A Conceptual Model of Pain: TREATMENT MODALITIES

Part three of this series discusses the choice of treatment approaches depending on the diagnosed source(s) of pain.

by James Woessner, MD, PhD

In part one of this series,[1] the author described a conceptual model of pain based on electrical principles: sensors (free nerve endings), wires (axons/nerves) and the perceptron (spinal cord and brain). Pain was described as either nociceptive (normal functioning of pain fibers), neuropathic (misfiring of axons/nerves), or central dysfunctions (central nervous system), the latter includes the pain pathways in the spinal cord and the brain. Part two of this series discussed methods to measure and quantify functioning of the pain nerve pathways with a view to understanding the underlying pathology causing the pain.[2]

Overview

The concept that pain results from mechanically- and chemically-caused physical changes that become more and more difficult to reverse is well-accepted throughout Medicine. With the passage of time, the reasons for the pain also become multi-factorial and overlapping, as well as more difficult to cure. Thus, early treatment is better to avoid permanent physiologic and structural changes and facilitate a cure.

While the pain mechanism(s) may become more complicated over time,[1,2] as more than one of the basic mechanisms becomes active (i.e. nociceptive pain may progress to neuropathic pain and then to central pain), the physician can address one mechanism at a time by choosing treatment methods that are logically most effective and logistically most convenient. Patient perception of treatment "reasonableness" also plays a role in the initial treatment adopted.

Pain Patterns Related to Different Pathologies

Having pathology is not the same as having pain from that pathology. Without visible tissue changes, there may not be a peripheral pain generator, leaving neuropathic and/or central pain as the probable cause. There could also be a microscopic pathology and/or local metabolic reason. Ultimately, there must always be a mechanism whereby some pathology or dysfunction causes the perception of pain. There are, however, a multitude of pain-pathology referral patterns. Most physicians only recognize dermatomal patterns; there are also sclerotomal, myofascial, viscerotomal, thermatomal, myotomal, as well as other referral patterns.

Dermatomal pain suggests nerve root involvement from a herniated disc or other physical or chemical pathology at the nerve root exit from the spinal canal.[3] While these distributions are usually unambiguous, specific mapping of the sensory distributions of thoracic dermatomes and the anatomic locations of the innervating nerves clearly show overlapping and highly individualized patterns.

Sclerotomal pain is deep bone pain referred from specific vertebral segments that may be interpreted as non-physiological. Bone pain may be either local or referred from ipsilateral spinal segments.[3]

Pain referred from tendinous and/or ligamentous interfaces with bone surfaces has no specific name that may also be interpreted as non-physiological. Hackett[4] mapped pain referred from ligamentous and tendon attachments to bones.

Drs. Travel and Simons[5,6] have provided physicians and patients with detailed maps of referred pain patterns from myofasical trigger points. While individual variations certainly occur, in general, these patterns of referred pain can be recognized in physician practice, and may sometimes be incorrectly referred to as "non-physiologic" pain patterns.

Likewise, the pain referral patterns of pathology in the internal organs are well-known across multiple field of medicine. Of course, there is an embryologic basis for these fairly consistent patterns of pain.[5,6]

There are also thermal patterns of pain, which are probably related to the distribution of sympathetic nerves (see Figure 1).[7]

Butler[8] has mapped referred pain from the spinal dura, which is also probably related to stimulation/irritation of the sympathetic C-fibers on the dura. Pain referred from the spinal dura is reminiscent of thermatomes in being diffuse, but these referral patterns are unique.

Bonica and Loeser describe "myotomal" pain as involving problems with the fascial tissue planes that surround muscle groups.[3] While "myotomal" may not be the correct description, when muscles were injected with hypertonic saline, which is an experimental substance known to produce pain, the above-mapped patterns of referred pain emerged.

Sometimes the myofascial pain referral patterns follow dermatomes, to some degree.[9] Dermatomes are somatic sensory nerve distributions whereas trigger point pain referral patterns are more related to sympathetic C-fiber distributions.

There is much to be investigated and considered before an integrated theory really useful to pain management can be advanced.

These different pain referral patterns may even occur simultaneously. If the physician does not pick out the correct primary pathology, treatment is — at best — a hit-or-miss "shotgun" approach. This approach is demonstrated on a daily basis as many physicians routinely — but consistent with the standard of care and training they've received — prescribe muscle relaxants, pain-killers (opioid/acetaminophen), NSAIDs (non-steroidal anti-inflammatory drugs) and sleeping pills to patients in acute and chronic pain.

It is important to note that "curing" the pain, as opposed to "masking" it, requires a specially trained physician to precisely and effectively decide the primary cause of a patient's pain problem and to pick the best and most effective treatment early in their care. This exercise is the essential first step in deciding on a theoretically-based and pragmatically-possible treatment plan.

Interestingly enough, these different pain etiologies and patterns are most directly helpful in dealing with nociceptive pain. In other words, these pain sources and referral patterns basically represent normal neurophysiologic functioning and, by and large, provide the patient and the physician with useful information in determining a good working diagnosis for nociceptive pain. However, actual clinical presentations are usually more complex.

Complicating Factors

While somewhat arbitrary, acute and chronic pain are concepts that must be considered and are useful in the sense that changes of real consequence occur over time. There are typically many, more complex, and permanent changes that do occur. Certainly, most physicians have seen the very visible changes that can occur in the natural progression of CRPS or RSD.

Neuropathic changes can also occur with CRPS and other pain conditions as illustrated in the 2nd of this series.[2] If efferent pathways are either damaged or are responding in a reflex manner to aberrant afferent signals, then easily visible anatomic and structural changes can occur. These changes become more notable, complex, and difficult to cure over time. Anti-nociception can be a dysfunctional result in any type of pain.

Environmental influences are certainly recognized to influence pain. Cold, wet days make neuropathic pain (including CRPS, myofascial, and fibromyalgia), worse. Just as old arthritics often comment that they "can feel" weather changes in their "bones," patients with neuropathic conditions often complain of more achy pain during bad weather. If consistent across these types of pain patients, this phenomenon would support the concept that myofascial pain and fibromyalgia have, at least, a neuropathic component.

Pre-morbid and secondary psychological/psychiatric conditions do often complicate diagnosing a pain condition. While depression may only sometimes be considered a cause of pain, the converse is certainly true. Dissatisfaction, psychosocial emotional stress and desire for secondary gain can occur concomitantly with objective physical pathology. In other words, the patient may present with a chronic condition that, in some ways, is exacerbated by a new injury.[10]

Basic individual personalities and cultural background have a significant affect on the perceived degree of pain and dysfunction, i.e. the patient's reaction to the pain. Chronic pain conditions are also often exacerbated by the withdrawal of family and friends support.[10] Financial pressure to pay doctor's bills and maintain life generates stress, raises cortisol levels and consequently lowers pain thresholds.

Pain and discomfort can essentially cause fatigue and sleep dysfunction, which further slows healing and increases suffering. Metabolic diseases, such as diabetes, may either be a primary cause of pain, contribute in varying degrees to the pain, may exacerbate a psychological component or, in other cases, may have nothing to do with the pain for which the patient presents.

Neuropathology

As presented in the second article of this series, the pain fibers can transmit — or be perceived as transmitting — less or more

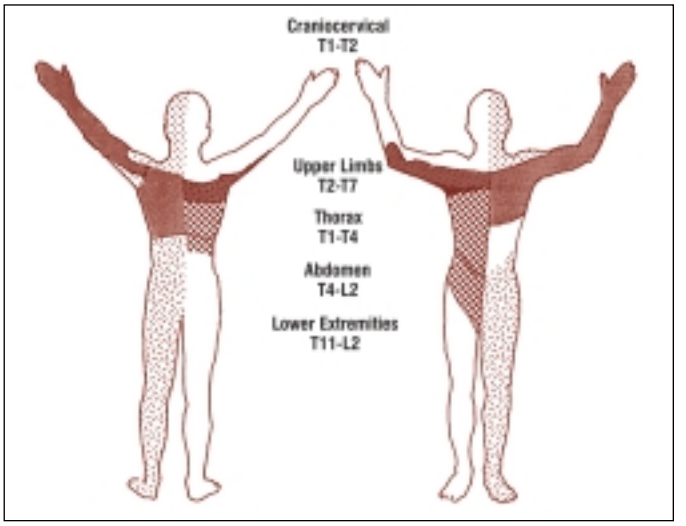

FIGURE 1: *Hooshmand[7] has coined the word "thermatomes" to describe referred pain patterns related to the circulatory distribution of sympathetic nerves. These relatively amorphous distributions are consistent with the observation that these C-fiber nerve pathways end up seeing pain "through fogged glass."*

signals than normal (damaged/dead and irritated fibers, respectively). In addition, there can be mixture of functional levels in a population of axons; the summation of hypo- and hyper-function can result in average function that mimics normal range.

Small pain nerve (A-delta and C-fiber) pathology should intuitively have several etiologies. Sudden trauma to a body part would seem to also have the potential to damage by crushing the small pain nerves, resulting in acute and then chronic compressive neuropathy. An acute compressive neuropathy may cause physical and chemical changes that can become a chronic non-compressive and/or traction neuropathy. Chronic repetitive rubbing can end up causing nerve dysfunction from similar physical and chemical consequences.

These physical insults often cause local chemical changes manifest by swelling, redness and hotness, i.e. inflammation. Inflammation causes certain chemicals to be released in the damaged tissues. There are numerous such identified chemicals; a few examples are prostaglandins, peripheral serotonin, kinins, histamines, etc.[11]

The Problem with Treatment Protocols

Treatment protocols, as well as scientific experimental results, are problematic because each assumes that there is a range of normal that must apply to every individual pain patient, whereas aspects of each individual patient's problem are absolutely unique. Pain is usually different every day, and it changes unpredictably over the course of the day.

It is well known that even when it comes to the mu-receptors in the spinal cord, there are at least 10 types and each individual has different proportions of these types. Obviously, it is impossible to predict for an individual pain patient which opioid will be effective and at what dose; different individuals will have widely different opioid requirements for their pain. Further, opioid requirements will change over the course of the day, every day, requiring more or less to control pain.

Treatment history can also have infinite possible courses and happenings. If multiple previous chemical blocks have preceded efforts with electromedical nerve blocks,[12] the resultant scar tissue from the chemicals around the stellate ganglion will likely interfere with penetration of the electric current to the underlying sympathetic C-fibers, making the procedure less effective.

How can one really predict in each individual case? Scientific results can be supportive, but individualized, artful decisions are the modus operandi throughout Medicine, particularly in Pain Management. Protocols are to be viewed as guides — not the last word.

Treatment Approaches

No matter how complex the pain problems of any individual patient, patterns of pathology do emerge and treatment options can be chosen. A framework must be developed for approaching a pain problem starting with diagnoses. Among these diagnoses, the physician must decide which is primary, causative and/or dominant.

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By and large, most acute pain is nociceptive. On the other hand, trauma can also damage the small pain nerves causing immediate neuropathic problems. For example, the perceptron/central pathology for phantom pain, resulting from amputation or central disconnection, is probably established at the instant of trauma, but realized or perceived days, weeks, or months later.

Chronic pain most likely, but not necessarily, involves all three types of pain — nociceptive, neuropathic, and central. Varying degrees and patterns of these dysfunctions occur to result in the different pain conditions. In some cases of arthritis, neither neuropathy nor central dysfunction occurs. Fibromyalgia could be completely central, but not psychogenic. CRPS likely involves all three, i.e. structural tissue changes that stimulate nociceptors, malfunction of small pain neurons, and central neuronal changes consistent with central hypersensitivity.[1,2]

Treating Nociceptive Pain

Disease, pathology and pathophysiological processes cause mechanical or chemical pain, which is usually nociceptive. Physicians are most skilled at identifying nociceptive pain as the pain-causing pathology. Unless the nerves themselves are damaged or central pathways physiologically altered, curing or removing the cause is the physician's primary concern.

When it comes to cure, traditional allopathic physicians are most successful in treating nociceptive pain problems — as long as neuropathic and central problems do not develop too quickly. For instance, if a benign cyst is pressing on a nerve root, it can be surgically removed and we would expect resolution of the pain — unless neuropathic and/or central pain problems have developed.

Neuron blockade and pain-killers of all sorts may be used initially to create "windows of opportunity" for cure. Chronic use of pain-killers is condoned and medically honorable once the physician and the patient have made an honest effort to cure and to recover, respectively.

The following presents some of the author's experience as an outpatient physical medical physician in treating nociceptive pain:

RICE: Rest, Ice, Compression and Elevation are the elements of the traditional approach in caring for acute sprain/strains. The physician and the patient are basically treating swelling, redness, hotness and pain. These modalities result in less pain and expedite recovery. The experienced physician may also include pharmaceuticals.

Physical Therapy: All of the PT modalities, including passive manual therapy and therapeutic exercises, are the best curative approach. All sorts of pain-killers and injections may very well provide windows of opportunity for these efforts to be effective. The unifying principle of Physical Medicine — i.e. tissue remolding — is facilitated and achieved, however, by physical therapy.

Therapeutic Exercise: The most effective tissue remolding technique is therapeutic exercise under professional Physical Therapist supervision or at home. In-

fluencing the micro-environment of the tissue planes of the body by moving tissues with respect to other tissues, possibly in conjunction with other procedures and therapies, is the key to cure. These exercises include stretching, strengthening and endurance training-type of movements that vary in intensity, repetitions, sets, duration and session frequency.

Manual Therapies: Medical myotherapy, deep soft tissue massage, rolfing, neural flossing,[8] the Gunn technique[13] and numerous other strengthening exercise techniques can be artfully integrated with other above-mentioned treatments for resolution of a patient's pain.

Chiropractic Care: Chiropractic care usually includes modalities and therapeutic exercise identical to those used in physical therapy. Unique, but not proprietary, aspects of chiropractic care include applied kinesiology, activator adjustments, high-velocity and low-velocity joint manipulations of various descriptions and the use of multiple modalities. Chiropractic can be very a useful facet of a multidisciplinary pain management approach.

Injections: There are injections done primarily to reduce pain, to reduce inflammation or to stimulate natural processes. Local anesthetics, catabolic steroids and proliferative agents are used, respectively. The efficacy of the injections described below depend on the correctness of the diagnosis, the physician's understanding of the utility and effect of the injected substances, and finally whether the injected substance reaches the target tissue.

Local anesthesia ideally blocks the pain and provides a window of opportunity for sleep, reduced stress, and various therapeutic activities.

Catabolic steroids, by definition, break down tissue. If the physician does not want tissue breakdown, steroids should not be used. Reducing abject inflammation and/or softening pain-causing scar tissue are reasonable goals for steroid injection.

Proliferative agents are intended to increase healthy collagenous tissue. Prolotherapy is beginning to receive scientific support[14] and wider recognition among physicians.[15]

Radio Frequency Ablation: If peripheral pathology is chronic, purely nociceptive, without removable pathology and without neuropathic or central disease, burning or cutting the offending nerve pathways makes sense and many patients are happy with the results. Radio frequency ablation is the preferred way to burn or cut the offending nerves. Recurrence, on the other hand, happens frequently. Three possibilities come to mind: 1) a new transmission pathway develops, 2) local neuropathology develops from the cut nerves, and/or 3) delayed central hypersensitivity sets in.

IDET: Intradiscal electrothermal reduction of herniated nucleus pulposus is a procedure that would seem to reduce the morbidity of full-blown surgical procedures. However, the author's experience has been that third party payors have resisted accepting this procedure. In the situations that IDET is unsuccessful, the problems may be due to microscopically rough surfaces remaining after disc material is destroyed and possibly from the resulting reduced disc height. This assumes that the diagnosis was correct in the first place since discography is often not predictive of the causative pathology.

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Surgery: Whole textbooks are written about lumbar surgery. Short-term outcomes have been reasonable, but long-term results have been disappointing. Microdiskectomy has about the same drawbacks as IDET. Metaphorically speaking, laminectomies and various types of fusion surgeries are really major trauma. Like many things in Medicine, sometimes a poisonous medication or a traumatic procedure is used to benefit when other, more conservative, approaches fail.

Spinal Column Stimulators: SCSs are probably not stimulators at all but, more likely, continuous neuron blockade of the pain nerve pathways in the dorsal columns. If these signals were indeed stimulating, they would be stimulating pain. The classic gate theory does not apply in the author's opinion. Patients with SCSs seldom state that pain relief in 100%; they more often describe the sharp pains as being reduced but with the nagging, burning and aching pains remaining.

Intrathecal Drug Pumps: Distribution ports are surgically placed in the epidural space, where combinations of various painkillers and muscle relaxants are delivered. In the author's opinion, these pumps are probably overused. Instead, optimized use of slow release opioid preparations and muscle relaxants are preferred.

When nothing can be done to correct the underlying cause, the pain can, of course, be dysfunctional and require traditional and well-accepted pharmaceutical pain control.

The Pharmaceutical Approach

These pharmaceutical suggestions are the author's preferences based on the known mechanisms of actions (pharmacokinetics) and location of action inside the body.

Oral Opioids: Opioids are probably the safest of all the pain-killers. However, for those patients suffering from neuropathic pain alone, pain management health care professionals recognize that opioids merely "take the edge off," while many patients recognize no help at all. For this specific population, patients reporting that opioids "take the edge off" may, in fact, be potentially addicted. On the other hand, opioids typically do legitimately benefit those patients who have nociceptive pain (with or without neuropathic pain). The author's professional experience confirms that when the nociceptive pain patient is freed from the distractions of the pain, there is commonly an improvement in mental function.

NSAIDs: Non-steroidal anti-inflammatory drugs (both COX-1 and COX-2) inhibit inflammation and provide analgesia.[16] Inhibiting the inflammatory cascade may be beneficial to prevent tissue damage for the first few days. During more advanced healing phases, a normally functioning inflammatory process is necessary for the best possible tissue recovery. While the NSAIDs are not recommended beyond the first days of an acute injury, they may

be useful in clearly chronic disease for analgesia, but the side effects of GI problems, kidney dysfunction, and possibly heart problems with the COX-2 NSAIDs, must be closely monitored — especially in elderly and immune-compromised patients. Ibuprofen and Naproxen are over-the-counter NSAIDs.

Other OTC Meds: Acetaminophen and aspirin are the main remaining OTC pharmaceuticals. Both are underappreciated yet are effective pain-killers and can be excellent low level pain control agents for mild pain, depending on the individual patient. Each can be used on a daily basis for long periods. However, chronic use of acetaminophen can cause liver and/or kidney failure, while chronic use of aspirin can cause acute GI bleeding.

Muscle Relaxants: Lioresal (Baclofen®), carisoprodol (Soma®), chlorzoxazone (Paraflex®), cyclobenzaprine (Flexeril®), diazepam (Valium®), methocarbamol (Robaxin®), orphenadrine (Norflex®) and tizanidine (Zanaflex®) are all commonly used muscle relaxants.[17] Lioresal works at the GABA receptors discussed below and could, via antinociceptive mechanisms, reduce reflex muscle contraction. Carisoprodol is preferred by many patients as it often helps with sleep, yet poses problems due to its addictive characteristics. Cyclobenzaprine is related to the tricyclic antidepressants and probably works centrally and it can also be useful for sleep. The author seldom uses chlorzoxazone, methocarbamol and orphenadrine, each of which is in a pharmodynamic class of its own. Tizanidine (discussed in a subsequent section) works at receptors on peripheral nerves, spinal cord neurons and central neurons.[18]

Lidoderm: While there are analgesic creams, Lidoderm, at present, is the only topical preparation that comes as a patch. When using all topicals, the physician must remember that the depth of the pain nerves can be a problem; in other words, these preparations work better when causative pathology is near the skin surface. The chemicals do not penetrate or diffuse in effective quantities deeper, because the circulatory system absorbs and gradually disperses the active ingredients as the chemical penetrates deeper.

SSRIs and Other Antidepressants: Tricyclic antidepressants (TCAs) include amitriptyline (Elavil®), imipramine (Tofranil®), nortriptyline (Pamelor®, Aventil®) and desipramine (Norpramine®, Pertofrane®). TCAs have data to support some effcicacy in fibromyalgia. The SSRIs include fluoxetine (Prozac®), paroxetine (Paxil®), citalopram (Celexa®), sertraline (Zoloft®) and venlaxine (Effexor®). The biochemical precursor to Serotonin is the amino acid, tryptophan, which is available in turkey meat. Supplementation may be reasonable in those depressed, not sleeping, and with resulting exacerbated pain.

Anticonvulsants and Antiarhythmics: Rowbothan & Petersen[19] only mention one antiarhythmic, i.e. mexiletine. It along with carbamazepam (Tegretol®), gabapentin (Neurontin®), lamotrigine (Lamictal®), phenytoin (Dilantin®), topiramate (Topamax®) and valproic acid (Depakote®) can be considered membrane-stabilizers in the sense that most of these medications reduce ectopic extraneous nerve firing by blockade of sodium channels. Clonazepam is a benzodiazepine that is included by Rowbothan and Petersen, but works mostly like diazepam. Carbamazepam is the only one of these indicated as safe and efficacious for pain by the FDA. Tegretol and Neurontin may also work synergistically and are also used for mood disorders.

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Sites of Pharmaceutical Antinociceptive Action

Pain signals from free pain nerve endings and from dysfunction peripheral nerves are conveyed to the perceptron through the synapse of the peripheral nerve on the dorsal horn of the spinal cord. Theoretically, if those signals are blocked by antagonizing actions at the presynaptic terminal, neither nociceptive nor neuropathic pain signals should be perceived by the brain.

Since the physician's best efforts are frequently unsuccessful, understanding of pain transmission must be less than perfect. What is known is that the pain signals are weakened by encephalin-induced dynorphin activity in the spinal cord. Dynorphin activation of kappa receptors on inhibitory interneurons causes the release of GABA, which hyperpolarizes dorsal horn cells and inhibits further transmission of the pain signal. This latter mechanism is especially important in modulating visceral pain. Medications that mimic the efforts of endorphins and encephalins are the mainstays of chronic pain therapy. Newer drugs that mimic or potentiate the effects of GABA or alpha2-receptor agonists have made it possible to target therapy for chronic pain syndromes more specifically than in the past."[20]

Most utilized pharmaceutical mechanisms are basically antinociceptive in nature. It may be that all of the antagonists must be supplied simultaneously. Further, Brookhoff[20] suggests more complex interactions involving sympathetic and parasympathetic nervous systems that, being poorly understood at this time, are without pharmaceutical approaches.

Treating Neuropathic Pain

Radiological imaging of the spine and brain are rarely helpful in determining neuropathic, central, or even nociceptive pain. Nerve damage can occur via an infinite number of mechanisms, and result in several outcomes, i.e. hyperesthesia and/or hyperalgesia, paresthesias and/or allodynia, or hypoesthesia; the ultimate hypoesthesia is the complete inability to experience any pain at all. Remembering that neuropathic pain is related to nerve (wire) dysfunction itself, curative treatment must, therefore, focus on reversing that pathology.

Other than trying to mask the pain by means mentioned above, nutritional approaches should be primary and synergistic. Omega fatty acids (6 to 3) in the ratio of 4 to 1 have been shown to optimize nerve function. Since Omega fatty acids are the building blocks for nerve membranes, we would expect that supplementing a neuropathic pain patient's diet would be a reasonable approach to suggesting cure. We would expect 4 to 6 months to

elapse before the patient or the doctor may see any noticeable improvement.

In a previous article,[12] the author reported that medium frequency, especially 20,000 Hz, alternating current across a tissue culture resulted in utilization of cyclic AMP.[21] Understanding the role of cyclic AMP suggests that normalization of nerve function can occur by stimulating anabolism. Masking neuropathic pain can also occur via electric neuron blockade. In both cases, we would expect that the unmyelinated C-fibers would benefit more than the A-delta fibers.

Supplemental to the above approaches, is the use of so-called membrane stabilizing medications; these medications appear to stabilize nerve membranes by antagonizing signal transmission at specific receptors on pain nerves to prevent hyperactive flow related to transmission of pain signals. These medications are mostly anticonvulsants, but also include tricyclic antidepressants and antiarrhythmics. Zonegran blocks sodium, T-type calcium and K-evoked glutamate receptors. Neurontin (gabapentin) and Gabatril are reported by Brookhoff[20] to have actions unrelated to GABA receptors shown above.

With knowledge of the nerve fiber type involved, specific, focused treatments may be possible. Neuropathic pain, as it's usually used, refers to a burning, aching, non-localized pain which points to involvement of the C-fibers. The usual treatments are pharmaceutical. Thus, when the area pain is regional in nature, the physician must, in consultation with the patient, decide, depending on the character of the neuropathic pain present, whether bathing the whole body in a pharmaceutical, the possibility of dependence and the expense are worth the minimal general pain relief and/or pain relief in a single region.

Treating Central Pain

Central pain, according to the author's definition, is any pain resulting from dysfunction of neurons of the central nervous system, i.e. the brain and the spinal cord. Thalamic pain and phantom pain fall in this category. Perceived body pain in complete spinal cord injured patients must be central in origin and maintenance, also.

Because elevated cortisol is known to be anti-inflammatory in the human body, we would thus also expect that any stress causing increased cortisol will also be anti-natural-healing and anti-immune. It is well known that increased cortisol lowers pain threshold. Psychophysiological factors with complex interactions are obviously involved in pain perception.

The most logical treatment approach is to use methods that directly affect neurons in the central nervous system. Transcranial and body stimulation, auricular and traditional acupuncture, reflexology, applied kinesiology, yoga, imagery, and a whole range of psychological techniques are valid possibilities.

Nutritionals, such as gingko, may also play a role.[22,23] We would expect nutritionals to be the building-blocks of repair and normalization of function. Since subtle nutritional deficiencies or medicinal needs take time to develop, we would also expect that repair would likewise take months to years (see the section on the role of nutritionals).

Sometimes psychiatric conditions, such as depression, anxiety and Post-Traumatic Stress Disorder (PTSD) are the cause of pain and discomfort. It has been scientifically confirmed that depression, at least, can be correlated to central neurochemical changes. Such chemistry can be modulated via Selective Serotonin Re-Uptake Inhibitors (SSRIs) and other antidepressants.

Pharmaceuticals that pass the blood-brain barrier may also have potential for cure, but so far appear to only suppress the pain sensation. In the same sense of membrane stabilization, anticonvulsants and other pharmaceuticals mentioned above, have also been documented to be useful for treating pain with central components.

Because mechanisms are still in the early stages of discovery, psychogenic causes of pain may very well be eventually understood to be either chemical or anatomic (neuronal) changes in central pain perceptor systems.

Treating Combined Pain

As indicated previously, almost all chronic pain is a combination of the nociceptive, neuropathic and central pain without a clear single pain generator. Books have been written considering all aspects of various pain syndromes, yet protocols and set recipes are too restrictive for the infinite variations found in patients. Each patient is an unique individual, whose condition varies from minute to minute. There is no substitute for a knowledgeable, flexible physician who has adequately educated the pain patient. Even so, a couple of examples may be instructive at this juncture.

Complex Regional Pain Syndrome (CRPS), previously named Reflex Sympathetic Dystrophy (RSD) usually starts with neuropathology of the A-delta and C-fibers caused by acute or repetitive trauma. Damage to efferent nerves causes visible physical changes that are well-described in CRPS/RSD. Also many researchers have noted intracranial changes,[24] which are most likely subcortical. CRPS/RSD is a non-standard, variable disease, and as stated, varies among individual patients. Even before the name of Reflex Sympathetic Dystrophy was changed to Complex Regional Pain Syndrome, it has been appreciated that these neuropathies involve more than one type of nociceptive fiber.

Fibromyalgia is another common chronic disease which, in the authors opinion, has probable involvement of the three pathologies supported by the pain model described in this series. However, because of the dynamics of post-traumatic fibromyalgia and the patchiness that the author has observed, it is suggested that fybromyalgia probably starts peripherally. But fibromyalgia also surely has central components because of the associated cognitive and emotional sequelae and concommitant symptoms.[25]

While not curative, Zanaflex® has been found by the author to be the best pharmaceutical for directly treating combined nociceptive, neuropathic and central causes of pain with the least side-effects. Zanaflex® is a basic alpha2 adrenergic agonist active in the polysynaptic pathways in the spinal cord and in the locus ceruleus and is unique in its widespread sites of action.[18]

Tissue Remolding and Tissue Plane Microenvironments

Physical Medicine includes numerous techniques to remold tissue. These include modalities and body movement implemented by both active and passive means to change the micro-environments — both intra-cellular and extra-cellular.

Tissue remolding, in a microscopic sense, is the changing of the microenvironment. This phenomenon is mostly collagen remolding. However, other aspects of this microenvironment are likely involved. Temperature, pH and other chemical parameters almost certainly come into play. Nutritional building

MANAGING CHRONIC PAIN IN TEN EASY STEPS	
Step 1	**Be Realistic.** Be honest with yourself and learn all you can about your physical condition. You may well have to deal with the fact that your will need to deal with pain every day. Dealing with anger, frustration and change is an important part of the process.
Step 2	**Get Involved.** Take an active role in dealing with your condition. Find out about all options available to you and move from a passive to an active role in your healthcare. You may wish to look at non-medical options for support and help. Alternatives such as acupuncture, homeopathy and looking at diet may be useful.
Step 3	**Learn Relaxation and the Value of Distraction.** This isn't about booze and smokes! Learning to breathe and relax properly distracts your mind and gives mind and body a break from the suffering associated with pain.
Step 4	**Recognize Thoughts and Feelings.** The mind affects the body and the body affects the mind. Identifying your thoughts and feelings is vital if you want to change how you relate to your pain.
Step 5	**Safe Movement.** Safe movement combined with deeper breathing can improve mobility and make you feel more positive.
Step 6	**Set Priorities.** With limited energy and mobility, it is important to look at what matters in your life. Ask yourself: "What do I want?" Never mind the "should's".
Step 7	**Set Realistic Goals.** Break big tasks into smaller more manageable steps that you can achieve. Pace yourself; continually review pain and energy levels relative to activity. you will feel more in control.
Step 8	**Know Your Basic Rights.** You have the right to be treated with respect, to say "no" without guilt, to do less than humanly possible.
Step 9	**Communicate.** Communicating clearly and effectively with family and friends and colleagues reduces anxiety, tension, stress, and suffering. Learning how to get your needs med is an important part of pain management.
Step 10	**Rediscover Hope.** By using these strategies you will find that you can: Regain control; Increase your sense of well-being; Step out of the pain-tension-anxiety-stress-cycle; Begin to get your needs met; Lessen suffering.

Table 1. *Self-help steps in managing chronic pain developed by the Pain Association Scotland.*

blocks, as well as fibroclastic and fibroblastic cells, must be present.

Circulation changes affect microenvironmental chemistry. If circulation is modified, then it's fairly certain to change the biochemical environment of the peripheral areas involved. More blood means more nutrients and more dispersal of metabolites, and vice versa. Likewise, microenvironmental chemistry affects circulatory changes thereby illustrating the complex interrelationships.

Efferent sympathetic C-fibers control peripheral microenvironmental circulation. This makes microenvironmental conditions directly related to local and systemic sympathetic nervous system function — via reflex actions or centrally. This can be understood starting first with central control of the peripheral circulation.

Microenvironments can be intracellular, where metabolism is controlled or regulated by second messengers, or extracellular. The most important extracellular micro-environments are the tissue planes between tissue systems. As stated above, these microenvironments contain the A-delta and C-fibers that carry pain signals. If these micro-environments are altered, logically we would expect that the fiber would become hyperactive (irritated) and/or hypoactive, depending on the axon within the "cable" of the whole nerve.

These tissue plane micro-environments may be mobilized by stretching, neural flossing,[8] strengthening, manual therapies to include various massage techniques, rolfing, other deep soft tissue techniques, craniosacral techniques, etc., and therapeutic exercise. The unifying principle of physical medicine for the cure of soft tissue pathology is tissue remolding.

Chronic Pain in Perspective

Chronic pain includes CRPS/RSD, fibromyalgia, central pain conditions and any pain that is present for long periods of time, is not likely to resolve, and manifests in anatomic/physiologic changes. Chronic pain of any kind almost certainly includes combinations of the above pathologies, simply because one can precipitate another.

In general, chronic stimulation of nociceptors results in permanent physiologic and microanatomic changes. While acute pain response is in the nociceptor terminal and is facilitated by glutamate, chronic pain is more involved and complex. Most chronic conditions include malfunctioning sympathetic C-fibers. It is well known that there are numerous C-fibers in tissue planes and around other structures such as nerves. Because these are unmyelinated, it makes sense that electrical energy, as a treatment modality, would more likely penetrate these nerves and thereby provide immediate pain relief while promoting recovery of any C-fiber pathology and malfunction.

Changes occur even at the nociceptor terminal level in any chronic pain condition. Brookhoff[20] gives a detailed description, including the production/release of natural painkillers in the chronic pain situation. Methods to naturally stimulate the release of native pain-killers such as endorphins and enkephalins would seem to be an ideal way to promote natural pain control. Brookhoff also shows how potent inflammatory and vasodilating agents are released following prolonged sensitization of the cells in the dorsal horn.

Successful treatment, of course, depends on the exact cause. However, even with clear peripheral pathology causing nociceptive pain, most of the treatments mentioned above probably have less probability of providing a complete cure because of the neuropathic and central components.

In reality, the only proven approach for chronic pain to date is counseling the pa-

tient to deal with the pain and developing a pain management plan involving long-acting opioids.[26] After all else has failed, covering up the pain in the context of a chronic pain program is an accepted and honorable approach to improving the quality of life of the pain sufferer. A comprehensive self-help program for managing chronic pain, developed by the Pain Association Scotland,[27] is presented in Table 1.

The Role of Nutritionals

Proteins, carbohydrates, fats, vitamins and minerals are all building blocks for tissues and cells. Nutritional precursors are necessary to allow the body to metabolize appropriate bi-products for cure and normalization of function and structure. Basic nutrition promotes good health. However, there is another approach that can be used separately or concomitantly. In the face of disease, medicinal doses are necessary and useful. This approach is to encourage the patient to supplement his or her diet with so-called building block nutrients.

Glucosamine sulfate is a known building block for collagen. Besides being a logical nutritional for arthritis, it could play a role in neuropathic pain, because collagen has been shown to form the sheaths around nerves — the micro-environment of nerves.

Omega fatty acids have roles in the health of many body systems. Here, we are interested in its presence in nerve membranes. Certainly, for the body to heal damaged nerves (i.e. neuropathy), omega fatty acids should be in abundant supply. When it comes to nerves, the proper balance of omega fatty acids can reconstitute the walls of irritated and damaged sympathetic C-fibers. Healthy nerve membranes may very well equal more normal nerve function.

DL phenylalanine has been shown to facilitate the production of endorphins in humans. Since it is an essential amino acid, it could very well be an ingredient in the endorphin recipe.[28]

Vitamin B6 is well-known biochemically to be a co-enzyme in the energy cycle. Energy is required for metabolism. Healing is a metabolic process. It has been used for years by general practitioners and nutritional experts for various kinds of soft tissue pain.

The association between vitamin B12 and abnormal fatty acid synthesis provides a rationale for the neuropathy of cobalamin deficiency. Odd-chain fatty acids would build up in membrane lipids of nervous tissue, resulting in altered myelin integrity and demyelination, leading eventually to impaired nervous system functioning.

It is reasonable to postulate that the use of nutritionals effects the entire pathway, including the peripheral nervous system and the central nervous system — all the way through the spinal cord and into the brain.

The Role of Electric Medicine

That there are electrical aspects to human physiology is well-accepted. Note that EKG, EEG, EMG, nerve conduction studies, evoked potentials, pace makers, TENS, SCS, etc. are used throughout Medicine. The scientific basis for electric nerve blocks has previously been reviewed by the author.[12]

> *"Nutritional precursors are necessary to allow the body to metabolize appropriate bi-products for cure and normalization of function and structure."*

Intra-cellular changes[21] are most likely promoted by so-called medium frequency alternating current applied along body parts where cellular dysfunction occurs, and nutritionals. We cannot rule out the importance of changes in intracellular chemistry that are caused by stress and other psychological phenomena.

For best results, the right diagnoses are necessary so that the specific pathology can be treated and the electrodes correctly placed. Treatment history also can have unanticipated results. For example, multiple previous chemical blocks — resulting in chemical-induced scar tissue around the stellate ganglion — will likely interfere with penetration of electric current to the sympathetic C-fibers by any subsequently attempted electromedical nerve block. Note that electromedical nerve blocks of the stellate ganglion are more difficult to confirm than chemical blocks, in part because the Horner's sign is subtler.

In the face of allodynia and hyperesthesia, electromedical treatments and other therapy may also directly help decrease disuse atrophy and cure some diseases that otherwise cause muscle atrophy, skin color changes, and functional decreases in strength and ROM.

The Role of Complementary/ Alternative Medicine (CAM)

All kinds of acupuncture (traditional, auricular and electrical), reflexology, koryo (Korean hand acupressure), etc. likely result in reprogramming neurons to normal function. These techniques, when they work, would then logically work better for central nervous system pain dysfunctions.

Herbal approaches are by and large not proven in a Western scientific sense. The role and value of nutritional is gradually finding scientific support, but the "proof" is slow in coming.

A recently published 656-page reference volume deals specifically with the subject of using Oriental Medicine techniques to treat pain.[29] The pain etiology is based on the Chinese concepts of exogenous factors.

The Role of Science

The basis of science is manipulating one variable at a time and measuring the result as manifest by another single variable. Applying science to the function of an individual variable, such as nutritionals, is antithecal to actual pain presentation. Real-world patient presentation is very complex and involves multiple variables working synergistically or antagonistically to give multiple results of interest.

Certainly science helps physicians objectively analyze things happening in health care world around us. However, many physicians, especially those with research training and advanced scientific degrees, recognize that a very small percentage of clinical medicine is based on scientific, double-blinded, controlled, peer-reviewed proof. Certainly, no such evidence exists for the effectiveness of appendectomies. Deductive reasoning and experience allows physicians to accept

and use this surgical technique as the "standard of care."

Logic and scientific information can be applied and the results can be valuable without a rigorous scientific experiment being done. In fact, the real world of medicine is not a place where "real" science can be done, because the real world is complex and the best medicine is practiced on individuals — not populations. The population approach, based on the mathematics of statistics, has spawned "guidelines," "protocols" and "hard-and-fast" rules. "Protocols" are helpful, but should not be controlling.

Multidisciplinary/Integrated Care As a Beginning

Integrated or Blended Medicine is a concept that is gaining credence in recent years. Clinics are including "integrated" in their names. Understanding that the CAM portion of Integrated Medicine is still in its infancy (in a scientific sense) logically means that Integrated Medicine must also be in its infancy. However, in the opinion of the author, this is the direction that is most likely to advance pain care, now and in the future.

Synthesis, Summary and Conclusions

With this conceptual model of pain, we have described a practical and more direct way of analyzing the function of small pain nerves. Deductively, depending on the pattern and consistency of dysfunction, neuropathic and central pain can now be analyzed in a more logical fashion.

Medicine, particularly allopathic medicine, has concentrated on curing nociceptive pain, i.e., removing the pathology. Meanwhile, Oriental Medicine and CAM have — serendipitously — dealt with dysfunction of the sympathetic nervous system of which the C-fibers are a part. Medicine as a whole should integrate the best of CAM, Oriental and Western Medicine to push forward with the curative practice of Pain Medicine.

CAM and Oriental Medicine treatments that mostly did not make "sense" in the past, are starting to make "sense" now as we learn more. These treatments include "tissue remolding," psychophysiological (mind-body), electrical, herbal and nutritional approaches. With these integrative approaches and scientific deduction, it is becoming increasingly clear that physicians can begin retarding, maintaining, and regressing neuropathic and central pathology towards a cure rather than cover-up.

With the realization that pathology, particular in chronic pain, can involve nociceptive, neuropathic and perceptron (central) pathology together and in complex individually varying patterns, integrated medical treatment is the only way to have reasonable hope of optimizing pain care. These pain conditions can be so complex that we fully expect a new field of medicine to be developed, such as Pain Medicine.

Each of the opinions stated above can be supported from the published literature; however, a careful presentation of the arguments on both sides would require publication of several books. The intent here is to stimulate new and more correct approaches in fashioning a custom solution for individual patients to attempt cure or, at the very least, improve their condition. ■

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