Functional Electrical Stimulation and Neuromuscular Electrical Stimulation AHM

Clinical Indications

- **Functional electrical stimulation** (FES) is considered (e.g., Parastep I System) medically necessary durable medical equipment (DME) to enable patients with spinal cord injury (SCI) [A] to ambulate when **ALL** of the following criteria are met [B]
  - Patient has intact lower motor units (L1 and below)
  - Patient can bear weight on upper and lower extremities to maintain an upright posture independently
  - Patient demonstrated brisk muscle contraction to neuromuscular electrical stimulation and has sensory perception of electrical stimulation sufficient for muscle contraction
  - Patient is highly motivated and has the cognitive ability to use such devices for walking
  - Patient can transfer independently and stand for at least 3 minutes
  - Patient possesses hand and finger function to manipulate the controls
  - Patient is at least 6 months post recovery of spinal cord injury and restorative surgery
  - Patient does not have hip and knee degenerative disease and has no history of long bone fracture secondary to osteoporosis
  - The patient has successfully completed a training program, which consists of at least 32 physical therapy sessions with the device over a 3-month period

- **Functional electrical stimulation for walking** (Parastep I System) has no proven value for patients with SCI with **1 or more** of the following
  - Patients with cardiac pacemakers
  - Patients with severe scoliosis or severe osteoporosis
  - Patients with skin disease or cancer at area of stimulation
  - Patients with irreversible contracture
  - Patients with autonomic dysreflexia

- **Neuromuscular electrical stimulators** (NMES) [C] is considered medically necessary DME for disuse atrophy where the nerve supply to the muscle is intact and the patient has any **1 or more** of the following non-neurological reasons for disuse atrophy
  - Contractures due to burn scarring
  - Major knee surgery (when there is failure to respond to physical therapy)
- Previous casting or splinting of a limb
- Recent hip replacement surgery (NMES is covered until physical therapy begins)

- **FES of the upper extremities** (e.g., NESS H200) is considered experimental and investigational for all indications, including improvement of muscle strength, reduction of spasticity and atrophy, and facilitation of functional motor movement due to any of the following conditions:
  - Spinal cord injury
  - Stroke (cerebrovascular accident/CVA)
  - Traumatic brain injury
  - Other upper motor neuron disorders (e.g., Parkinson's disease)

- **FES** and **NMES** is considered experimental and investigational for all other indications, including any of the following:
  - Bell's palsy
  - Cerebral palsy
  - For cardiac conditioning
  - For general muscle strengthening in healthy individuals
  - For the treatment of denervated muscles

- **Form-fitting conductive garment** medically necessary DME only when it has been approved for marketing by the FDA, has been prescribed by a physician for use in delivering NMES that is considered medically necessary, and any 1 or more of the following criteria is met:
  - The patient cannot manage without the conductive garment due to the large area or the large number of sites to be stimulated, and the stimulation would have to be delivered so frequently that it is not feasible to use conventional electrodes, adhesive tapes, and lead wires
  - The patient has a skin problem or other medical conditions that precludes the application of conventional electrodes, adhesive tapes, and lead wires
  - The patient requires electrical stimulation beneath a cast to treat disuse atrophy, where the nerve supply to the muscle is intact
  - The patient has a medical need for rehabilitation strengthening following an injury where the nerve supply to the muscle is intact

- **Diaphragmatic/phrenic pacing** (e.g., the NeuRx DPS RA/4 Respiratory Stimulation System) is considered medically necessary for **ALL** of the following indications:
  - For improvement of ventilatory function in stable, non-acute patients with SCI when **ALL** of the following criteria are met:
    - Patient has high quadriplegia at or above C-3
    - There are viable phrenic nerves
    - Patient's diaphragm and lung function are adequate
  - For the treatment of central alveolar hypoventilation
For individuals with amyotrophic lateral sclerosis

- **Electrical stimulation of the sacral anterior roots** (by means of an implanted stimulator, the Vocare Bladder System[^E]) in conjunction with a posterior rhizotomy medically necessary for patients who have clinically complete spinal cord lesions (American Spinal Injury Association Classification) with intact parasympathetic innervation of the bladder and who are skeletally mature and neurologically stable, to provide urination on demand and to reduce post-void residual volumes of urine. **ALL** of the following selection criteria must be met
  - 3 months (female patients) after or 9 months (male patients) after complete supra-sacral spinal cord injury
  - A phasic detrusor pressure rise of 35 mm H2O (female patients) or 50 cm H2O (male patients) on cystometry
  - Presence of 3 of the 4 non-vesical sacral segment reflexes (i.e., ankle jerks, bulbocavernous reflex, anal skin reflex, and reflex erection)

**Indications considered Not Medically Necessary**

- **Electrical stimulation of the sacral anterior roots** in conjunction with posterior rhizotomy (Vocare Bladder System) is considered investigational for all other indications
- Transurethral electrical stimulation is considered investigational for the management of neurogenic bladder dysfunction and all other indications because its effectiveness for these indications has not been established
- **Peroneal nerve stimulator** (e.g., the WalkAide device, the Bioness, and the NESS L300 Foot Drop System) is considered investigational for persons with foot drop and for all other indications because of insufficient evidence to support its use for these indications.
- Threshold (or therapeutic) electrical stimulation is considered investigational for the management of cerebral palsy and other motor disorders and knee osteoarthritis because its effectiveness for these indications has not been established.
- FES and NMES is considered investigational for improving ambulatory function and muscle strength for progressive diseases (e.g., cancer, chronic heart failure, chronic obstructive pulmonary disease, multiple sclerosis) in persons without spinal cord injury.
- FES and NMES is considered investigational the treatment of denervated muscles for the treatment of knee osteoarthritis.
Evidence Summary

Background

- Spinal cord injury can (SCI) cause various degrees of neurological impairment depending on the location and severity of the injury. One method of categorizing the degree of injury is by a neurological examination that explores the segments of the cord which are still functional. The most caudal segment of the cord with normal sensory and motor functions is denoted as the neurological level of injury. The American Spinal Injury Association (ASIA) Impairment Scale is a classification system used to describe the extent of SCI.
- The ASIA Impairment Scale
  - A Complete: No motor or sensory function is preserved in the sacral segments S4 - S5
  - B Incomplete: Sensory but not motor function is preserved below the neurological level and includes the sacral segments S4 - S5
  - C Incomplete: Motor function is preserved below the neurological level, and more than half of key muscles below the neurological level have a muscle grade less than 3
  - D Incomplete: Motor function is preserved below the neurological level, and more than half of key muscles below the neurological level have a muscle grade less than 3
  - D Incomplete: Motor function is preserved below the neurological level, and at least half of key muscles below the neurological level have a muscle grade of 3 or more
  - E Normal: Motor and sensory function are normal
- Another factor that influences the severity of impairment is the neurological extent of injury, namely the degree of tissue trauma to the spinal cord at the level of injury. If the spinal cord is seriously damaged at the injury site, there is complete loss of sensation and voluntary muscle control below the level of lesion. On the other hand, if the damage is not complete, some sensory and/or motor functions may still be preserved. Thus, a complete injury to the cervical spine will result in quadriplegia, while an incomplete injury to the cervical spine will result in quadriparesis. Similarly, a complete lesion in the thoracic or lumbar spine will produce paraplegia, whereas an incomplete lesion at these levels will produce paraparesis. Spinal cord injury can result in damage to upper motor neurons (UMN), lower motor neurons (LMN), or a combination of both. The cell bodies of UMN originate from the primary motor area of the cerebral cortex and the brain stem, with their axons descending downward and terminating at each segmental level throughout the entire length of the spinal column to synapse with LMN which arise in the spinal cord and connect to a muscle or organ. The brain, through the UMN, exerts an inhibitory influence on the LMN so that they do not become hyperactive to local stimuli. The cell bodies of LMN are located in the central gray matter throughout the entire length of the spinal column, and their axons extend out via the spinal nerve roots and peripheral nerve branches to innervate skeletal muscles throughout the body.
- Neuromuscular electrical stimulation (NMES) can be grouped into 2 categories: (i) stimulation of muscles to treat muscle atrophy, and (ii) enhancement of functional activity in neurologically impaired individuals. These devices use electrical impulses to
activate paralyzed or weak muscles in precise sequence and have been utilized to provide SCI patients with the ability to walk (e.g., The Parastep I System). Neuromuscular electrical stimulation used in this manner is commonly known as functional electrical stimulation (FES).

- The Parastep I System, a transcutaneous non-invasive and micro-computerized electrical stimulation system built into a battery-powered unit, is controlled by finger-touch buttons located on a walker's hand-bars for manual selection of stimulation menus. The microcomputer shapes, controls, and distributes trains of stimulation signals that trigger action potentials in selected peripheral nerves. Walker support is used for balance. The patient can don the system in less than 10 minutes. At least 32 training sessions are required.

- Klose, et al. (1997) described performance parameters and effects on anthropometric measures in SCI patients (13 men and 3 women) training with the Parastep I system, Subjects with thoracic (T4 - T11) motor-complete SCI, mean age of 28.8 years, and mean duration post-injury of 3.8 years underwent 32 functional neuromuscular stimulation ambulation training sessions using the Parastep I System. The authors concluded that the Parastep I System enabled persons with thoracic-level SCI to stand and ambulate short distances but with a high degree of performance variability across individuals. Furthermore, Graupe and Kohn (1998) reported that about 400 patients have used the Parastep I System and essentially all achieved standing and at least 30 feet of ambulation, with a few reaching as much as 1 mile at a time.

- Bonaroti, et al. (1999) compared FES to long leg braces (LLB) as a means of upright mobility for children with motor-complete thoracic level SCI (n = 5). The authors found that FES system generally provided equal or greater independence in seven mobility activities as compared with LLB, provided faster sit-to-stand times, and was preferred over LLB in a majority of cases.

- In addition to enhancement of walking abilities in SCI patients, other clinical applications of FES include diaphragmatic/phrenic pacing, and spasticity control. Functional electrical stimulation has had some success in improving ventilatory function in adult patients with SCI (Glenn, et al., 1984; Carter, et al., 1987; Glenn, et al., 1988). Hunt, et al. (1988) reported that diaphragmatic pacing is also helpful for infants and children who need ventilatory support. Furthermore, in a 1992 review on the rehabilitation of children with SCI, Flett (1992) stated that diaphragmatic/phrenic pacing is indicated for children with quadriplegia at C3 or higher if they have viable phrenic nerves and adequate diaphragm and lung function. Candidates for diaphragmatic pacing should be stable and out of the acute phase of injury. The author stated that this approach of assisting ventilation in these patients resulted in psychological benefits to both the children and their families. Currently, bilateral stimulation at low frequency is more frequently used instead of stimulation of only one hemidiaphragm at a time, and adequate ventilation can be attained with 5 to 9 stimuli per minute.

- Diaphragmatic pacing has also been used to treat patients with central alveolar hypoventilation syndrome. Yasuma and associates (1998) noted that the respiratory assistance by the diaphragm pacemaker or the use of a mechanical ventilator as a backup was highly useful for the home care of a patient with central alveolar hypoventilation.
Garrido-Garcia and colleagues (1998) presented a series of patients with chronic ventilatory failure treated with electrophrenic respiration: 13 males and 9 females with a mean age of 12 +/- 11.5 years. The etiology was: 13 tetraplegia, 5 sequelae of surgical treatment of intracranial lesions, and 4 central alveolar hypoventilation. The mean duration of the conditioning period was 3 - 4 months. Eighteen patients (81.8 %) achieved permanent, diaphragmatically-paced breathing with bilateral stimulation and in 4 (18.2 %) patients, pacing was only during sleep. Five patients died (22.7 %): 2 during the hospital stay and 3 at home; 2 deaths had unknown cause and 3 were due respectively to, lack of at-home care, recurrence of an epidermoid tumor, and sequelae of accidental disconnection of the mechanical ventilation before beginning the conditioning period. Two cases were considered failures: 1 patient had transitory neurapraxia lasting 80 days, and the other had an ischemic spinal cord syndrome with progressive deterioration of the left-side response to stimulation. One patient had right phrenic nerve entrapment by scar tissue and 4 suffered infections. These results demonstrated that complete stable ventilation can be achieved using diaphragmatic pacing and that it improves the prognosis and life quality of patients with severe chronic respiratory failure.

- Girsch, et al. (1996) noted that ventilatory insufficiency due to central hypoventilation syndrome and SCI can be treated even in children with diaphragm pacing, provided the indication for implantation, containing medical and social aspects, was made correctly. Additionally, Flageole et al (1995) stated that pediatric surgeons should be aware of congenital central hypoventilation syndrome (CCHS) because it may be treated with surgically implanted electrodes that allow for pacing of the diaphragm. The technique has an acceptable complication rate, and it can greatly decrease the impact of the disease on the lifestyle and activity of the patient. Shaul, et al. (2002) stated that diaphragmatic pacing can provide chronic ventilatory support for children who suffer from CCHS or cervical SCI.

- Chen and Keens (2004) reported that all patients with CCHS require lifelong ventilatory support during sleep but some will be able to maintain adequate ventilation without assistance while awake once past infancy. However, some CCHS patients require ventilatory support for 24 hours/day. Modalities of home mechanical-assisted ventilation include positive pressure ventilation via tracheostomy, non-invasive positive pressure ventilation (bi-level ventilation), negative pressure ventilation and diaphragmatic pacers. Furthermore, Creasey, et al. (1996) reported that electrical stimulation has been used for over 25 years to restore breathing to patients with high quadriplegia causing respiratory paralysis and patients with central alveolar hypoventilation. Three groups have developed electrical pacing systems for long-term support of respiration in humans. These systems consist of electrodes implanted on the phrenic nerves, connected by leads to a stimulator implanted under the skin, and powered and controlled from a battery-powered transmitter outside the body. The systems differ principally in the electrode design and stimulation waveform. Approximately 1,000 people worldwide have received one of the three phrenic pacing devices, most with strongly positive results: reduced risk of tracheal problems and chronic infection, the ability to speak and smell more normally, reduced risk of accidental interruption of respiration, greater independence, and reduced costs and
Neuromuscular respiratory failure is the cause of death in the majority of patients with amyotrophic lateral sclerosis (ALS). Respiratory muscle dysfunction impacts on quality of life and survival. Yun and associates (2007) noted that closed loop systems may facilitate the implementation of diaphragmatic pacing for the treatment of many indications. They may allow for wider adoption of ventilatory support in central sleep apnea and improve quality of life in diseases of chronic hypoventilation, such as ALS.

Onders and colleagues (2009a) summarized the complete worldwide multi-center experience with diaphragm pacing stimulation (DPS) to maintain and provide diaphragm function in ventilator-dependent SCI patients and respiratory-compromised patients with ALS. It highlighted the surgical experiences and the differences in diaphragm function in these 2 groups of patients. In prospective FDA trials, patients underwent laparoscopic diaphragm motor point mapping with intra-muscular electrode implantation. Stimulation of the electrodes ensued to condition and strengthens the diaphragm. From March of 2000 to September of 2007, a total of 88 patients (50 SCI and 38 ALS) were implanted with DPS at 5 sites. Age of patients at implantation ranged from 18 to 74 years. Time from SCI to implantation ranged from 3 months to 27 years. In 87 patients the diaphragm motor point was mapped with successful implantation of electrodes with the only failure the second SCI patient who had a false-positive phrenic nerve study. Patients with ALS had much weaker diaphragms identified surgically, requiring trains of stimulation during mapping to identify the motor point at times. There was no peri-operative mortality even in ALS patients with forced vital capacity (FVC) below 50 % predicted. There was no cardiac involvement from diaphragm pacing even when analyzed in 10 patients who had pre-existing cardiac pacemakers. No infections occurred even with simultaneous gastrostomy tube placements for ALS patients. In the SCI patients, 96 % were able to use DPS to provide ventilation replacing their mechanical ventilators; and in the ALS studies, patients have been able to delay the need for mechanical ventilation up to 24 months. The authors concluded that this multi-center experience has shown that laparoscopic diaphragm motor point mapping, electrode implantation, and pacing can be safely performed both in SCI and in ALS. In SCI patients it allows freedom from ventilator and in ALS patients it delays the need for ventilators, increasing survival.

Onders and co-workers (2009b) summarized the largest series of surgical cases in ALS during multi-center prospective trials of the laparoscopic DPS to delay respiratory failure. The overall strategy outlined includes the use of rapidly reversible short-acting analgesic and amnestic agents with no neuromuscular relaxants. A total of 51 patients were implanted from March 2005 to March 2008 at 2 sites. Age of patients ranged from 42 to 73 years and the percent predicted FVC ranged from 20 % to 87 %. On pre-operative blood gases, Pco(2) was as high as 60. Using this protocol, there were no failures to extubate or 30-day mortalities. The DPS system increases the respiratory system compliance by decreasing posterior lobe atelectasis and can stimulate respirations at the end of each case. The authors concluded that laparoscopic surgery with general anesthesia can be safely performed in patients with ALS undergoing DPS.
• It has not been consistently shown that spasticity decreases with long-term FES. Yarkony, et al. (1992) claimed that no definitive statement can be made regarding the type, the magnitude, or even the direction of the effect of electrical stimulation on the spasticity of patients with SCI. Current management strategy for this condition ranges from rehabilitative physical therapy, re-education therapeutic exercise, oral medications such as Dantrium, Valium, and Lioresal (baclofen), intrathecal infusion of baclofen, motor point blocks or nerve blocks, to destructive neurosurgical procedures (Merritt 1981).

• Functional electrical stimulation exercise training has been claimed to strengthen and increase endurance of muscles paralyzed following UMN injuries, thereby improving physical fitness and health of individuals with SCI. However, fatigue of electrically stimulated muscles is a principal limiting factor in the applications of FES. Glaser (1986) stated that more research is needed to ascertain the mechanisms of fatigue of this type of peripherally induced exercise, and to substantiate the potential fitness and health benefits of FES exercise training. Sipski, et al. (1989) examined patient perceptions of FES bicycle ergometry. These researchers suggested that future studies should include a placebo control group. They also found that 6 of 9 patients with a history of neurogenic pain reported an increase in this pain which caused them to drop out of the training program. The cause of this intensification of pain was unclear. Leeds, et al. (1990) reported that bone mineral density did not increase in quadriplegic men who had undergone 6 months of FES cycle ergometry training. Sipski, et al. (1993) stated that more research is needed to document the benefits, if any, of the use of bicycle ergometry to justify the use of this equipment. Pentland (1993) claimed that much more research in FES techniques and treatment protocols is needed before this approach can be used widely as a means to provide cardiorespiratory fitness for quadriplegics.

• The principal goal of stroke rehabilitation is to improve the functional abilities of these patients, thus affording them greater independence in activities of daily living and improving their quality of life. Conventional modalities of stroke rehabilitation comprise various combination of range of motion and muscle strengthening exercises, mobilization activities, and compensatory techniques. Other therapies include neurophysiological and/or developmental based methods in which the therapeutic program incorporates neuromuscular re-education techniques. In this regard, FES has been employed in the rehabilitation of stroke patients. It has been utilized to manage contracture of joints, maintain range of motion, facilitate voluntary motor control, and reduce spasticity. However, there is insufficient evidence that FES is effective as a rehabilitative tool for patients who suffered strokes. In particular, there is little data supporting the long-term effectiveness of this modality for stroke rehabilitation.

• In a review on the clinical applications of FES, Kumar, et al. (1995) stated that advances in electrode technology and control and command sources activation systems as well as development of close-loop systems are needed if wide patient acceptance of this modality (FES) is to be ensured. The Agency for Health Care Guideline and Research's clinical guideline on “Post-stroke Rehabilitation” maintains that neither research evidence nor expert consensus adequately supports recommendation concerning the use of FES in the rehabilitation of stroke patients (Gresham, 1995). Furthermore, Hummelsheim, et al.
(1997) reported that repetitive electrical muscle stimulation did not improve biomechanical or functional motor parameters of the centrally paretic hand and arm of stroke patients.

- In a randomized controlled study, Yan and colleagues (2005) evaluated whether FES was more effective in promoting motor recovery of the lower extremity and walking ability than standard rehabilitation alone. Forty-six patients were assigned randomly to one of three groups receiving standard rehabilitation with FES or placebo stimulation or alone (control). They received treatment for three weeks, starting shortly after having the stroke. Outcome measurements included composite spasticity score, maximum isometric voluntary contraction of ankle dorsi-flexors and planter-flexors, and walking ability. After 3 weeks of treatment, those receiving FES plus standard rehabilitation did better on several measures of lower limb functioning compared to the other two groups. All patients in the FES group were able to walk after treatment, and 84.6% of them returned home, in comparison with the placebo (53.3%) and control (46.2%) groups. However, these authors stated that generalization of the results from this study should be performed with caution because of subject selection criteria, which did not cover all stroke categories or subjects aged younger than 45 or older than 85 years. Further studies are now needed to see whether FES can work with a wide range of stroke patients.

- Although a number of studies suggested that electrical stimulation may be effective for reducing shoulder pain and subluxation or improving the function of wrist and finger extensors following stroke (Chantraine et al, 1999, Wang et al, 2002, and Yozbatrian et al, 2006), more research is needed to validate these findings. Chantraine et al (1999) reported that FES program was significantly effective in reducing the severity of subluxation and pain and possibly may have facilitated recovery of the shoulder function in hemiplegic patients. However, they noted that more research addressing the mechanism of the actions of FES on pain and subluxation of the hemiplegic shoulder is needed.

- Chae and Yu (2000) critically evaluated the clinical effectiveness of neuromuscular electrical stimulation in treating motor dysfunction in hemiplegia. Three distinct applications were reviewed in the areas of motor relearning, shoulder dysfunction, and neuroprostheses. Assessment of clinical effectiveness and recommendations on clinical implementation were based on the weight of published scientific evidence. With respect to motor relearning, evidence supports the use of neuromuscular electrical stimulation to facilitate recovery of muscle strength and coordination in hemiplegia. However, effects on physical disability are uncertain. With respect to shoulder dysfunction, neuromuscular electrical stimulation decreases shoulder subluxation, at least in the short term. However, effects on shoulder pain and disability are also uncertain. With respect to neuroprosthesis systems, clinically deployable upper extremity systems must await the development of more sophisticated control methods and greater fundamental understanding of motor dysfunction in hemiplegia. The evidence for clinical feasibility of lower extremity neuroprostheses is stronger, and investigations on clinical effectiveness should be pursued. The authors concluded that the application of neuromuscular electrical stimulation for motor relearning and shoulder dysfunction are ready for more rigorous scientific and clinical assessment via large, multi-center, randomized clinical trials.
• In a Cochrane review, Price and Pandyan (2000) ascertained the effectiveness of any form of surface electrical stimulation (ES) in the prevention and/or treatment of pain around the shoulder at any time after stroke. These investigators concluded that the evidence from randomized controlled studies so far does not confirm or refute that ES around the shoulder after stroke influences reports of pain, but there do appear to be benefits for passive humeral lateral rotation. A possible mechanism is through the reduction of glenohumeral subluxation. The authors stated that further studies are needed.

• Turner-Stokes and Jackson (2002) noted that although a wide variety of physical changes are associated with hemiplegic shoulder pain (HSP), these can be categorized into two presentations; (i) "flaccid", and (ii) "spastic". Management should vary accordingly; each presentation requiring different approaches to handling, support and intervention. In the "flaccid" stage, the shoulder is prone to inferior subluxation and vulnerable to soft-tissue damage. The arm should be supported at all times and FES may reduce subluxation and enhance return of muscle activity. In the "spastic" stage, movement is often severely limited. Relieving spasticity and maintaining range requires expert handling; over-head exercise pulleys should never be used. Local steroid injections should be avoided unless there is clear evidence of an inflammatory lesion. The authors concluded that HSP requires coordinated multi-disciplinary management to minimize interference with rehabilitation and optimize outcome. They stated that more research is needed to determine effective prophylaxis and document the therapeutic effect of different modalities in the various presentations.

• The New Zealand Guidelines Group's guideline for management of stroke (2003) stated that the use of FES and transcutaneous electrical nerve stimulation for post-stroke patients is not recommended. Furthermore, Van Peppen, et al. (2004) determined the evidence for physical therapy interventions aimed at improving functional outcome after stroke. These researchers reported that while strong evidence was found regarding neuromuscular stimulation for glenohumeral subluxation, no or insufficient evidence in terms of functional outcome was found for functional and neuromuscular ES aimed at improving dexterity or gait performance; orthotics and assistive devices; and physical therapy interventions for reducing hemiplegic shoulder pain and hand edema. Furthermore, in a review on therapeutic orthosis and ES for upper extremity hemiplegia after stroke, Aoyagi and Tsubahara (2004) stated the longer term effectiveness after discontinuation as well as the motor recovery mechanism of ES or robotic devices remains unclear. More research is needed to determine the evidence-based effectiveness of ES or other devices for stroke survivors.

• In a Cochrane review on electrostimulation for promoting recovery of movement or functional ability after stroke, Pomeroy et al (2006) concluded that "[a]t present, there are insufficient robust data to inform clinical use of electrostimulation for neuromuscular re-training. Research is needed to address specific questions about the type of electrostimulation that might be most effective, in what dose and at what time after stroke".

• Functional electrical stimulation is being investigated as a means to improve hand and arm function after stroke-related paralysis or spinal cord injury. The NESS H200 hand rehabilitation system (Bioness, Valencia, CA), formerly the Handmaster, is a
neuroprosthesis that uses mild electrical stimulation in an attempt to activate muscle
groups in the forearm to produce functional movement patterns in the hand. It is designed
to be used as part of a self-administered home-based rehabilitation program for the
treatment of upper limb paralysis from hemiplegic stroke, traumatic brain injury or C5 –
C6 spinal cord injury. The system contains a custom-fitted orthosis and a control unit.
The control unit allows the user to adjust the stimulation intensity and training mode.
Exercise sessions can be gradually increased to avoid muscle over-fatigue.

- Initial case studies have indicated that the use of FES as an adjunct to physical therapy
can improve patient outcomes (Weingarden, et al., 1998; Alon, et al., 2002; Alon, et al.,
2003; Berner, et al., 2004). However, the studies lacked a control group, involved small
study populations with limited periods of follow-up. Thus, it is difficult to ascertain the
significance of the treatment effects and their durability.

- De Kroon, et al. (2002) systematically reviewed the evidence for electrical stimulation to
improve motor control and functional abilities of the upper extremity after stroke. The
authors reported that "[t]he results suggest that electrical stimulation has a positive effect
on motor control, although it is not known if this improvement is clinically relevant." The
review stated that "[n]o conclusions can be drawn concerning the effect of electrical
stimulation on functional abilities."

- Ring and Rosenthal (2005) evaluated the effects of daily neuroprosthetic (NESS
Handmaster) FES in sub-acute stroke. Patients were clinically stratified to 2 groups: (i)
no active finger movement, and (ii) partial active finger movements, and then were
randomized to control and neuroprosthesis groups. Observer blinded evaluations were
performed at baseline and completion of the 6-week study. A total of 22 patients with
moderate to severe upper limb paresis 3 to 6 months after stroke were enrolled in this
study. They were in day hospital rehabilitation, receiving physical and occupational
therapy 3 times weekly. The neuroprosthesis group used the device at home. The
neuroprosthesis group had significantly greater improvements in spasticity, active range
of motion and scores on the functional hand tests (those with partial active motion). Of
the few patients with pain and edema, there was improvement only among those in the
neuroprosthesis group. There were no adverse reactions. These investigators concluded
that supplementing standard outpatient rehabilitation with daily home neuroprosthetic
activation improves upper limb outcomes.

- In a systematic review, Meilink et al (2008) evaluated if electromyography-triggered
neuromuscular electrical stimulation (EMG-NMES) applied to the extensor muscles of
the forearm improves hand function after stroke. A total of 8 studies, selected out of 192
hits and presenting 157 patients, were included in quantitative and qualitative analyses.
The methodological quality ranged from 2 to 6 points. The meta-analysis revealed non-
significant effect sizes in favor of EMG-NMES for reaction time, sustained contraction,
dexterity measured with the Box and Block manipulation test, synergism measured with
the Fugl-Meyer Motor Assessment Scale and manual dexterity measured with the Action
Research Arm test. The authors concluded that no statistically significant differences in
effects were found between EMG-NMES and usual care. Most studies had poor
methodological quality, low statistical power and insufficient treatment contrast between
experimental and control groups. In addition, all studies except 2 investigated the effects
of EMG-NMES in the chronic phase after stroke, whereas the literature suggests that an early start, within the time window in which functional outcome of the upper limb is not fully defined, is more appropriate.

- In a retrospective cohort study, Meijer, et al. (2009) evaluated the short-term and long-term use of a hybrid orthosis for NMES of the upper extremity in patients (n = 110) after chronic stroke. The Modified Ashworth Scale (0-5) for wrist (primary outcome) and elbow flexor hypertonia, visual analog scale (0-10) for pain, edema score (0-3), and passive range of wrist flexion and extension (pROM, degrees) were assessed prior to Handmaster orthosis prescription (T0), after 6 weeks try-out (T1) and a subsequent 4 weeks withhold period (T2). Long-term use was evaluated using a questionnaire. Non-parametric analyses and predictive values were used for statistical analyses. Of the 110 patients, 78.2% were long-term Handmaster orthosis users. Long-term users showed significant short-term (T0-T1) improvements on all impairment scores and a significant relapse of wrist and elbow Modified Ashworth Scale (T1-T2). Non-users showed significant short-term effects on elbow Modified Ashworth Scale and visual analog scale only. Positive predictive values of short-term effects for long-term use varied between 75% and 100%, with 85% (95% confidence interval (CI) 0.72 - 0.93) for wrist Modified Ashworth Scale. Negative predictive values were low (11 - 27%). The authors concluded that short-term Handmaster orthosis effects were generally beneficial for hypertonia, pain, edema, and pROM, especially in long-term users and that short-term beneficial effects were highly predictive for long-term use, but not for non-use.

- The results of these studies are promising, however, these findings need to be validated by further investigation with more patients and follow-up data.

- On the other hand, NMES has been shown to be an effective rehabilitative regimen for patients following ligament/knee surgery. It prevents muscle atrophy associated with knee immobilization, enables patients to ambulate sooner, and reduces the use of pain medication as well as length of hospital stay (Arvidsson, 1986; Lake, 1992; Gotlin, et al., 1994; Snyder-Mackler, et al., 1995).

- Bax, et al. (2005) systematically reviewed the available evidence for the use of neuromuscular electrical stimulation in increasing strength of the quadriceps femoris. The authors concluded that limited evidence suggests that NMES can improve strength in comparison with no exercise, but volitional exercises appear more effective in most situations. The authors' cautious conclusions reflect the general poor quality of the included studies.

- Neurogenic bladder dysfunction is due to lesions of the innervation either within the central nervous system or in the peripheral nerves of the bladder and urethra. The Lapides Classification is the scheme most frequently used by urologists to classify patients with neuropathic voiding dysfunction. This classification system is divided into five categories: (i) sensory neurogenic bladder, (ii) motor paralytic bladder, (iii) uninhibited neurogenic bladder, (iv) reflex neurogenic bladder, and (v) autonomous neurogenic bladder.

- A sensory neurogenic bladder is caused by diseases that selectively disrupt the sensory fibers between the bladder and spinal cord or the afferent pathways to the brain. This is commonly observed in patients with peripheral neuropathies such as diabetes mellitus,
tabes dorsalis, folic acid avitaminosis, and pernicious anemia. A motor paralytic bladder is the consequence of diseases/processes that interrupt the parasympathetic motor innervation of the bladder. It can be produced by extensive pelvic surgery or trauma or herpes zoster. An uninhibited neurogenic bladder is due to the absence of cerebral inhibition of the micturition reflex as a result of injury or disease in the corticoregulatory tract. Cerebral lesions such as stroke, tumors, arteriosclerosis, and traumatic lesions are the most common causes of this type of voiding disorder. A reflex neurogenic bladder is often observed in the post-spinal shock condition existing following the complete transection of the sensory and motor tracts between the sacral spinal cord and the brain stem. This is often the result of traumatic SCI and transverse myelitis, but may also occur with severe demyelinating disease or tumor. An autonomous neurogenic bladder is caused by complete motor and sensory separation of the bladder from the sacral spinal cord. Diseases that destroy the sacral spinal cord or cause extensive damage to the sacral roots or pelvic nerves can produce this type of disorder. It should be noted that many patients do not exactly fit into one or another of these categories because of gradations of sensory, motor, and mixed lesions. Thus, the patterns produced after different types of peripheral denervation may vary greatly from those that are classically described (Barrett & Wein, 1991).

- Neurogenic bladder dysfunction can also be associated with other neurological diseases including cerebellar ataxia, multiple sclerosis, Parkinson's disease, and Shy-Drager syndrome. In children, the common causes of neurogenic bladder dysfunction are sacral agenesis, tethered cord syndrome, and myelomeningocele. The main results of neurogenic bladder dysfunction are renal damage and urinary incontinence (UI). The former is due to either high intravesical pressure or the association of vesicoureteral reflux and infection. The mechanisms for UI are multiple including (i) overflow incontinence caused by detrusor atonia with a non-relaxing sphincter, (ii) lack of storage capacity caused by hyperreflexia or poor compliance, and (iii) low urethral resistance caused by denervation of the sphincters. Oftentimes, the causes of UI are mixed (Wein 1992; Fernandes et al, 1994).

- The management of patients with neurogenic bladder dysfunction entails clean intermittent catheterization, pharmacotherapy (e.g., oxybutynin, phenoxybenzamine, and anti-cholinergic medications such as tolterodine), and surgical interventions (e.g., urinary diversion or bladder augmentation). Moreover, stimulation of sacral anterior nerve roots in association with posterior rhizotomy has been used in the treatment of patients with suprasacral SCI. The FDA approved the Vocare Bladder System as a humanitarian use device based on a study of 23 patients who received device in association with posterior rhizotomy and were followed for a minimum of 3 months. Comparisons were made with the implanted stimulator turned either on or off; thus patients served as their own controls. The primary outcome measures were improvement in bladder emptying as evidenced by the ability to void more than 200 ml on demand with post-void residual urine volumes of less than 50 ml. Secondary endpoints included reduction in the use of urinary catheters, number and severity of episodes of UI, reduction in incidence of urinary tract infections, and results of a user satisfaction survey.
After 3 months, 90% of the patients were able to urinate more than 200 ml on demand and 81% had post-void residual urine volumes of less than 50 ml. A total of 73% of patients reported fewer urinary tract infections and at 6 months, about 50% of the patients were using the device exclusively for micturition, and no external devices (e.g., catheters) were needed. The results reported in this study were in agreement with those reported by Van Kerrebroeck, et al. (1996) as well as Egon, et al. (1998). The former group of investigators reported on the outcomes of 47 patients who were followed for a minimum of 6 months. Complete continence was observed in 43 of the 47 patients, and 41 of the 47 patients used only the stimulator for bladder emptying. The residual urine volume also decreased to less than 50 ml in 41 patients. The incidence of urinary tract infections also decreased. The latter group of researchers reported on a case series of 93 patients. A total of 83 of the 93 patients used their implants for micturition with residual volumes of less than 50 ml.

Jamil (2001) stated that the Finetech-Brindley stimulator can be recommended to female patients after 3 months and to male patients after 9 months of complete supra-sacral SCI. The presence of 3 of the 4 non-vesical sacral segment reflexes (ankle jerks, bulbocavernous reflex, anal skin reflex, and reflex erection) and a phasic detrusor pressure rise of 35 mm H2O in the female and 50 cm H2O in the male on cystometry indicates intact efferent nerve supply to the bladder and consequently the possibility of success of the implanted stimulator.

A less widely used method for the treatment of neurogenic bladder is transurethral electrical bladder stimulation (TEBS). This modality was first introduced in Europe by Katona and Berenyi (1975) to treat patients with myelomeningocele. It was introduced in the United States by Kaplan and Richards (1986). This procedure has been utilized with the theory that bladder stimulation promotes new sensory awareness of bladder filling and a restoration of detrusor contractility (i.e., disappearance of uninhibited bladder contractions and replacement with normal contractions). Briefly, this procedure involves the filling of the bladder to approximately half capacity with normal saline via an electrocatheter under sterile conditions. The catheter is then connected to a pressure recorder for continuous monitoring of bladder pressure. A rectal balloon catheter is employed to subtract abdominal pressure and a ground electrode is placed on the leg. Stimulation parameters are as follow: (i) voltage -- 0.5 to 10 mA, (ii) frequency -- 40 to 100 Hz, (iii) duration -- 2 to 8 msec, and (iv) interval -- 1 to 10 sec. Patients undergo one or more series of bladder stimulation. The first series of stimulation begins with an evaluation session, which is followed by 10 to 30 90-minute daily sessions. Each of these sessions comprises a 15-minute period of monitoring of bladder activity followed by 60 minutes of bladder stimulation and then another 15 minutes of observation of bladder activity. Between series there is a rest period of 3 to 6 months during which no stimulation is given. Following the rest interval, a subsequent series consisting of 5 to 15 daily sessions will commence (Boone, et al., 1992; Kaplan & Richards, 1988; Kaplan, et al., 1989).

Although earlier reports (Katona & Berenyi, 1975; Kaplan & Richards, 1986; Kaplan & Richards, 1988; Kaplan, et al., 1989) claimed that TEBS is effective in treating patients with neurogenic bladder dysfunction, recent studies (Boone, et al., 1992; Decter, et al.,
1992; Lyne & Bellinger, 1993; Decter, et al., 1994) have not been able to replicate such findings. The two most relevant outcome measures in assessing the effectiveness of TEBS are restoration of normal detrusor contractility and urinary continence. Lyne and Bellinger (1993) treated 17 patients with neurovesical dysfunction with TEBS. Overall, only 5 (41.7 %) of the 12 patients with fully standardized serial cystometry experienced a durable increase in bladder capacity, and no patient achieved volitional voiding. Decter, et al. (1992) treated 21 patients with neurogenic bladder dysfunction using TEBS. They found that 20 % of the patients showed an increase in bladder capacity and 30 % experienced a decrease in end filling pressures. However, these effects did not significantly change patients' daily voiding regimens. In a follow up study, Decter, et al. (1994) stated that TEBS is a time consuming and labor intensive procedure. Additionally, the limited urodynamic benefits attained by patients have not changed their daily routine of bladder management. Because of the afore-mentioned factors, these investigators are not accepting any new patients in their TEBS program. In an earlier study, Nicholas and Eckstein (1975) reported their findings of TEBS in the treatment of 20 patients with neurogenic bladder dysfunction due to spina bifida. No patient attained bladder sensation and the essential pattern of detrusor activity in these patients was unchanged by TEBS.

- Boone et al (1992) performed the only prospective, randomized, sham controlled and blinded clinical trial on the use of TEBS in 36 children with myelomeningocele. Patients were allocated to either a 3-week period of TEBS or sham treatment, which was followed by a 3-month rest period, and then all patients were treated with TEBS for an additional 3 weeks. Bladder capacity, sensation, and compliance as well as continence were evaluated. Transurethral electrical bladder stimulation did not produce any beneficial effects even in patients who had undergone a total of 6 weeks of active stimulation.

- Van Balken, et al. (2004) reviewed the literature on the application of various devices and techniques for the electrical stimulation treatment of lower urinary tract (e.g., bladder) dysfunction with respect to mechanism of action and clinical outcome. These investigators concluded that randomized clinical trials to compare different techniques and evaluate placebo effects are urgently needed, as are further studies to elucidate modes of action to improve stimulation application and therapy results. The introduction of new stimulation methods may provide treatment alternatives as well as help answer more basic questions on electrical neurostimulation and neuromodulation.

- Cerebral palsy (CP) refers to a wide variety of non-progressive brain disorders resulting from insults to the central nervous system during the perinatal period. Infants born prematurely and full-term infants with low birth weight have the highest risk of developing CP. Infants whose birth weights are less than 2,500 g account for approximately one-third of all babies who later demonstrate signs of CP. Moreover, the rate of CP is about 30 times higher in babies who weigh less than 1,500 g at birth than in full-term babies with normal weight (Kuban and Leviton, 1994). Traditionally, the adverse effects of spasticity are managed by means of pharmacotherapy, physical therapy, bracing, casting, splinting, orthopedic surgeries, and more recently selective posterior rhizotomy. Various forms of electrical stimulation have also been employed for the management of patients with CP including neuromuscular electrical stimulation.
(NMES), which has been used to increase range of motion, decrease spasticity, and enhance muscle rehabilitation.

- The exact mechanisms by which NMES might improve motor function in children with CP remain unclear. It may be related to its ability to increase range of motion, temporarily decrease spasticity, and enhance muscle rehabilitation. Moreover, Pape, et al. (1993) suggested that NMES applied during sleep might encourage the differential growth of atrophic non-spastic antagonistic muscles. As a result, the decreased imbalance at the end-organ level might improve motor function.

- Pape, et al. (1993) reported their findings regarding the use of NMES for improving motor deficits in children with CP. Six patients with mild ambulatory spastic hemiplegia or diplegia underwent a study of overnight low intensity sub-threshold transcutaneous electrical stimulation (ES). Only 5 of the 6 patients completed the study. After 6 months of ES, significant improvement was observed on the Peabody Developmental Motor Scales scores in gross motor, locomotor, and receipt/propulsion skills. However, balance and non-locomotor scores showed no significant changes. On the other hand, when ES was withdrawn for 6 months, there was uniform partial regression in scores. Moreover, reinstitution of treatment by ES resulted in additional improvement in total gross motor, balance, locomotor, and receipt/propulsion skills, but not for non-locomotor skills. The authors concluded that in selective cases, especially children with mild CP, overnight ES may be a useful adjunct to conventional rehabilitation services. Although the findings by Pape et al appear to be encouraging, this was an uncontrolled study with 5 children who were 3 to 5 years old, a time when rapid changes are expected in these children. More importantly, no attempt was made to standardize physical therapy throughout the study. All but one subject continued to receive rehabilitative procedures which may have a confounding effect on the outcome of the study. It is unclear whether these improvements were translated into improvements in activities of daily living. Additionally, there were no data regarding the long term effects of this treatment modality.

- Hazlewood, et al. (1994) evaluated the effectiveness of ES in treating children with hemiplegic CP. Ten patients were given ES of the anterior tibial muscles by their parents daily for 1 hour for 35 consecutive days in conjunction with their physical therapy (PT) regimen. Ten patients who were matched for age, severity of gait pattern, and for limitation of range of passive dorsiflexion of the ankle served as controls and continued with their current PT program. Active and passive ranges of movement of the ankle, as well as knee and ankle motion during ambulation were recorded by means of electrogoniometers before and after ES. For passive joint-range measurements, there were no significant changes in the range of ankle plantar-flexion, or dorsiflexion with the knee flexed for patients who received tibial muscles ES. However, there was a significant increase in dorsiflexion of the ankle with the knee extended. The mean ranges of the stimulated group of patients for dorsiflexion with the knee extended increased from 40 to 60 % of the range of the non-affected side. For active joint-range measurements, there was a significant difference in the range of voluntary dorsiflexion when the patient was sitting, comparing the experimental and control groups post-test, but no significant differences comparing the pre-and post-changes of the two groups. Furthermore, gait analysis and ankle motion showed little change. The authors concluded that because of
the complex and diverse pathology associated with CP, the application of ES for the treatment of children with this disorder requires further investigations to determine which types of CP patients are likely to benefit from ES as well as the desired parameters of stimulation before this modality should be used widely in the clinical setting.

- Steinbok, et al. (1997) concluded that therapeutic ES may be beneficial in children with spastic CP who have undergone a selective posterior rhizotomy more than 1 year ago. However, the authors concluded that more research is needed to confirm these results. More importantly, it must be emphasized that these findings cannot be extrapolated to the larger population of children with spastic CP who have not undergone selective posterior rhizotomy.

- In a systematic review of the literature on electrical stimulation for cerebral palsy, Kerr, et al. (2004) concluded that "[t]here is more evidence to support the use of NMES than TES [threshold electrical stimulation]. However, the findings should be interpreted with caution as the studies had insufficient power to provide conclusive evidence for or against the use of these modalities." An earlier systematic evidence review by Boyd, et al. (2001) reached similar conclusions about the paucity of evidence for the use of electrical stimulation for cerebral palsy.

- Acute idiopathic facial paresis is often known as Bell's palsy. Treatment of idiopathic Bell's palsy is still not well-defined. Conservative approaches entail physiotherapies such as facial exercises, massage, and muscle relaxation, which may support rehabilitation and possibly reduce the production of pathological synkinesia. Medical treatments include botulinum toxin type A (Botox) as well as a combined regimen of cortisone, virostatic agents, hemorrhheologic substances, and possibly antibiotics. Moreover, available evidence from randomized controlled trials does not show significant benefit from treating Bell's palsy with corticosteroids (Salinas, et al., 2002). Surgical decompression of the facial nerve remains controversial.

- Adour (1991) stated that decompression of the facial nerve and electrotherapy are not advised for the management of patients with idiopathic (Bell's) palsy. This is in agreement with Wolf who stated that ES should not be used in the treatment of Bell's palsy. Buttress and Herren (2002) reviewed the medical literature to ascertain whether ES had any advantages over facial exercises in promoting recovery after Bell's palsy. Of the 270 papers reviewed by the authors, only 1 presented the best evidence to answer the clinical question. The authors stated that there is no evidence to suggest that either facial exercises or ES is beneficial to patients with acute Bell's palsy. However, evidence does exist to suggest the use of ES in patients with chronic Bell's palsy, although the study design was not rigorous.

- Individuals with stroke, CP, multiple sclerosis, and SCI/traumatic brain injury may exhibit foot drop, a condition caused by weakness or paralysis of the muscles involved in lifting the front part of the foot. The WalkAide is a product of Myo-Orthotics Technology, a term coined by the manufacturer, Innovative Neurotronics (Austin, TX). According to the manufacturer, it represents the convergence of orthotic technology (which braces a limb) and electrical stimulation (which restores specific muscle function). The WalkAide device is intended to counteract foot drop by producing dorsiflexion of the ankle during the swing phase of the gait. The device attaches to the
leg, just below the knee, near the head of the fibula. During a gait cycle, the WalkAide stimulates the common peroneal nerve, which innervates the tibialis anterior and other muscles that produce dorsiflexion of the ankle. The WalkAide is designed to offer persons with foot drop increased mobility, functionality and independence. It was cleared by the FDA through the 510(k) process. However, there is currently insufficient evidence to support its use for foot drop and other indications. Prospective clinical studies of the WalkAide device are necessary to evaluate whether it improves function and reduces disability compared to standard bracing in persons with foot drop.

- Sheffler and associates (2007) reported the findings of peroneal nerve stimulation in patients with hemiplegia. Two chronic stroke survivors who utilized an ankle foot orthosis (AFO) prior to study entry were evaluated at baseline and after 4 weeks of daily use of a surface peroneal nerve stimulator. Participants were assessed without their dorsiflexor assistive device, using the modified Emory Functional Ambulation Profile (mEFAP). The participants demonstrated improvement in all 5 components of the mEFAP relative to baseline. These case reports indicated that enhanced functional ambulation may be an important therapeutic effect of peroneal nerve stimulation. The authors stated that controlled trials are needed to demonstrate a cause-and-effect relationship.

- In a randomized controlled study, Kottink and colleagues (2008) examined the effect of an implantable peroneal nerve stimulator for 6 months versus an AFO in patients with chronic stroke and foot drop (n = 29). The mean time from stroke was 7.3 years (SD = 7.3), and all subjects were community ambulators. The FES group received the implantable stimulation system for correction of their foot drop. The control group continued using their conventional walking device (i.e., AFO, orthopedic shoes, or no walking device). All subjects were measured at baseline and at 4, 8, 12, and 26 weeks in the gait laboratory. The therapeutic effect of FES on the maximum value of the root mean square (RMSmax) of the tibialis anterior (TA) muscle with both flexed and extended knees and walking speed were selected as the primary outcome measures. The RMSmax of the peroneus longus (PL), gastrocnemius (GS), and soleus (SL) muscles with both flexed and extended knees and muscle activity of the TA muscle of the affected leg during the swing phase of gait were selected as secondary outcome measures. A significantly higher RMSmax of the TA muscle with extended knee was found after using FES. No change in walking speed was found when the stimulator was not switched on. A significantly increased RMSmax of the GS muscle with both flexed and extended knees was found after using FES. The authors concluded that functionally, no therapeutic effect of implantable peroneal nerve stimulation was found. However, the significantly increased voluntary muscle output of the TA and GS muscles after the use of FES suggested that there was a certain extent of plasticity in the subjects in this study.

- The American Association of Neuromuscular and Electrodiagnostic Medicine, the American Academy of Neurology, and the American Academy of Physical Medicine & Rehabilitation (Bril et al, 2011) developed a scientifically sound and clinically relevant evidence-based guideline for the treatment of painful diabetic neuropathy (PDN). The basic question that was asked was: "What is the efficacy of a given treatment (pharmacological: anticonvulsants, antidepressants, opioids, others; non-
pharmacological: electrical stimulation, magnetic field treatment, low-intensity laser treatment, Reiki massage, others) to reduce pain and improve physical function and quality of life (QOL) in patients with PDN"? A systematic review of literature from 1960 to August 2008 was performed, and studies were classified according to the American Academy of Neurology classification of evidence scheme for a therapeutic article. Recommendations were linked to the strength of the evidence.

- The results indicated that pregabalin is established as effective and should be offered for relief of PDN (Level A). Venlafaxine, duloxetine, amitriptyline, gabapentin, valproate, opioids (morphine sulfate, tramadol, and oxycodone controlled-release), and capsaicin are probably effective and should be considered for treatment of PDN (Level B). Other treatments have less robust evidence, or the evidence is negative. Effective treatments for PDN are available, but many have side effects that limit their usefulness. Few studies have sufficient information on their effects on function and QOL.

- In a case-series study, Wahls et al (2010) examined if NMES would improve gait disability in patients with secondary progressive multiple sclerosis (SPMS) or primary progressive multiple sclerosis (PPMS). Participants were treated using NMES coupled with a home-exercise program (HEP) to treat MS-related gait disability. Between June 2007 and June 2009, a licensed physical therapist used NMES coupled with a HEP to work with patients who had SPMS/PPMS and MS-related gait disability. All of the cases in which an NMES test session of NMES was conducted were included in the case series. Data regarding MS symptoms, treatment, gait, and function were abstracted from the PT clinic notes.

- Results of assessment with the expanded Kurtzke Disability Status Scale (EDSS) at presentation and at most recent visit were abstracted from the clinical record by the treating physical therapist. A total of 9 patients (7 with SPMS and 2 with PPMS) met inclusion criteria for review. Mean of years of diagnosis was 10.4 (range of 4 to 15), and mean EDSS score at presentation was 5.9 (range of 4.5 to 6.5). Mean of days of NMES was 140 (range of 22 to 495). Mean EDSS scores improved by 0.78 (range of 0 to 2.0). The authors concluded that NMES was associated with measurable gains in ambulatory function in patients with gait disability associated with SPMS and PPMS. Moreover, they stated that additional studies are needed.

- Giggins et al (2012) evaluated the effectiveness of surface NMES in the treatment of knee osteoarthritis. A systematic review and meta-analysis of randomized controlled trials (RCTs) and controlled clinical trials was performed. Studies were identified from databases (MEDLINE, EMBASE, CINAHL, Sports Discus, PEDro and the Cochrane Library) searched to January 2011 using a battery of keywords. Two reviewers selected studies meeting inclusion criteria. The methodological quality of the included studies was assessed using the Thomas Test and the strength of the evidence was then graded using the Agency for Health Care Policy and Research guidelines. Data were pooled and meta-analyses were performed.

- A total of 9 RCTs and 1 controlled clinical trial, studying a total of 409 participants (n = 395 for RCTs, and n = 14 for controlled trial) with a diagnosis of osteoarthritis were included. Inconsistent evidence (level D) was found that NMES has a significant impact on measures of pain, function and quadriceps femoris muscle strength in knee
osteoarthritis. The authors concluded that the role of NMES in the treatment of knee osteoarthritis is ambiguous. Thus, future work is needed in this field to clearly establish the role of NMES in this population.

- Threshold electrical stimulation (also known as therapeutic electrical stimulation) entails the use of low-intensity ES, usually at night. For patients with CP, threshold electrical stimulation (TES) aims to (i) strengthen muscles weakened by non-use and (ii) increase joint mobility, thus, resulting in improved voluntary motor function.

- In a randomized, controlled, cross-over trial, Sommerfelt et al (2001) evaluated the effect of TES applied to antagonists of spastic leg muscles on gross motor function in children with spastic diplegic CP. A total of 12 children between 5 and 12 years of age completed a 24-month cross-over study in which 6 were randomly assigned to receive TES for the first 12 months and the remaining 6 for the last 12 months. Physiotherapy and a home training program were not altered. All were evaluated blindly in terms of tests of motor function and video recordings at the start and at 12 and 24 months. At the end of the study parents/carers gave a subjective assessment of the effect of TES.

  - No significant effect of TES on motor or ambulatory function was found on the blinded evaluation, but parents of 11 of the 12 children stated that TES had a significant effect. The authors concluded that it is unlikely that TES has a significant effect on motor and ambulatory function in children with spastic diplegia CP.

- In a randomized, double-blind, placebo-controlled clinical trial, Dali et al (2002) studied whether a group of stable children with CP (36 boys, 21 girls; mean age of 10 years 11 months with a range of 5 to 18 years) would improve their motor skills after 12 months of TES; 2/3 received active and 1/3 received inactive stimulators. The primary outcome was change in summary indices of the performance measurements in a set of motor function tests. Tests were videotaped and assessed blindly to record qualitative changes that might not be reflected in performance measurements. Fifty-seven of 82 subjects who were able to walk at least with a walker, completed all 12 months of treatment (hemiplegia n = 25; diplegia n = 32). There was no significant difference between active and placebo treatment in any of the tested groups, nor combined.

  - Visual and subjective assessments favored TES (non-significant), whereas objective indices showed the opposite trend. The authors concluded that TES in these patients did not have any significant clinical effect during the test period.

- In a randomized placebo-controlled study, Kerr et al (2006) examined the effectiveness of NMES and TES in strengthening the quadriceps muscles of both legs in children with CP. A total of 60 children (38 males, 22 females; mean age of 11 years [SD 3 years 6 months]; age range of 5 to 16 years) were randomized to one of the following groups: NMES (n = 18), TES (n = 20), or placebo (n = 22). Clinical presentations were diplegia (n = 55), quadriplegia (n = 1), dystonia (n = 1), ataxia (n = 1), and non-classifiable CP (n = 2). Thirty-four children walked unaided, 17 used posterior walkers, 6 used crutches, and the remaining 3 used sticks for mobility. Peak torque of the left and right quadriceps muscles, gross motor function, and impact of disability were assessed at baseline and end of treatment (16 weeks), and at a 6-week follow-up visit. No statistically significant difference was demonstrated between NMES or TES versus placebo for strength or function.
• Statistically significant differences were observed between NMES and TES versus placebo for impact of disability at the end of treatment, but only between TES and placebo at the 6-week follow-up. The authors concluded that further evidence is needed to show whether NMES and/or TES may be useful as an adjunct to therapy in ambulatory children with diplegia who find resistive strengthening programs difficult.

• In a systematic review with meta-analysis of randomized trials, Scianni et al (2009) examined if strengthening interventions increase strength without increasing spasticity and improve activity, and if there is there any carry-over after cessation in children and adolescents with CP? Children with spastic CP between school age and 20 years were included in this analysis. Strengthening interventions involved repetitive, strong, or effortful muscle contractions and progressed as ability changed; and they included biofeedback, ES, and progressive resistance exercise. Strength was measured as continuous measures of maximum voluntary force or torque production. Spasticity was measured as velocity-dependent resistance to passive stretch. Activity was measured as continuous measures, e.g., 10-m Walk Test, or using scales e.g., the Gross Motor Function Measure.

• A total of 6 studies were identified and 5 had data that could be included in a meta-analysis. Strengthening interventions had no effect on strength (SMD 0.20, 95 % CI: -0.17 to 0.56), no effect on walking speed (MD 0.02 m/s, 95 % CI: -0.13 to 0.16), and had a small statistically-significant but not clinically-worthwhile effect on Gross Motor Function Measure (MD 2 %, 95 % CI: 0 to 4). Only 1 study measured spasticity but did not report the between-group analysis. The authors concluded that in children and adolescents with CP who are walking, the current evidence suggests that strengthening interventions are neither effective nor worthwhile.

• Cauraugh et al (2010) performed a systematic review and meta-analysis using the International Classification of Functioning to determine the summary effect of ES on impairment and activity limitations relevant to gait problems of children with CP. These researchers identified 40 CP and ES studies, and 17 gait studies qualified for inclusion. Applying enablement classification methods to walking abnormalities created 2 subgroups: impairment (n = 14) and activity limitations (n = 15). Overall, 238 subjects experienced ES treatments and 224 served as a no stimulation control group. Calculations followed conventional data extraction and meta-analysis techniques: (a) individual standardized mean differences, (b) summary effect size, (c) I^2 heterogeneity test, (d) fail-safe N analysis and (e) moderator variable analyses. The authors cited reservation about recommending ES as an effective intervention for individuals with CP.

• Outside of the laboratory-testing experiments, "no quantitative, functional immediate or longitudinal effects beyond the testing situations were reported in the studies. Thus, long-term effects of various types of electrical stimulation on gait challenges in children with cerebral palsy would advance our understanding."

• Pereira et al (2012) conducted a systematic review on the effectiveness of FES in improving lower extremity function in chronic stroke. Multiple databases (PubMed, CINAHL, EMBASE, and Scopus) were searched for relevant articles. Studies were included for review if (i) greater than or equal to 50 % of the study population has sustained a stroke, (ii) the study design was a RCT, (iii) the mean time since stroke was
greater than or equal to 6 months, (iv) FES or NMES was compared to other interventions or a control group, and (v) functional lower extremity outcomes were assessed. Methodological quality was assessed using the PEDro tool. A standardized mean difference (SMD +/- SE and 95 % CI) was calculated for the 6-min walk test (6MWT). Pooled analysis was conducted for treatment effect of FES on the 6MWT distance using a fixed effects model.

- A total of 7 RCTs (PEDro scores 5 to 7) including a pooled sample size of 231 participants met inclusion criteria. Pooled analysis revealed a small but significant treatment effect of FES (0.379 +/- 0.152; 95 % CI: 0.081 to 0.677; p = 0.013) on 6MWT distance. The authors concluded that FES may be an effective intervention in the chronic phase post-stroke. However, its therapeutic value in improving lower extremity function and superiority over other gait training approaches remains unclear.

- In a Cochrane review, Maddocks et al (2013) evaluated the effectiveness of NMES for improving muscle strength in adults with advanced disease. The secondary objective of this study was to examine the acceptability and safety of NMES, and changes in muscle function (strength or endurance), muscle mass, exercise capacity, breathlessness and health-related quality of life. Studies were identified from searches of The Cochrane Library, MEDLINE, EMBASE, CINAHL and PsycINFO databases to July 2012, citation searches, conference proceedings and previous systematic reviews. These investigators included RCTs in adults with advanced chronic obstructive pulmonary disease (COPD), chronic heart failure, cancer or human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) comparing a program of NMES as a sole or adjunct intervention to no treatment, placebo NMES or an active control.

- They imposed no language restriction. Two review authors independently extracted data on study design, participants, interventions and outcomes. They assessed risk of bias using the Cochrane Collaboration's tool; and calculated mean differences (MD) or standardized mean differences (SMD) between intervention and control groups for outcomes with sufficient data; for other outcomes these researchers described findings from individual studies. A total of 11 studies involving 218 participants met the inclusion criteria across COPD, chronic heart failure and thoracic cancer. Neuromuscular ES significantly improved quadriceps strength by a SMD of 0.9 (95 % CI: 0.33 to 1.46), equating to approximately 25 Newton meters (Nm) (95 % CI: 9 to 41).

- Mean differences across various walking tests, favoring NMES, were 40 m (95 % CI: -4 to 84) for the 6MWT, 69 m (95 % CI: 19 to 119) for the incremental shuttle walk test and 160 m (95 % CI: 34 to 287) for the endurance shuttle walk test. Limited evidence was available for the assessment of other secondary outcomes. The authors concluded that NMES appears an effective means of improving muscle weakness in adults with progressive diseases such as COPD, chronic heart failure and cancer. Moreover, they stated that further research is needed to clarify its place in clinical practice, by determining the optimal parameters for a NMES program, the patients most likely to benefit, and its impact on morbidity and service use.

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Reviewed by a Board Certified Internist
Reviewed by David Evans, MD, Medical Director, Active Health Management-Nov 2016
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Footnotes

[A] The American Spinal Injury Association (ASIA) Impairment Scale is described in the background section below [A in Context Link 1]

[B] These criteria are adapted from the Food and Drug Administration (FDA) labeling for Parastep I System as well as information provided in published studies. [B in Context Link 1]

[C] More than 2 hours of NMES per day is considered not medically necessary; protocols reported in the literature recommend no more than 2 hours of NMES treatment within a 24-hour period. [C in Context Link 1]

[D] FES devices such as the FES Power Trainer, ERGYS, REGYS, NeuroEDUCATOR, STimMaster Galaxy, RT300 motorized FES ergometer, and SpectraSTIM are all considered to be exercise equipment. Most plans exclude coverage of exercise equipment; please check benefit plan descriptions for details [D in Context Link 1]

[E] The Vocare Bladder System, also known as the implantable Finetech-Brindley stimulator, is different from the InterStim device (sacral nerve neuromodulation, see CPB 223 - Urinary Incontinence Treatments). The Vocare Bladder System is patient-activated and
is designed to elicit functional contraction of the innervated muscles. Implantation of the Vocare device is frequently performed in conjunction with a dorsal rhizotomy. The rhizotomy results in an areflexive bladder, limiting incontinence and autonomic hyperreflexia. [E in Context Link 1]

**Codes**