In the October 2014 issue of *Topics in Pain Management* (vol. 30, no. 3), we presented an update and review of the mechanisms at work in complex regional pain syndrome (CRPS). In that article, entitled “Complex Regional Pain Syndrome: An Update and Review of Mechanisms,” we discussed the diagnosis of CRPS and the data to support several of the proposed contributing factors of the syndrome. We reviewed and summarized the literature to demonstrate how epidemiology, genetics, psychosocial factors, immobilization, central nervous system changes, autonomic dysfunction, neurogenic inflammation, psychological factors, and autoimmunity may be associated with this condition.

In this article, we review the recommended interdisciplinary treatment algorithms, along with data to support some of the

Learning Objectives: After participating in this CME activity, the physician should be better able to:
2. Educate the patient and supporting family members about interdisciplinary treatment of CRPS.
3. Implement pharmacologic treatments to aid the patient to progress in therapy.
4. Compare some of the interventions used in psychotherapy.

Key Words: Budapest Criteria, Complex regional pain syndrome, Restoration therapy, Pharmacotherapy

In the October 2014 issue of *Topics in Pain Management* (vol. 30, no. 3), we presented an update and review of the mechanisms at work in complex regional pain syndrome (CRPS). In that article, entitled “Complex Regional Pain Syndrome: An Update and Review of Mechanisms,” we discussed the diagnosis of CRPS and the data to support several of the proposed contributing factors of the syndrome. We reviewed and summarized the literature to demonstrate how epidemiology, genetics, psychosocial factors, immobilization, central nervous system changes, autonomic dysfunction,
CRPS Subtypes

CRPS is a chronic pain condition most often affecting one of the limbs (arms, legs, hands, or feet), usually after an injury or trauma to that limb. As noted in our previous article, there are 3 subtypes of CRPS:

1. CRPS I: causation by an initiating noxious event, such as a crush or soft tissue injury, immobilization, tight cast, or surgery;
2. CRPS II: associated with a major nerve lesion; and
3. CRPS-NOS (not otherwise specified): symptoms consistent with CRPS in which a specific injury or lesion has not been isolated as the cause.

CRPS has also been staged chronologically, but it has been demonstrated that the severity of CRPS does not necessarily correlate and support patients and families, prescribe evidence-based drug therapies to manage this painful condition, and consider referring the patient for other interventions such as psychotherapy.

The continuing education activity in Topics in Pain Management is intended for clinical and academic physicians from the specialties of anesthesiology, neurology, psychiatry, physical and rehabilitative medicine, and neurosurgery as well as residents in those fields and other practitioners interested in pain management.
follow staging, with some patients experiencing severe symptoms immediately.1 The Budapest Criteria tool takes into consideration sensory, vasomotor, sudomotor, and trophic changes that are noted by the clinician during the visit and subjectively noted by the patient.

**Clinical Diagnosis**

Clinical diagnosis using the Budapest Criteria can be made when the following 4 criteria are met:

1. Continuing pain disproportionate to any inciting event.
2. At a minimum, 1 symptom must be reported in at least 3 of the 4 following categories:
   - Sensory: hyperesthesia or allodynia;
   - Vasomotor: temperature asymmetry, skin color changes, or skin color asymmetry;
   - Sudomotor/edema: edema, sweating changes, or sweating asymmetry; and
   - Motor/trophic: decreased ROM, motor dysfunction (eg, weakness, tremor, and dystonia), or trophic changes (eg, hair, nail, and skin).
3. Patients must display at least 1 sign at the time of evaluation in at least 2 of the following categories:
   - Sensory: evidence of hyperalgesia (to pinprick) or allodynia (to light touch, temperature sensation, deep somatic pressure, or joint movement);
   - Vasomotor: evidence of temperature asymmetry (>1°C), skin color changes, or asymmetry
   - Sudomotor/edema: evidence of edema, sweating changes, or sweating asymmetry; and
   - Motor/trophic: evidence of decreased ROM, motor dysfunction (eg, weakness, tremor, and dystonia), or trophic changes (eg, hair, nail, and skin).
4. No other diagnosis better explains the signs and symptoms.

For research purposes, the diagnostic decision rule should be the finding of at least 1 symptom in all 4 symptom categories and at least 1 observed sign.

**Management**

There is no gold standard treatment for CRPS. In the 4th edition of *CRPS: Practical Diagnostic and Treatment Guidelines,*3 the integration of physical therapy focusing on functional restoration in combination with pharmacotherapy, psychotherapy, and interventions was proposed. The emphasis is on prompt diagnosis, early treatment, and avoidance of implementing drug therapy alone to prevent disuse of the affected limb and the psychological consequences of living in pain.4

**Functional Restoration Therapy**

The therapy algorithm is based on functional restoration of the presensorimotor cortices. Gradual desensitization goes hand in hand with increased functionality: less pain, more ROM, and increased strength. Medications and interventions should only be added if patients cannot proceed to the next step in therapy.3 Four steps have been defined within a functional restoration therapy algorithm:

1. Mirror visual feedback, graded motor imagery, reactivation, contrast baths, desensitization, exposure, and therapy;
2. Edema control, flexibility (active), isometric strengthening, postural correction, diagnosis, and treatment of secondary myofascial pain;
3. Stress loading, isotonic strengthening, ROM (gentle, passive), general aerobic conditioning, postural normalization, and balanced use; and

**Pharmacotherapy**

Pharmacotherapy is most effective used in combination with functional restoration. Monotherapy is best to minimize side effects and maximize compliance,3 but comorbidities such as depression must be considered. Because CRPS differs from other nociceptive or neuropathic pain conditions and can affect an individual’s central pathway, motor function, and autonomic function, no single medication treats all components of the syndrome.

If a patient cannot progress in therapy because of pain, edema, inflammation, or immobility, medications can be considered on the basis of symptoms (Table 1). Various types of medications used to provide relief of the CRPS symptoms include:

- **Anti-inflammatories.** In acute CRPS, pro-inflammatory cytokines [tumor necrosis factor-α, interleukin-2 (IL-2), IL-1β, and IL-6] are upregulated; in contrast, anti-inflammatory cytokines (IL-4 and IL-10) are diminished.5 Although it has been customary to start patients on anti-inflammatories, there are conflicting data regarding these agents as treatment for CRPS. Inflammation in CRPS is largely thought to be due to neurogenic inflammation initiated by inflammatory mediators from the terminals of afferent nociceptors, and nonsteroidal anti-inflammatory drugs have mixed success in neuropathic pain.3,6,7 Some data demonstrate that oral corticosteroids are beneficial in acute CRPS.8 (Suggested dose: naproxen 250–500 mg orally 2 times/day.)
- **Immune modulators.** Dimethyl sulfoxide (DMSO) cream, a free-radical scavenging agent, has anti-inflammatory, analgesic, mast-cell inhibition, and muscle-relaxing effects, and is thought to be beneficial for CRPS-I.7 A study of 29
patients demonstrated that topical application of DMSO 50% decreased pain intensity according to a visual analog score with results approaching absence of pain, and it led to higher scores on the quality-of-life questionnaire. The authors concluded that topical DMSO 50% is an additional tool for use in treating CRPS-I, providing an overall sense of relief and decreased rigidity with few side effects.9

- **Capsaicin cream.** The mechanism of action of capsaicin was thought to be related to substance P, but it is now thought to be due to the decrease of the transient receptor potential cation channel subfamily V member 1 (TRPV1), the capsaicin receptor. There is good evidence demonstrating that capsaicin treats neuropathic pain.10 (Suggested dose: capsaicin topical 4 times/day over painful regions.)

- **Vitamin C.** The exaggerated inflammatory response in CRPS generates excess free radicals. One literature review concluded that routine, daily administration of vitamin C may be beneficial after foot and ankle surgery or injury to avoid CRPS.11 A review of vitamin C prophylaxis in 40 patients with stage II or III trapeziometacarpal arthritis requiring joint replacement revealed that no CRPS-I occurred, compared with 13% cases of CRPS-I after the same implant without vitamin C prophylaxis.12 (Suggested dose: vitamin C 500 mg orally for 50 days.)

- **Antidepressants.** The psychogenic association of depression to CRPS continues to be debated, with no data proving that depression causes pain. Antidepressants can treat the consequential depression of the patient, which can lower the pain threshold. Serotonin-norepinephrine reuptake inhibitors are FDA-approved for various chronic pain conditions, but they have not been trialed for CRPS. Tricyclic antidepressants (TCAs) such as nortriptyline and amitriptyline can be used for neuropathic pain; nortriptyline has fewer adverse effects.

- **Calcitonin.** Despite conflicting evidence, calcitonin is often prescribed.13-15 Intramuscular calcitonin was researched for poststroke patients and demonstrated to suppress the onset of CRPS when started immediately after the stroke.16 (Suggested dose: nasal calcitonin 200 units 2 times/day.)

- **Bisphosphonates.** These agents relieve spontaneous and stimulus-evoked pain and improve functional status in patients with early disease (<6 months). (Suggested dose: neridronate IV 100 mg 4 times over 10 days or pamidronate IV 90 mg 4 times over 10 days.)17

- **Dystonia treatment.** Dystonia and contractures can occur in severe CRPS, leading to pain, decreased ROM, and disability. The mechanism differs from dystonia seen in patients who have central nervous system pathologies. Baclofen is generally a first-line agent. Trihexyphenidyl and Botox can also be considered. (Suggested dose: Botox 40 sites or 200 units.)

- **Opioids.** This class should be used as second- or third-line agents. Opioids can be used for neuropathic pain, with methadone having advantages because of N-methyl-D-aspartate (NMDA) antagonism. The practitioner must be vigilant about managing tolerance, and the risks of opioid-induced hyperalgesia or overdose. The practitioner should be aware that using short-acting opioids for rescue dosing remains controversial.3

- **NMDA antagonist, ketamine infusion.** NMDA antagonists have promising results, but there are toxic side effects and it is a drug with potential for abuse.18 Optimum dose, route, and timing of administration remain to be determined.18-20

- **IV magnesium.** In a pilot study of 8 patients, IV magnesium significantly improved pain, impairment, and quality of life. It was also well-tolerated.21

- **IV immunoglobulin.** The autoimmune theory for CRPS hypothesizes that injury facilitates the binding of preexisting

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**Table 1. Pharmacotherapy for Pain, Edema, Inflammation, or Immobility in Patients Who Cannot Otherwise Progress in Therapy**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild to moderate pain</td>
<td>Simple analgesics and/or interventional blocks</td>
</tr>
<tr>
<td>Excruciating, intractable pain</td>
<td>Opioids, interventional blocks</td>
</tr>
<tr>
<td>Inflammation, edema</td>
<td>Corticosteroids (systemic or targeted, acute), nonsteroidal anti-inflammatory drugs (chronic), immune modulators</td>
</tr>
<tr>
<td>Depression, anxiety, insomnia</td>
<td>Sedative, analgesic antidepressant/anxiolytics, and/or psychotherapy</td>
</tr>
<tr>
<td>Significant allostynia/hyperalgesia</td>
<td>Anticonvulsants and/or other sodium channel blockers and/or N-methyl-D-aspartate antagonists</td>
</tr>
<tr>
<td>Significant osteopenia, immobility, and trophic changes</td>
<td>Calcitonin, bisphosphonates</td>
</tr>
<tr>
<td>Profound vasomotor disturbance</td>
<td>Calcium channel blockers, sympatholytics, and/or interventional blocks</td>
</tr>
</tbody>
</table>
autoantibodies to target structures, enhancing central sensitization. (Suggested dose: IV immunoglobulin 0.5 g/kg over 10 days.)

- **Mannitol + corticosteroid + gabapentin.** A recent study compared the clinical results of 4 treatment modalities for CRPS-I associated with various types of upper extremity fractures. In comparing the groups (NSAID, gabapentin, IV mannitol with corticosteroid, or IV mannitol with corticosteroid and gabapentin), the authors concluded that a protocol including a combination of IV 20% mannitol and corticosteroid with oral gabapentin is an acceptable and effective treatment for CRPS-I.

### Pain Interventions

Interventional management of CRPS can be categorized into 3 main approaches:

1. Minimally invasive approaches, which include sympathetic nerve blocks, IV regional nerve blocks, and somatic nerve blocks;
2. More invasive approaches, which include epidural and plexus catheter blocks, neurostimulation, and intrathecal drug infusion; and
3. Surgical and experimental interventions, which include sympathectomy and motor cortex stimulation.

#### Minimally Invasive Approaches

Sympathetic block of the stellate ganglion or the lumbar sympathetic chain has demonstrated pain relief that outlasts the local anesthetic effects. One study reviewed a treatment that included IV regional anaesthetic block with lidocaine and methylprednisolone. In this study, 168 patients with CRPS-I of the upper extremity were treated in a 5-year period. At the end of treatment, 88% of the patients reported minimal or no pain. After a mean follow-up of 5 years (range, 28 months to 7 years), complete absence of pain was reported by 92% of the patients in the study.

A 2013 analysis that summarized Cochrane and non-Cochrane reviews revealed moderate evidence that sympathetic nerve blocks with anesthetics and IV regional blocks with guanethidine are not effective. Despite conflicting research outcomes, sympathetic blocks continue to be widely used internationally to treat CRPS. In a study of 14 patients who had joint stiffness caused by CRPS-I, the authors concluded that the nerve block is a valuable diagnostic and therapeutic option for the management of joint stiffness caused by CRPS-I.

#### More Invasive Approaches

Neurostimulation can be considered if a patient has had no response to conventional treatment (eg, pharmacotherapy) within 12 to 16 weeks.

Spinal cord stimulation (SCS) has been demonstrated to be highly effective in the treatment of CRPS-I, resulting in significant, long-term reduction in pain and improvement in quality of life. SCS, because of costs and invasiveness, has been used as a last resort when treating CRPS. Authors of a 2013 literature review, which considered safety, efficacy, cost-effectiveness, and cost neutrality, concluded that SCS should not be considered a therapy of the last resort for CRPS but rather should be applied earlier (eg, 3 months) as soon as more conservative therapies have failed.

A case series of 5 patients demonstrated that combined SCS and intrathecal baclofen neuromodulation decreased pain...
reduced pain fluctuations.\textsuperscript{31} Abnormal dystonic posture and movement disorders and intensity in refractory CRPS cases or improved associated primary gain must also be recognized. Depression and anxiety can be consequences of becoming disabled or experiencing chronic pain, and secondary gain can also be noted.\textsuperscript{32}

**Surgical and Experimental Approaches**

Sympathectomies are thought to be effective CRPS treatments. No randomized controlled trials have been carried out to study sympathectomy in patients with CRPS, but a military study in 2000 included 1564 patients with nerve injuries. The data from this study demonstrated that 89\% of patients experienced pain relief from a sympathetic block. Of these patients, 100\% had complete relief of symptoms in the immediate postoperative period and for follow-up from 1 to 6 years.\textsuperscript{33} In a 2003 meta-analysis, 94\% of the patients undergoing sympathectomy were cured of CRPS symptoms.\textsuperscript{34}

Animal studies have demonstrated that the pathophysiology of CRPS involves coupling between nociceptive fibers and sympathetic fibers.\textsuperscript{35} In a study of 16 patients with CRPS-II who had ineffective pain treatment for more than 6 months, subcutaneous venous sympathectomy was performed, and 75\% of the patients achieved significant improvement in limb function.\textsuperscript{36} Amputation for long-standing, therapy-resistant CRPS-I continues to remain controversial. A 2011 literature review demonstrated that recurrence of CRPS-I in the stump occurred in 31 of 65 patients, and 15 patients had phantom pain. Patient satisfaction was reported in 8 studies, although the definition of “satisfaction” was not clear.\textsuperscript{37}

**Psychotherapy**

A 2012 systematic review analyzed psychosocial factors associated with CRPS and concluded that research does not reveal evidence to support any specific personality or psychopathology predictors of the condition.\textsuperscript{38} However, depression and anxiety can be consequences of becoming disabled or experiencing chronic pain, and secondary gain must also be recognized.

Psychological interventions for CRPS are theorized to be palliative and possibly have a pathophysiologic impact on the disease.\textsuperscript{39} CRPS affects adrenergic mechanisms and inflammatory mediators, both of which can be affected by the psyche.

Although the sample sizes have been small, the research behind adding psychotherapy to physical therapy and pharmacotherapy in the efficacy of treating CRPS has been promising, demonstrating improvements in skin temperature, pain, ROM, and edema. A literature review reveals the positive efficacy of behavioral interventions for CRPS, demonstrating that modalities such as thermal biofeedback, hypnotic imagery, physical therapy, and relaxation training can reduce pain and, in some cases, completely resolve symptoms.\textsuperscript{3} Other modalities, such as eye-movement desensitization and reprocessing, hypnosis, and meditation, have also been used.\textsuperscript{3}

Harden et al\textsuperscript{3} used the following psychological interventional step-by-step algorithm to help address issues such as pain-related fears, incorrect beliefs, expectations, and family education:

1. Patient and family education about CRPS.
   - Pathophysiology in lay language;
   - Disuse issues;
   - Reactivation;
   - Self-management focus; and
   - Possible psychophysiological interactions.

2. Psychological evaluation (core issues).
   - Comorbid axis I psychiatric disorders;
   - Cognitive, behavioral, emotional response to CRPS;
   - Ongoing life stressors; and
   - Responses of significant others to CRPS.

   - Relaxation training with biofeedback;
   - Cognitive intervention;
   - Behavioral intervention; and
   - Family intervention.

4. If axis I psychiatric disorders or major life stressors are identified, the practitioner should conduct focused cognitive behavioral therapy targeting these issues.

**Integrative Medicine**

Very little research has been done in the field of complementary alternative medicine for CRPS. However, we know that specific treatments and remedies relieve pain with a good side-effect profile. Modalities such as acupuncture,\textsuperscript{40,41} craniosacral therapy, and osteopathic manipulations have been demonstrated to decrease perceived pain, reduce inflammation, and relax the stressed mind.

In addition, food and supplements have been demonstrated to affect pain in the following ways:

- **Consuming the ideal ratio of omega-3 to omega-6 polyunsaturated fatty acids.** Omega-6s are important for the body's immune system. They have a proinflammatory effect that may contribute to chronic inflammation. Omega-3s reduce...
these proinflammatory responses and have been demonstrated to decrease inflammation in rheumatoid arthritis and reduce progression of osteoarthritis. (Suggested dose: fish oil 1–2 g by mouth daily.)

- **Magnesium.** Overactivation of the NMDA receptor system plays a role in central sensitization. NMDA receptor antagonists have undesirable side effects; an alternative strategy to reducing the effect of NMDA is to reduce dietary polyamine intakes. Polyamines originate from diet and gut bacterial metabolism. Magnesium is an NMDA receptor blocker that has been suggested for brain function, including the reduction of pain paroxysms in patients with neuropathic pain.

- **Vitamin C.** Vitamin C reduces free radicals and can prevent the onset or worsening of nerve injury in neuropathic pain. (Suggested dose: vitamin C 500 mg by mouth per day.)

- **Vitamin B complex.** Vitamins B₆ and B₁₂ are necessary for nerve function. Several studies indicate that the use of vitamin B may help neuropathic pain. (Suggested dose: vitamin B complex 1–2 tablets by mouth daily, with a typical B-complex formula containing vitamin B₁ 100 mg, vitamin B₆ 100 mg, and vitamin B₁₂ 100 mcg.)

- **Alpha-lipoic acid.** Alpha-lipoic acid has been studied extensively for neuropathic pain, especially in Australia and Europe. Its mechanisms include free-radical scavenging, and recent studies show it may also be a T-type calcium channel blocker. One systematic literature review demonstrated that vitamin-B complex IV 600 mg over 3 weeks is administered, a significant and clinically relevant reduction in neuropathic pain is noted (grade of recommendation: A). It can also be taken orally and purchased over the counter. (Suggested dose: alpha-lipoic acid 100 mg by mouth daily.)

- **Acetyl-L-carnitine (ALC).** ALC is a molecule derived from acetylation of carnitine in the mitochondria. ALC represents the basis of epigenetic mechanism, open new pathways in the inflammatory polyamine intakes. Polyamines originate from diet and gut bacterial metabolism. Magnesium is an NMDA receptor blocker that has been suggested for brain function, including the reduction of pain paroxysms in patients with neuropathic pain.

## Conclusion

There have been many advances in CRPS research, with literature demonstrating evidence to support the integration of functional restoration therapy, pharmacotherapy, and psychotherapy. Despite all of the modalities available, a significant number of patients with CRPS experience long-lasting symptoms. Early detection and treatment is key, and prevention of disease worsening should be considered.

**Acknowledgment.** This article was reviewed and edited by Elizabeth A.M. Frost, MD, Professor, Department of Anesthesiology, Icahn Medical Center at Mount Sinai, New York, New York.

**References**


Woman With Rare Genetic Disorder Elects Amputation to End Chronic Pain

The Portland Press Herald (Portland, Maine) published a 3-part article about a local woman who elected to amputate her left foot after 11 years of refractory chronic pain in both feet, caused by the genetic disorder Ehlers-Danlos syndrome.1

Her decision had been controversial, with many surgeons she contacted unwilling to consider amputation. After having the surgery and completing rehabilitation with a prosthetic foot, the patient is happy with her decision and more active, finding that the solution of amputating one foot allows her to put less stress on her other foot, leading to manageable pain and a decision not to pursue amputating her right foot.2,3

According to the Ehlers-Danlos National Foundation (EDNF) website,4 people with Ehlers-Danlos syndrome (EDS) have a genetic defect in their connective tissue, resulting in fragile skin and unstable joints due to faulty or reduced amounts of collagen. There are 6 major subtypes classified under this syndrome. The most common type—classical—has been estimated to occur in fewer than 1 of every 10,000 individuals, though other estimates indicate the occurrence could be as low as 1 in 40,000 individuals.4

The EDNF website contains several resource guides for medical professionals, in addition to several pages with information for patients.

Gymnastics, Cheerleading, and Running

The woman profiled by the Portland Press Herald, Elisha Morgan, 35, was a gymnast as a child and a cheerleader in high school. By college, she had become a runner who logged 30 miles a week. Her pain became noticeably bad during her last year in college, but it wasn’t correctly diagnosed until years later.1

Once the EDS diagnosis was made, Morgan told the newspaper, she was still a bit skeptical, as her physicians had been wrong so many other times. But after she read about EDS, it made sense—she had always been particularly flexible as a gymnast and was able to perform a “snake-like” trick with her hands pressed together. The syndrome is marked by hyperflexibility in the joints.

That hyperflexibility and tissue fragility, combined with her running, had worn out the ligaments of her feet, causing her to feel knife-like pain.

Before physicians finally reached the EDS diagnosis, they prescribed several strategies and performed several surgeries: Morgan was first told she needed to stretch more, which she did. She underwent cortisone injections and nerve blocks in her spine. She received shockwave therapy, being told it would break up the tissue in her feet and promote healing. Surgeons cut ligaments in her feet and tendons of her calves to make them longer and stronger, they said.

Meanwhile, Morgan went from easy athlete to someone who carefully planned to spend as little time as possible on her feet. The pain affected her marriage, social life, work, and other aspects of her life. After being told there was no cure, she considered amputation. Her biggest obstacle turned out to be finding a surgeon.

Willing to Risk Phantom Limb Pain

Morgan’s biggest fear with this choice had been phantom limb pain, but she felt it was a risk worth taking. Her biggest obstacle turned out to be finding a surgeon who would perform the amputation. None of the Maine surgeons she contacted approved of her decision.1,2

She ultimately went to the Lahey Hospital and Medical Center in Boston, where Margaret Lobo, MD, director of foot and ankle surgery, agreed amputation was a valid option but recommended she find a surgeon with more experience. Morgan ultimately turned to Blake Ohlson, MD, in South Carolina, the same surgeon who had amputated the feet of the runner, Richard Blalock, whose blog Morgan had followed.

According to the second of the 3-part series, Ohlson performs about 3 or 4 elective amputations a year. He told the
newspaper that Morgan wasn’t a typical candidate for the procedure—she didn’t even limp. Morgan explained the reason for this to the newspaper, saying she could not favor one foot over the other when both burned in pain.2

Ohlson required Morgan obtain a second opinion and a psychiatric evaluation, which she did. Although Morgan had wanted both feet amputated, Ohlson told her he would amputate one. He performed an Ertl procedure, using part of the amputated bone to create a bridge between the ends of the tibia and fibula, holding them with a long screw until they grew and fused together. Morgan underwent a long recovery and rehabilitation visits over several months back home in Maine.

**Prosthetic Left Foot Alleviates Stress on Right Foot**

Morgan told the newspaper in the third article of the series that she is happy, active, and glad of her choice. Phantom limb pain did not develop. She has decided not to amputate her right foot, however. With the prosthetic on her left leg, she is able to favor that leg, leading to less stress and therefore less pain in the right foot.

The article also describes the larger problem of chronic pain in the United States, quoting figures from the 2011 Institute of Medicine report for the monetary cost of such pain: $560 billion to $635 billion annually in health care costs and lost productivity. In the microcosm of one medical center, the article says, chronic pain accounts for 300 referrals a month at the Mercy Pain Center in Portland.1

**References**


1. Which one of the following is clinically assessed by the physician when making a clinical diagnosis of CRPS using the Budapest Criteria?
A. Sensory, hyperalgesia, skin changes
B. Sensory, proprioceptive, decreased hair, shiny skin
C. Sensory, vasomotor, sudomotor, edema, motor/trophic
D. Sensory, sudomotor/edema, motor/trophic, mood

2. Which one of the following is the gold standard in treatment of CRPS?
A. Neuropathic agents
B. Physical therapy
C. There is no gold standard treatment
D. Psychiatric treatment

3. Which one of the following describes the appropriate steps and exercises in the functional restoration therapy algorithm?
A. Step 1, mirror visual feedback; step 2, ergonomics; step 3, edema control; step 4, vocational rehabilitation
B. Step 1, reactivation; step 2, isometric strengthening; step 3, ROM (gentle, passive); step 4, movement therapies
C. Step 1, edema control; step 2, flexibility; step 3, aerobic conditioning; step 4, mirror visual feedback
D. Step 1, reactivation; step 2, isometric strengthening; step 3, ROM (gentle, passive); step 4, vocational rehabilitation

4. How does pharmacotherapy work best for patients with CRPS?
A. When it is used as a first-line agent to make the patient more comfortable
B. When used in combination with functional restoration
C. When used in combination with pain interventions
D. When 2 to 3 medications are combined to maximize synergistic effects

5. Which one of the following describes the medication with the appropriate mechanism of action for CRPS?
A. DMSO cream: immune modulator, a free-radical scavenging agent that has anti-inflammatory, analgesic, mast cell inhibition, and muscle relaxing effects
B. Capsaicin: increase of TRPV1 receptor (capsaicin receptor)
C. Ketamine infusion: NMDA agonist
D. Vitamin C: NMDA antagonist

6. Despite wide use internationally for CRPS, research outcomes with use of sympathetic blocks have been varied.
A. True
B. False

7. A recent systematic review revealed strong correlation between depression and anxiety before onset of CRPS and predictors for improvement.
A. True
B. False

8. There is no evidence that dorsal root ganglia stimulators are effective in treating CRPS.
A. True
B. False

9. Which one of the following groups of over-the-counter supplements may decrease pain in patients with CRPS?
A. Magnesium, vitamin C, vitamin B complex, ACL
B. Milk, magnesium, vitamin C, vitamin B complex
C. Milk, magnesium, vitamin C, vitamin D
D. Fish oil, vitamin B complex, vitamin C, aspirin 80 mg

10. A 2011 literature review demonstrated that amputation for long-standing CRPS-I has great results with high patient satisfaction.
A. True
B. False
Website Intends to Promote Collaboration Among Pain Researchers

The Interagency Pain Research Portfolio is a federal database launched in May 2014 that lists the federally funded pain-related research projects and training activities. The database encourages the dissemination of information regarding details on current federally supported research and promotes collaboration among investigators with the hopes of reducing duplication of effort.

“This database will provide the public and the research community with an important tool to learn more about the breadth and details of pain research supported across the federal government,” said Linda Porter, PhD, in a press release. Porter is a pain policy advisor at the National Institute of Neurological Disorders and Stroke Office of Pain Policy, which manages the database.

 “[The database] also can be helpful in identifying potential collaborators by searching for topic areas of interest or for investigators,” Porter said.

The Pain Research Portfolio has collected information regarding more than 1200 projects funded by the Agency for Healthcare Research and Quality, the Centers for Disease Control and Prevention, the Department of Defense, the Food and Drug Administration, the National Institutes of Health, and the Department of Veterans Affairs.

The information is organized into 2 “tiers” of topic areas:

• Tier 1 contains basic, translational, and clinical research; and

• Tier 2 contains 29 specific scientific pain topics and research themes, including analgesic development, pain mechanisms, risk factors and causes, and training and education, among others.

Under the stipulations of the Patient Protection and Affordable Care Act that specified advancing pain care, education, and research, the Department of Health and Human Services created the Interagency Pain Research Coordinating Committee—an advisory committee of 19 federal and nonfederal members.

The committee aims to help support the advancement of pain research by coordinating the pain research efforts among the federal agencies. In its analysis of the federal research, the committee also identified critical gaps in research in a 2011 report. These tasks are designed to encourage collaboration among scientists and reduce redundancy of effort with the ultimate goal of furthering understanding of pain and improving treatment of pain.

The database can be found online at http://paindatabase.nih.gov.

Epidural Steroid Injections, Anticoagulants, and Safe Opioid Prescribing Among Leading Pain Topics at Post-Graduate Assembly

In future issues, Topics in Pain Management will explore some of the issues raised at the New York State Society of Anesthesiologists 68th Annual Post-Graduate Assembly, December 12–16, 2014.

At many of the pain-related panel discussions and workshops, the hot topics included epidural steroid injections (both the medications injected and how and whether to inject patients who are taking anticoagulants) as well as the continually evolving issue of safe opioid prescribing.

Experts weighing in on these topics included Terese Horlocker, MD; Subhash Jain, MD; Oscar De Leon-Casasola, MD; and David Wlody, MD, who also was co-chair of this year’s PGA, along with Richard A. Beers, MD.

Wlody has been a consultant to the FDA Center for Drug Evaluation and Research, which has been investigating the safety of medications for epidural steroid injections. Wlody is Professor of Clinical Anesthesiology and Vice Chair for Clinical Affairs at State University of New York and Chair of the Department of Anesthesiology at Long Island College Hospital.

To follow this topic on the FDA website and view transcripts, see http://www.fda.gov/AdvisoryCommittees/Calendar.ucm417300.htm.

Coming Soon:

• Compression Syndromes of the Lower Extremities, Part 2