHODS: This was a prospective study that enrolled 80 patients with open ulcers. Patients received stimulation with either an asymmetric biphasic (A) or symmetric biphasic (B) square-wave pulse. Amplitudes were set to activate intact peripheral nerves in the skin. Two other groups received either very low levels of stimulation current (MC), or no electrical stimulation (C). When

combined these groups were referred to as the control group. Treatment was carried out daily until the wound healed, the patient withdrew from the study, or the physician changed the overall wound management program. Average healing rates were calculated from weekly measures of the wound perimeter and were used for statistical comparison through a one-way analysis of variance. RESULTS: Stimulation with the A protocol significantly increased the healing rate, enhancing healing by nearly 60% over the control rate of healing. Stimulation with the B protocol did not increase the healing rate when compared with control subjects. CONCLUSIONS: Electrical stimulation, given daily with a short pulsed, asymmetric biphasic waveform, was effective for enhancement of healing rates for patients with diabetes and open ulcers.

Electrical stimulation to heal dermal wounds.

Gentzkow GD
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BACKGROUND. Numerous human and animal efficacy studies have demonstrated that electrical stimulation of the correct charge, density and total energy causes dramatically improved healing of dermal wounds. The investigations of biological actions (in vitro, animal, and human) demonstrate several effects that go a long way to explaining why electrical stimulation works. OBJECTIVE. To discuss recent research and advances in electrical stimulation of wound healing. RESULTS. Based on the latest scientific understanding of the wound healing process, one would expect a beneficial outcome from a therapy what decreases edema, debrides necrotic tissue, attracts neutrophils and macrophages, stimulates receptor sites for growth factors, stimulates growth of fibroblasts and granulation tissue, increases blood flow, stimulates neurite growth, induces epidermal cell migration, prevents post-ischemic oxygen radical-mediated damage, inhibits bacteria, and reduces numbers of mast cells. CONCLUSION. Taken together, the efficacy studies and the "mechanism of action" studies provide compelling, scientific evidence that electrical stimulation is safe and effective for promoting the healing of dermal wounds.

Alteration in alpha- and beta-adrenoceptor profile of rabbit knee joint blood vessels due to acute inflammation.

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Experiments were performed to investigate the nature of - and -adrenoceptors in blood vessels supplying the posterior capsule of the acutely inflamed rabbit knee joint, and results were compared to findings from previous experiments on the normal joint, to assess any alteration which may occur in the adrenoceptor profile due to the inflammation process. Electrical stimulation of the posterior articular nerve resulted in vasoconstriction which was reversed to vasodilatation by phentolamine and yohimbine. The dose-response curves to close intra-arterial injection of -adrenoceptor agonists showed a rank-order potency of: adrenaline = phenylephrine = clonidine. The adrenaline dose-response curve was shifted to the right by administration of antagonists with a rank-order potency of: phentolamine = yohimbine = prazosin. At this stage of the experiments there was an equal response of 1- and 2-adrenoceptors in blood vessels of the acutely inflamed rabbit knee joint. In another group of animals the neurally mediated vasodilatation, which appeared after administration of phentolamine, was completely blocked by propranolol, and was reduced by about 50 % by atenolol.

The dose-response curves to close intra-arterial injection of -adrenoceptor agonists showed a rank-order potency of: isoprenaline > salbutamol = dobutamine. The isoprenaline dose-response curve was shifted to the right by administration of antagonists with a rank-order potency of: propranolol > atenolol. These experiments also showed an almost equal response of 1- and 2-adrenoceptors in blood vessels of the acutely inflamed rabbit knee joint. Overall, compared to previous experiments on the normal joint in which 2- and 1-adrenoceptor responses predominated, acute inflammation resulted in a shift from 2- towards 1- and from 1- towards 2-adrenoceptor responses.

Sympathetically induced paradoxical increases of the cutaneous blood flow in chronically inflamed rats.

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In adjuvant arthritic (AA) rats, an abnormal responsiveness of nociceptors (C-fibre polymodal receptors) to sympathetic activities, i.e., alpha 2-adrenoceptor mediated activation of C-fibre polymodal receptors (CPRs), has been observed. The present investigations were undertaken to determine if a similar plastic change would occur in the cutaneous vascular system in the rat chronic inflammation model. The vascular responses were measured by a laser-Doppler flowmeter in the hindpaw skin of the AA rats after electrical stimulation of lumbar sympathetic trunk (sympathetic stimulation). In control non-arthritic rats, the sympathetic stimulation caused decrease in blood flow of the skin (SkBF) in all animals tested (n = 7). On the other hand, the sympathetic stimulation in the AA rats caused both increase (n = 15) as well as decrease (n = 11) in SkBF. In contrast to the abnormal responsiveness of CPRs, the intra-arterial injection of noradrenaline caused the expected decrease in SkBF in all animals tested, and in no instances increases in SkBF were observed. To determine whether activation of nitric oxide (NO), which is known to be a potent endogenous vasodilatation substance, was involved in the vasodilating effect to sympathetic stimulation, an inhibitor of NO synthase, NG-monomethyl-L-arginine (L-NMMA), was applied systemically. L-NMMA significantly increased baseline blood pressure in the control and the AA rats, but it did not significantly alter the SkBF in the control or the AA rats after the sympathetic stimulation, suggesting that NO is not a mediator in the vasoactive responses. The results of the current studies showed for the first time that electrical stimulation of the lumbar sympathetic trunk causes vasodilatation in the skin of the AA rats. This abnormal responsiveness of regional SkBF after sympathetic stimulation was not mediated by adrenergic or NO system.