A Conceptual Model of Pain: MEASUREMENT AND DIAGNOSIS

Part two of this series discusses the measurement and evaluation of patient data as an integral part of pain diagnosis.

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 & brain). Pain was described as either nociceptive (normal functioning of pain fibers), neuropathic (misfiring of axons/nerves), or central (dysfunctions of the central nervous system), the latter including the pain pathways in the spinal cord and the brain. In order to understand the underlying pathology causing pain, it is important to measure and quantify functioning of the pain nerve pathways.

Measuring pain is an ongoing goal of pain scientists. Recent reviews of some of these techniques, including PET, SPECT, fMRI and other neurometabolic and neurovascular tests, are discussed in Pain Imaging.[2] These techniques, while useful in understanding the physiological effects of pain, are typically research tools and not readily available to the general practitioner.

This article will therefore limit specific discussion to one of those instruments that are both cost-effective for the general practitioner and have a solid background as an investigational tool — as demonstrated by a preponderance of peer-reviewed studies.[3]

Nerve Anatomy

The peripheral nervous system is composed of nerve fibers of varying diameters — some myelinated (insulated) and others non-myelinated — performing different functions in the body. Nerve fibers, intertwined in nerve bundles (see Figure 1), are differentiated as either motor nerves, sensory nerves, or autonomic nerves.

A schematic illustrating the differentiation and functionality of various types of nerves is presented in Figure 2.

The nerve fibers identified in the middle tier of Figure 2 are summarized as follows:

A-beta fibers are intermediate size, myelinated, and fastest sensory conductivity. These fibers mediate the sensation of touch, mild pressure, vibration, and joint positioning sensations. These are measured in the sensory nerve conduction tests of standard electrodiagnostic studies (EMG/NCV).

A-delta fibers are small, myelinated, and moderate sensory conductivity speed. These fibers mediate the sensation of cold and the secondary components of cold sensation and pain.

C-fibers are the smallest diameter, non-myelinated, and slowest sensory and motor conductivity. These fibers mediate the sensation of heat and the primary components of hot sensation and pain.

Clinical experience dictates that there are macroscopic populations of nociceptive nerve fibers throughout the body[6] and individual axons within these populations must be dysfunctional to varying degrees — a range of normal functioning to nerve death (see Figure 3) in neuropathies.

Normal Nerve Function

Nerves are protoplasmic tubes or strands that conduct signals from a particular region of the body where the population of axons may be normal, irritated or basically dead. Such strands typically intertwine into a cable or bundle (see Figure 1), usually thought of as the nerve, and then feeds into the complex central nervous system (perceptron).

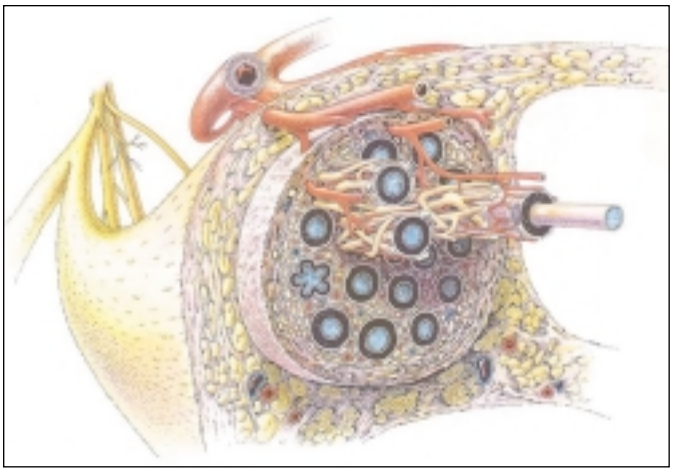


FIGURE 1. *Nerves are made up of axons and much other connective tissue with blood vessels intertwined.[4] Missing in this illustration are nerves that coat the surface of nerve bundles (mostly A-delta and C-fibers).*

When the small A-delta and C-fibers function normally, the subject can feel temperature changes rather quickly and can also tolerate thermal pain over a significant temperature range.

The known response of normal A-delta and C-fiber nerves to temperature provides a useful benchmark against which measurements of potentially damaged nerves can be compared. The importance of characterizing whether a nerve is more active than normal or less active than normal is that we can characterize to some extent the amount of damage to these nerves.

Although measuring temperature response is not a direct measure of mechanical or chemical nerve pain or dysfunction, thermal measurements do, however, directly measure thermal pain nerve dysfunction. Because these different nerve types are coincidental in size and location, direct and useful deduction can be made for the other types (mechanical and chemical) pain nerve/axon types.

Nerve Changes Over Time

In reality, nerve/axon damage is subjected to gradients[5] of insults over time and location. Trauma can cause tissue changes such as inflammation which, in turn, can damage nerves adjacent to the original trauma (or repetitive damage) site. These phenomena should be true for both the A-delta and C-fibers. It is fairly clear that not only does an axon and nerve evolve in degree and type of damage over time, but that a particular type of pain, from a pathway perspective (nociceptive, neuropathic, or central), can evolve into another type of pain or, alternately, involve another type of pain (see Figure 4).

Finally, it appears to the author that there may be cross-talk between these types of nerve fibers, resulting in an appropriate designation of Complex Regional Pain Syndrome.

Nerve/Axon Dysfunction

Figure 5 presents a simple, conceptual model of nerve/axon dysfunction. The anatomical distribution of damage, as well as the degree, is variable in different individuals with different pain conditions over time. Such damage can have immediate anatom-

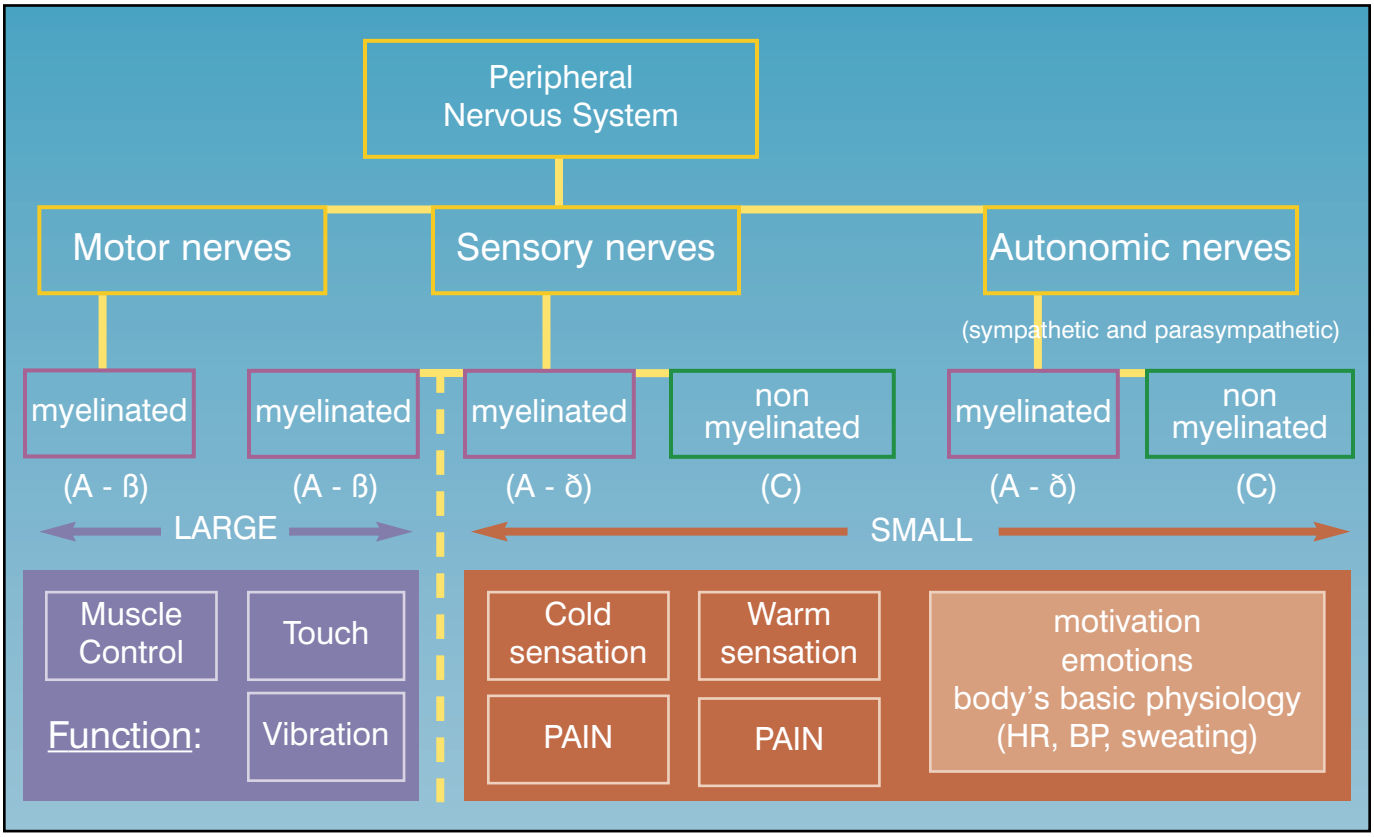


FIGURE 2. *Schematic of the peripheral nervous system. The top tier categorizes the peripheral nerves; the middle tier describes the state of myelination (insulation) of the different nerve/axon types; the bottom tier indicates the general function of each type of nerve.[5] With regard to pain, we are mostly interested in the A-delta and C-fibers.*

ic and physiologic consequences and/or chemical (inflammatory) reactions, which both often become locally chronic.

The distribution of damage is logically related to the direction and the character of mechanical and/or chemical insult to the nerve and axons. The mechanical insult can be acute traumatic or repetitive insults, such as rubbing, but is usually both acute and repetitive. The distribution of damage in nerves (nerve bundles) can be surface, regional, or diffuse.

The basic unit of damage is the axon, the single nerve fiber that extends from the nerve ending distally to the ganglia at the spinal cord proximally. The axon damage can be associated with A-delta fibers, C-fibers, or both. The degree, of course, is usually different depending on fiber type and varies over time. The degree of damage can be characterized as normal function, hyperactivity (such as irritation) and/or hypoactivity, and, ultimately, nerve death (see Figure 3).

Mixed Damage in Axon Populations

In the infinite possible mixtures of damage characteristics in nerves, we can easily project that — in pure nociceptive pain — all of the axons of both A-delta and C-fibers are functioning normally. We can also theoretically project that there could be a proportion of irritated and dead axons that would still result in perceived normal activity of the nerve.

If all the pain axons were dead, there would be no transmission of pain signals. If all the pain axons were irritated, the afflicted individual would likely have unbearable pain. Table 1 illustrates a mixed population of damaged and normal axons that exhibits normal function over-all. This phenomena has been clinically observed by the author among pain patients.

Electromyography and Nerve Conduction Velocity

Electromyography (EMG) and nerve conduction velocity (NCV) studies are gold standards for measuring nerve function. EMGs/NCVs are very helpful in identifying motor nerve dysfunction (i.e. A-alpha fiber and A-beta fiber), but not small fiber dysfunction (i.e. A-delta and C-fiber dysfunction).[7] Because these are medium- to large-sized myelinated nerves and are less fragile, they are typically damaged after the small fibers have already been damaged.

It is therefore apparent that EMGs/NCVs are far removed from measuring the pathophysiologic mechanism of pain generation. It behooves us to look for methods that more closely measure the actual function of the nerves — A-delta and C-fibers — that, in fact, transmit pain signals.

In Guyton's table[8] presented in part 1 of this series and in Figure 2, these fibers can have different functions in addition to transmitting pain — some of these small fibers even transmit information from the brain to small, involuntary motor fibers. Sweating, rapid heart rate, vasoconstriction, etc. are under sympathetic C-fiber control. Spindle muscle fibers and those that are trigger points are also under sympathetic C-fiber control.[9] Abnormal functioning of these efferent fibers, either hyper- or hypo-functioning, explain the findings in thermography, which are one step removed from the direct measurement of afferent pain function.

With or without mechanical impact that causes motor and large sensory nerve damage, sympathetic C-fiber and A-delta fiber irritation are certainly involved in the perception of pain. The primary pathology of major nerve pain almost certainly involves malfunctioning of sympathetic C-fibers[10] and probably also the A-delta fibers. Small fiber damage appears to occur even without motor and large sensory nerve fiber damage; electromyographic and nerve conduction studies may consequently be entirely normal even in the presence of small nerve fiber damage.

In addition, unless the pain nerves are irritated or damaged at the proximal end of a nerve root distribution and thus causing radiculopathy, the clinician often finds pain and sometimes other aberrant sensory phenomenon in so-called "non-physiologic" distributions.

Sensory Nerve Measurement Technology

The measure of pain developed in the field of psychology, the Visual Analog Score (VAS), is actually the best way overall to describe the severity of pain in each individual patient. However, pain scores do little to help us understand the underlying mechanisms of the pain. Parts of the History and Physical Examination can help the clinician suspect various kinds of pain prob-

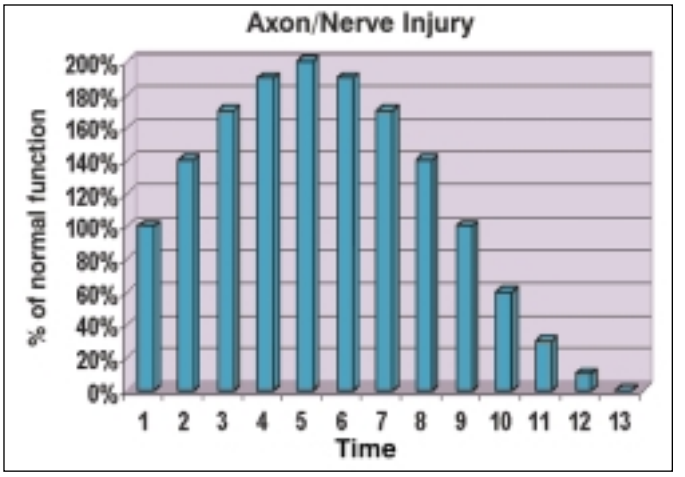


FIGURE 3: *While the time course can be anywhere from instantaneous to prolonged over months, the smooth course towards axonal death theoretically moves towards maximum irritation back through normal function — though not necessarily normal anatomy and physiology — to nerve death. In, reality this course is not likely smooth, linear nor necessarily culminate in axon/nerve death. Chronic pain is the state of persistently irritated nerve pathways.*

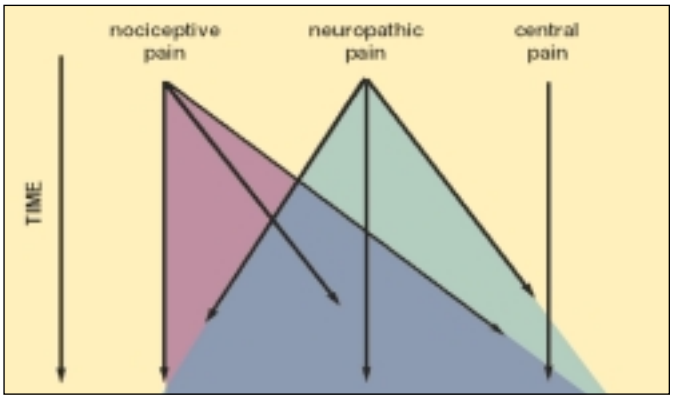


FIGURE 4. *This conceptual schematic suggests that the initial types of pain can evolve into other types over time (though not as smoothly as illustrated).*

Mixed Population of Axons			
Nerve state	**% of normal function**	**% of axons**	**weighted functionality**
Normal	100%	33%	33%
Irritated	200%	33%	67%
Dead	0%	34%	0%
Nerve total		100%	100%

TABLE 1. *Illustration of a mixed population of axons where one-third are normally-functioning, one-third are irritated (hyperfunctional at 200% of normal function) and one-third of the axons are dead. With equal populations of normal, irritated and dead axons the results could theoretically appear as normal nerve function. The specific percent of irritation was arbitrarily chosen for illustration purposes.*

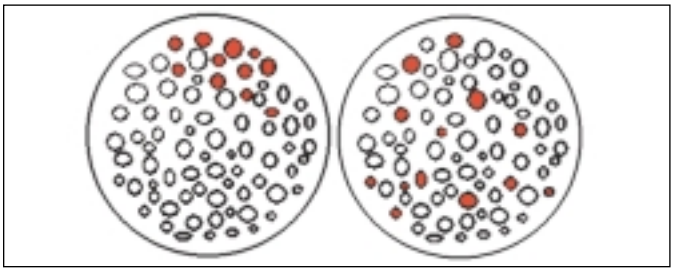


FIGURE 5. *Illustrations of nerve axon damage within a nerve bundle. The illustration on the left displays localized damage as probably typical in acute mechanical trauma, while the one on the right is more diffuse, and is probably more common in repetitive injury. Surface axon damage is not illustrated, but is probably the distribution of damage in neuritis of major nerves without motor changes.*

lems, but, as in most areas of medicine, great advantage is achieved by quantifying anatomic and physiologic changes.

In this discussion, scientific and detailed measurements are required in order to isolate the nerve dysfunctions. There are a number of clinical tests including quantitative sensory tests, autonomic tests, microneurography, and laser-evoked potentials, among others. Quantitative thermal sensory nerve pathway testing of small nerve fiber function includes the thermal stimulation testing and current perception threshold.[11] Below are brief descriptions of the various approaches to measuring the function of pain pathways, electrically, mechanically, vibrationally and thermally.

Electrical Testing. Because pain pathways are made up of nerves — the "wires" of the body — one would expect to measure or test nerve function electrically. Electrodiagnostic testing of the nervous system includes common, well-accepted methods that include EKG, EEG, galvanic skin response, evoked potentials, EMGs and nerve conduction velocity studies. None of these methods, however, precisely test the function of small nerves (A-delta and C-fibers) which are the fibers that conduct pain impulses.

Another measurement technique is electrical stimulation at the optimal transmission frequency of the various nerves types to reflect the function of those nerves, whether in the normal range, hyperactive or hypoactive. There are at least two technologies which use current perception threshold to evaluate small nerve fiber pathway function.[12] Nerve pathway sensitivity is then correlated to nerve pathology.

Mechanical Testing. There are several instruments that have been used clinically for years to isolate the functioning of these different fibers. Gross testing has included qualitative deductions from a patients' characterization of sensation and/or pain.

The most developed of these is the Semmes-Weinstein filament testing,[13] which are a set of different size fibers which, when brushed against the skin, are calibrated to represent different sensory nerve fiber hypofunction, depending on the response of the subject. While the function of various fiber sizes is very complex, light touch is, by and large, a measure of A-beta fiber function.

Algometry utilizes the patients' response to quantified skin surface pressure to evaluate mechanical pain threshold,[13] which is probably a measure of large sensory fiber function.[8]

Vibratory Testing. There are multiple devices that measure vibratory function. Since this methodology mainly measures A-beta fiber function,[8] it will not be considered in the context of nerve pain.

Thermography. Thermography is a technique for measuring skin temperature[14] since skin temperature reflects the function of efferent C-fiber function. However, interpretation becomes complex, because for some disease conditions there is no consistent pattern of hyper- and hypo-function to correlate with perceived pain and clinical disability.

Thermal Stimulation. As with light touch and pinprick, testing of nerve damage using hot and cold is basically as old as the discipline of Neurology itself. Computerized thermal measurement devices are commercially available that automate the testing process. The advantage over using a heated or cooled spoon or reflex hammer handle is that the response is measured precisely and multiple times to assure accuracy and precision. Diagnostic conclusions can only be made with confidence from consistent and unambiguous data.

Discussion of sensory testing in the following sections will concentrate on thermal stimulation methodology also referred to as Quantitative Somatosensory Testing (QST). As indicated previously, the transmission of cool sensation and cold pain signals are primarily along the A-delta fibers and warm sensation and hot pain signals are primarily along the C-fibers.

While ascertaining the thermal function of A-delta and C-fibers does not completely describe these fibers' responses to other stimuli, it does, however, provide a real-time measurement of the fibers' condition that, together with clinical observations, can lead to a valid diagnosis.

Quantitative Thermal Sensory Testing

C-fibers and A-delta fibers, responsible for both temperature sensing and pain transmission, allow the measurement of heat sensitivity (thermal sensory analysis) as an indirect indicator of nerve health. Both of these small nerve fibers, when tested for heat and cold sensitivity, yield quantitative data that is then compared to normal population values for an individual. Deviation from the norm can, therefore, indicate the existence of peripheral nerve pathway irritation or damage.

The author employs a thermal measurement device (Medoc's TSA II NeuroSensory Analyzer) to quickly and accurately measure the function of the small thermal and thermal pain signal transmission pathways of the body. This same equipment has been extensively used in the scientific community and is featured in approximately 300 scientific publications. The author has conducted over 100 clinical studies utilizing this machine to perform quantitative thermal sensory testing. Consequently,

test results from this instrument will be used to illustrate certain nerve pathologies that can be inferred from the thermal functionality of the A-delta and C-fiber nerves.

Utilizing the technique of QST, hypo- and hyper-activity can be accurately measured. In diagnosing neuropathic and central thermal sensory problems, this methodology directly measures the nerve pathways in question. However, while it provides pathway data (from the site of injury to the brain), it does not explicitly differentiate between central and peripheral neuropathology. This distinction is made by a trained and experienced clinician.

Deductive logic tells us that for mild cases where structural tissue damage is not, or cannot be, observed/documented, there is a likelihood of peripheral damage. If peripheral transmission is blocked and pain — not tenderness — is still preserved, then it is logical to project central nervous system involvement also. Central pain or central hypersensitization is suspected when the same pattern occurs over widespread areas of the body without direct clinical correlation.

Thermal Testing Methodology. Thermal testing employs a "thermode" (analogous to a surface electrode) that is held against the patient's skin serially as selected by the ordering clinician. The clinician will usually be testing a pain condition hypothesis by analyzing results from different neural pathways; comparison is essential for correct and useful diagnoses.

The thermode is capable of precisely cooling or heating the skin to one tenth of a Celsius degree. The subject/patient is instructed to push a button — much as in audiometry — to indicate perception of the cold and warm sensations, and then cold pain and hot pain.

Starting at an adaptation temperature between 30 and 32 degrees Celsius (at which the subject feels neither warmth nor cold), a calibrated increase in temperature of 1 to 2 degrees Celsius will be perceived by the subject as a warm sensation; this sensation is mediated by C-fibers. Further increasing the temperature to a threshold of about 45 degrees Celsius is normally perceived as heat-induced pain. Conversely, a calibrated decrease of 1 to 2 degrees Celsius below the adaptation temperature is perceived as a cold sensation; this sensation is mediated by A-delta fibers. A further decrease in temperature to a threshold of approximately 10 degrees Celsius is normally perceived as cold-induced pain.

While cold and hot pains are primarily mediated by C-fibers and A-delta fibers, respectively, there is some overlap — particularly in that A-delta fibers transmit some warm signals too. Clinically, in patients with neuropathic pain, a cold-induced pain, which is primarily A-delta fiber-mediated, is sometimes perceived as "hot" or "burning."

Thermal Data Analysis. While patient data collection, presentation, and analyses are automated, the practitioner, using the available software tools, needs to evaluate each patient's thermal thresholds by (1) comparing results with normative data (see Figure 6), (2) comparing results against the corresponding neural pathway on the opposite side of the body and in neighboring distributions, and (3) reviewing any significant variances in consecutive measurements to confirm repeatability and accuracy. Ideally, following changes over time with trend reports is helpful in evaluating the effectiveness of treatment outcomes.

While thermal testing provides valuable insight into the functioning of neural pathways, any diagnosis must also en-

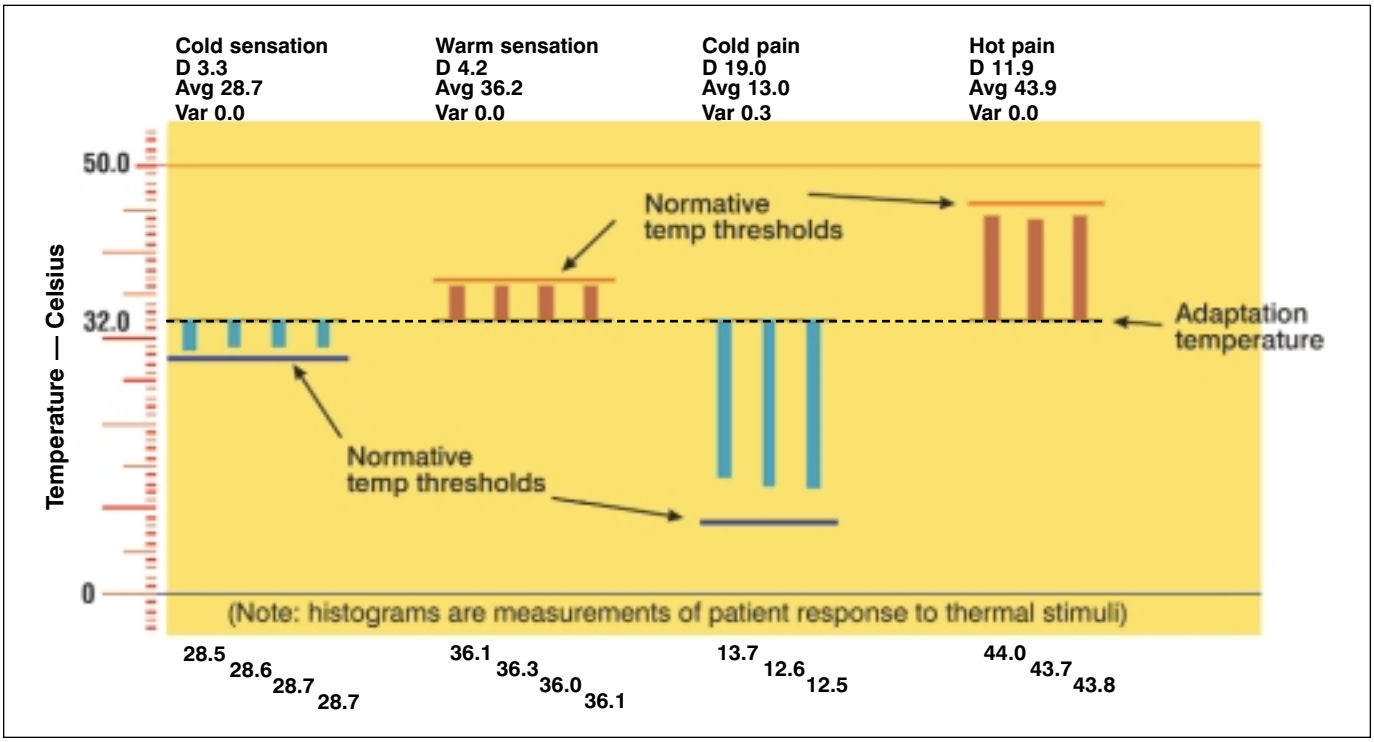


FIGURE 6. *This labeled illustration of an actual data printout shows how data may appear to the clinician in a normal case. We see that this subject responded within the normal range for all tested thermal parameters (cold, warm, cold pain, and hot pain) and the variances of multiple sampling indicate repeatability from one measurement to the next; for various reasons these are more consistent than most. Averages of each set can be used to analyze trends over time and is useful for outcomes measurement.*

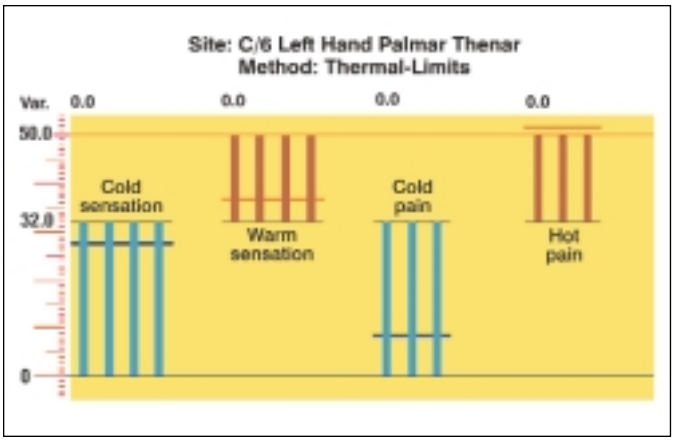


FIGURE 7. *These results either represent severe A-delta and C-fiber hypoactivity and essential death or an effort to convince the practitioner that the patient has severe nerve damage. From clinical information and inconsistencies, combined with the opinion of a clinical pain psychologist, it was determined that this patient was malingering.*

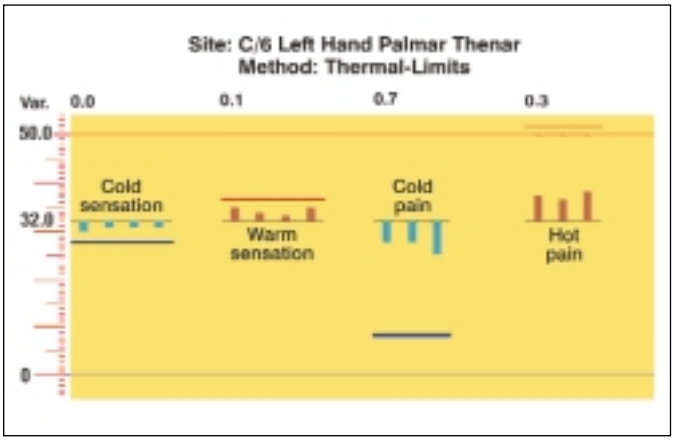


FIGURE 8. *While some exceptions may occur and the pattern over the body is, to some degree, patchy, these results — markedly increase thermal pain sensitivity without hypoactivity to sensation — are the quintessential findings in fibromyalgia.*

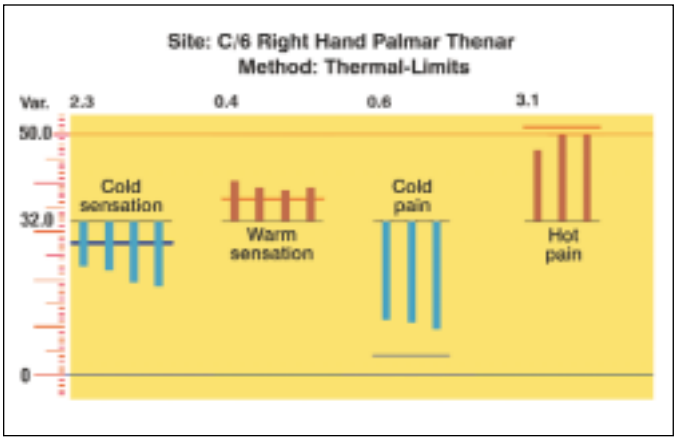


FIGURE 9. *In radiculopathy, A-delta cold- and C-fiber hot- sensation hypofunction is diagnostic. Cold- and hot-pain perception thresholds are usually in the normal range. If these latter thresholds decrease (ie. hypersensitivity to hot/cold pain) then CRPS can be suspected.*

compass the individual patient's History and Physical Examination and the practitioner's clinical observations.

Pathophysiology of Specific Pain Conditions

Building on the model presented in the first article of this series,[1] we see that all pain conditions can be understood as nociceptive, neuropathic, central, or combinations of these three types of dysfunction. This categorization is more meaningful than combining clinical symptoms together into syndromes, which are, by definition, poorly defined. The following sections will discuss observations and opinions regarding certain neural pathologies. These data are all of the C6 (left hand palmar thenar) distribution, because normal responses from the face, the back, and the lower extremities are significantly different.

Sample Thermal Test Results. The following sections present sample thermal sensory test results for Fibromyalgia, Radiculopathy, Polyneuropathy, Overuse Syndrome (also known as Repetitive Stress Syndrome), and Complex Regional Pain Syndrome (CRPS). All examples below are from the C6 (left hand palmar thenar) distribution to facilitate comparison. While not comprehensive enough to be utilized as clinical markers for the various disease states, the following samples serve to illustrate the usefulness of thermal measurements in diagnosing.

The Malingering/Feigning Patient. The requirement of patient cooperation is no different than the time-honored practice of physicians relying on patient response during the History and Physical Examination to form opinions, provide tentative or firm diagnoses and design a treatment plan. In practice, it is difficult to feign or otherwise malinger these test results in a manner that make any clinical sense.

In fact, one of the author's patients showed hypofunctional results that bore no relationship to the clinical presentation (see Figure 7).

Without clinical background, these results are consistent with marked hypofunction to both sensation and pain for the A-delta and C-fibers in the C6 distribution. The results for the lower extremities were the same, i.e. consistent with severe damage and death. With such severe damage, the clinician would expect to see gross skin abnormalities and odd movements in deference to these clearly abnormal and damaged nerve pathways. Yet the patient had only upper extremity complaints and no obvious skin changes nor abnormal mannerisms nor movements. Clearly the patient was not cooperating in good faith. Psychological testing was consistent also with this probable conclusion. It is always important for physicians to cross-correlate any measurements with clinical observations to arrive at a diagnosis.

Fibromyalgia. Review of the voluminous fibromyalgia literature reveals various abnormalities that commonly occur in fibromyalgia, including abnormalities in neural pathways as evidenced by thermal sensation perception.[15,16,17,18]

One common aspect are abnormalities that can be characterized as dysfunctions of primitive systems of the body, i.e. hormonal activity, immune function, emotion, the autonomic nerve pathways. If this disease actually starts from one subsystem, it may very well be one of these. For example, hormones affect basic physiology, which can alter microenvironments in the body (e.g. around nerves) which again affects basic physiology. The immune system usually responds to body imbalances caused by exogenous causes. Emotions, on the other hand, change stress proteins and increase native cortisol levels.

The most current information about fibromyalgia identifies — in a fair amount of detail — some of the consequences of the disease, but not the actual mechanisms of the disease nor any neuropathy involved.[19] While it is experimentally unclear whether the neuropathy is peripheral, central, or both, the dynamics of post-traumatic fibromyalgia and the patchiness that the author has observed seems to indicate that the neurogenic component of fibromyalgia is peripheral at the outset and progressive to more central disease.[1] Figure 8 presents typical thermal testing results for fibromyalgia. Additionally, fibromyalgia almost certainly has central components because of the commonly concomitant, associated cognitive and emotional symptoms.

In this author's opinion, fibromyalgia has no direct relationship to Myofascial Pain Syndrome, except that they may occur simultaneously in the same patient, and post-traumatic fibromyalgia often progresses from Myofascial Pain Syndrome.

Radiculopathy. Radiculopathy is primarily caused by herniated disc pressure on the nerve root near the spinal cord. At a minimum, the pressure is pinching off normal protoplasmic flow in the axons at the nerve root, and preferentially the small pain fibers that are on the surface of the nerve root. Since axons are continuous tubes of protoplasm from the ganglia near the spinal cord to the free nerve endings in the periphery, some degree of dysfunction should occur in the distal distribution of any axon affected.

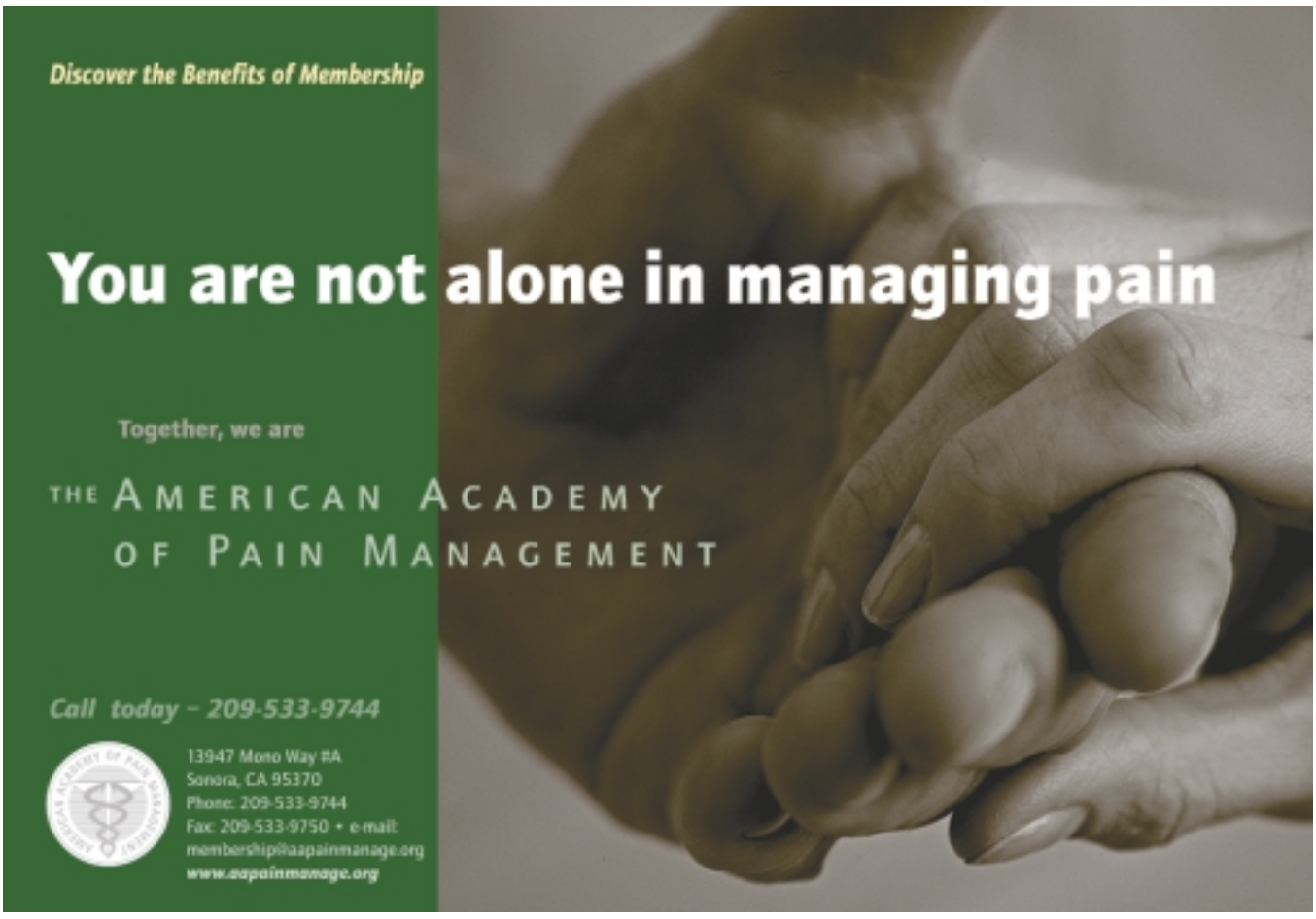
It is common for pain to also occur with radiculopathy indicating that the small pain nerves must also become irritated — whether mechanically or chemically — and thereby transmitting more signals than normal.

Thermal sensory testing has shown that the severity of radicular pain is indicated by the degree of thermal sensation hypofunction (see Figure 9) in the affected nerve root distribution or dermatome.[20]

Doing thermal sensory testing may turn out to be a very important pre-operative test because, according to Nygaard,[21] "The preoperative warmth detection threshold reflecting the function in small unmyelinated C fibres was significantly higher in the patients with a poor result and this may indicate that damage to C fibres before surgery is a *negative prognostic factor*."

Polyneuropathy. Damage to the peripheral nerves that can be described as "stocking and glove" decreased sensation to light touch and pin-prick is called "polyneuropathy." Polyneuropathy can be documented in detail and delineated from motor neuropathies in conjunction with large fiber electrodiagnostic testing. Sindrup, et al[22] confirm that, "quantitative testing of temperature sensation improves the diagnostic yield in patients examined for chronic polyneuropathy."

Overuse Syndrome. Repetitive Stress Syndrome is another term for Overuse Syndrome. Carpal Tunnel Syndrome is a subcategory of this bigger category. When only the median nerve is involved, motor and large sensory fiber involvement is necessary for this diagnosis.[23] Without large fiber involvement, small fiber damage measured by thermal sensory testing is often observable in multiple distributions. Figure 10 presents typical thermal test results for Overuse Syndrome.



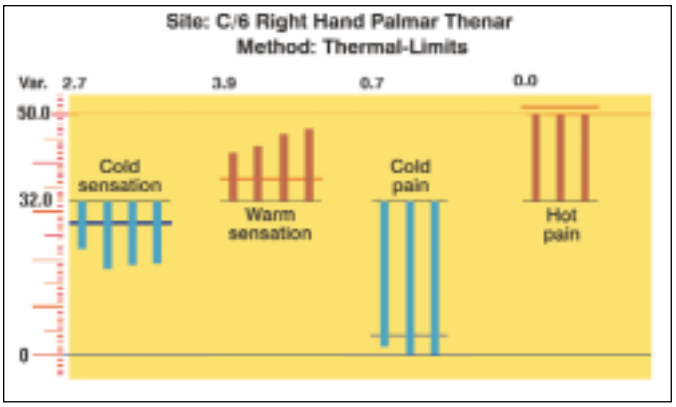


FIGURE 10. *Thermal sensory testing for Overuse Syndrome revealed hypofunction to sensation in this case. Since pain occurred with activity in this patient, tissue plane dysfunction resulting in nociceptive pain is suspected.*

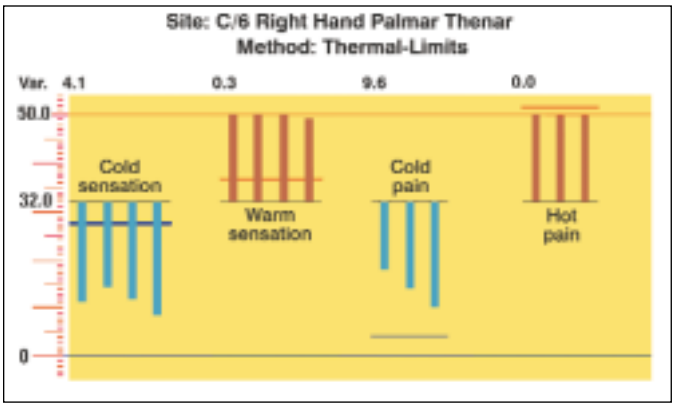


FIGURE 11. *Typical thermal test results for CRPS. Note that there is marked hypofunction to sensation and hypersensitivity to pain (at least for cold pain). Since the hot pain threshold is off-scale, we cannot know for certain that this subject is hypersensitive to hot pain. Experience and patient statement allows the author to project that there is indeed hypersensitivity to hot pain.*

Surprisingly, but in only a few patients evaluated by this author, Overuse Syndrome looks very similar to multiple level radiculopathies upon thermal testing. The difference from nerve root disease is distribution of abnormal thermal sensory findings in the face of no significant spinal pathology and the history of repetitive use of the involved body parts. If there is no pain with rest/inactivity, the pain must be nociceptive. If pain occurs, it is usually burning in nature — indicating C-fiber irritation. Without counter measures, Overuse Syndrome may be expected to progress to Complex Regional Pain Syndrome.

Complex Regional Pain Syndrome (CRPS). While CRPS was originally called reflex sympathetic dystrophy (RSD), the renaming to complex regional pain syndrome (CRPS) recognizes that these neuropathies involve more than one type of nociceptive fiber pathway. The hallmark of CRPS in small thermal nerve testing is both marked hypofunction to sensation and marked local hyperperception of pain. These abnormalities may be found, usually to a lesser degree, throughout the body, even in areas not thought to be painful by the patient (see Figure 11).

CRPS has been associated with local subcortical/central influences[13,24] and primitive or basic physiologic changes, characterized by the some or all of the following underlying basic physiologic phenomena:

- A-delta and C-fiber dysfunction
- sputter/static type discharge
- ephatic transmission
- spread and/or jumping of pain sensation, e.g. the mirror effect
- patchiness of pain sensation
- backfire — efferent reflex
- axon reflex
- abnormal reaction to external stimuli
- abnormal chemical hypersensitization
- efferent C-fiber dysfunction leading to circulatory changes

Other primary physiologic system changes and dysfunctions also occur:

- increase in alpha-adrenergic receptors
- increased levels of catecholamines
- estrogen receptor dysfunction
- testosterone receptor dysfunction
- cortisol receptor dysfunction
- circadian rhythm dysfunction

In general, small nerves/axons must be mechanically and/or chemically damaged leaving a mixed pattern of thermal hypoactivity manifested in reduced awareness of warming and cooling, and thermal hyperactivity manifested in the sensation of pain. If the C-fibers are irritated, one expects a continuous burning, achy pain. If the A-delta fibers are irritated, one expects occasional sharp, lancinating pains.

The author's experience with thermal testing indicates that the sympathetic C-fibers and A-delta fibers are concomitantly involved in CRPS. Dysfunction can involve more A-delta fibers in some patients and more C-fibers in other cases, but usually more or less equally. The pattern is markedly not uniform over the body when compared with the opposite side of the body and with neighboring asymptomatic areas, if available.

The balance of involvement between these types of fibers varies, and the balance between dead cells and irritated cells also varies. However, patterns do emerge and treatment options can be chosen. Due to the progressive nature of this condition, early intervention is desirable to avoid the accompanying progressive physiologic and structural changes.

If hypofunction occurs, one would not expect pain to be perceived. Three mechanisms can be hypothesized to explain the pain in the face of hypofunction to sensation: 1) the degree of axonal irritation and/or the number of hyperfunctioning axons must override the hypofunctioning thermal axons suggesting overall separate pathways for sensation and pain (supported by Abraham[25] and Becerra, et al[26]), 2) in the course of the pathology, locally sensitive central nerve pathways are already sensitized to the sensation signals, or 3) both. The second opinion seems to predominate since, as in Figure 11, the delta between sensation and pain thresholds is relatively large in the author's experience. Smaller sensation-pain deltas are more consistent with CRPS.

Myofascial Pain Syndrome. The author has concluded that myofascial pain syndrome is nociceptive in nature. Because the spindle muscle fibers, i.e. the nidi of trigger points, is innervated by C-fibers and the capsule is innervated by both A-delta and C-fibers and inflammation does not appear to be primary

in the pathology, we would expect — and the author has found — mostly normal small-nerve pathway function, as long as other concomitant nerve pathology does not occur.

Central Hypersensitivity Syndrome. Central Hypersensitivity Syndrome is neither a psychological nor a psychiatric disease. The author has observed that this condition develops over time due to sustained nerve insult from severe acute, recurrent acute, or chronic nociceptive and/or neuropathic pain. Gelnar, et al[27] have described an inkling of this phenomenon as "the functional connectivity across multiple cortical regions reorganizes dynamically with each task." Mailis, et al[28] states, "functional aberrations of brain function as part of dynamic CNS plasticity."

Upon thermal sensory testing without functional MRI correlation (Gelnar, et al[27]), this syndrome requires deductive decisions from the history, physical examination and general hyperfunction to pain. Because this central sensitivity is caused by peripheral pain usually with residual neuropathic pain, this diagnosis must be sorted out from the basic, underlying condition.

The author has seen wide distribution hyperfunction to pain with or without hypofunction to sensation on thermal sensory testing. With local peripheral distribution differences other, possibly causative, pain pathologies can also be identified.

Summary

Practitioners need a logical system as a guide to the most effective treatments, yet actual mechanisms are not yet thoroughly understood. In the meantime, some patients — having pain that is not clearly understood — forgo treatment for pain or are diagnosed as psychosomatic. These patients suffer twice: from the pain itself and the perception that their providers — and by extension, society — do not take their suffering seriously.

Without visible pathology, many patients fail to obtain definitive diagnoses or suitable treatments. Even in situations where the pathology was identified and treated, there may be ancillary nerve damage — either peripheral or central — as a result of sustained nerve irritation. Measurement of nerve health, utilizing commercially-available instruments can, at a minimum, point the practitioner in the right direction. In all cases, the diagnoses must encompass history, clinical observation, as well as objective measurement.

Thermal sensory testing is a study of small sensory nerves. These are the nerves that conduct sensation and pain signals to the brain. On the other hand, electromyography and nerve conduction studies test the function of motor and very large sensory fibers, which are not anatomically nor functionally related to the nerves transmitting pain signals to the brain. The thermal sensory testing machine directly measures the thermal function of small nerve fibers (A-delta fibers and C fibers) for warm and cold sensation along with hot- and cold-induced pain. Generally, the small, myelinated A-delta fibers transmit focal, lancinating, sharp, prickly pain sensation to the brain. Small, unmyelinated, primitive C-fibers transmit chronic, burning and/or aching pain from body regions.

It has been the clinical experience of the author that the graphical test results of the thermal sensory testing equipment are usually correct, but more complex and precise interpretations can only be done by trained and experienced clinicians. ■

Dr. James Woessner holds a doctorate in biological sciences in conjunction with a medical degree. His professional medical training includes neurology and physiatry. Dr. Woessner records and analyzes data on a daily basis in his solo practice; he frequently writes and lectures about pain and other subjects in Physical Medicine. Dr. Woessner may be contacted at Advanced Pain and Medical Rehab, 1090 Indian Canyon, Suite 104, Palm Springs, CA, 92262; phone, 760-778-8990.

Editor's Note: the final installment of this series (part three), will be presented in the next issue and cover treatment options suggested by the patient data, along with reiterative testing to further characterize a patient's complex disease state underlying the pain.

References

1. Woessner J. A Conceptual Model of Pain. *Practical Pain Management.* PPM Communications. 2002. 2:5, 8-16, 37.

2. Casey KL and Bushnell KL, editors. *Pain Imaging*. International Association for the Study of Pain. 2000. Vol. 18. 248 pp.

3. Stojanovic M. Quantitative Sensory Testing in Pain States. *Current Review of Pain*. World Institute of Pain. 1998.

4. Covino BG, Scott DB, and Lambert DH. *Handbook of Spinal Anesthesia and Analgesia*. W.B. Saunders, Philadelphia, PA. 1994. (p. 29.) 168 pp. Illustration reprinted with permission from Elsevier Science.

5. Medoc website. www.Medoc-web.com/peripheral-pic.html. October 2002.

6. Fishman S. *The War on Pain: How Breakthroughs in the New Field of Pain Medicine are Turning the Tide Against Suffering.* HarperCollins Publishers, New York. 2000. 301 pp.

7. Verdugo RJ and Ochoa JL. Use and misuse of conventional electrodiagnosis, quantitative sensory testing, thermography, and nerve blocks in the evaluation of painful neuropathic syndromes. *Muscle Nerve.* 1993. Oct;16(10):1056-1062.

8. Guyton AC and Hall JE. *Textbook of Medical Physiology*. WB Saunders, Philadelphia. 1996. 1148pp.

9. Hubbard DR, Jr. Chronic and Recurrent Muscle Pain: Pathophysiology and Treatment, and Review of Pharmacologic Studies. *Journal of Musculoskeletal Pain.* 1996. 4(1/2):123-143.

10. Schwartz RG. Electric sympathetic block: current theoretical concepts and clinical results. *Journal of Back and Musculoskeletal Rehabilitation*. 1996. 10:31-46.

11. Dotson M. Clinical neurophysiology laboratory tests to assess the nociceptive system in humans. *J Clin Neurophysiol.* 1997. Jan;14(1):32-45.

12. Chado HN. The current perception threshold evaluation of sensory nerve function in pain management. *Pain Digest*. 1995. 5:127-134.

13. Thimineur M, et al. Central nervous system abnormalities in complex regional pain syndrome (CRPS): clinical and quantitative evidence of medullary dysfunction. *Clin J Pain.* 1998. Sep;14(3):256-67.

14. Pochaczevsky R. Thermography in posttraumatic pain. *Am J Sports Med.* 1987. May-Jun;15(3):243-250

15. Kosek E. Somatosensory Dysfunction in Fibromyalgia: Implications for Pathophysiology Mechanisms. *PAIN*. 1996 Dec;68(2-3):375-383.

16. Lautenbacher S. and Rollman GB. Possible deficiencies of pain modulation in fibromyalgia. *Clin J Pain.* 1997. Sep;13 (3):189-196.

17. Weigent DA, et al. Current concepts in the pathophysiology of abnormal pain perception in fibromyalgia. *Am J Med Sci.* 1998. 315(6):405-412.

18. Hurtig IM, et al. Quantitative Sensory Testing in Fibromyalgia Patients and in Healthy Subjects: Identification of Subgroups. *The Clinical Journal of Pain.* 2001. 17: 316-322.

19. Staud R. Abnormal sensitization and temporal summation of second pain (wind-up) in patients with fibromyalgia syndrome. *Pain*. 2001. Mar;91(1-2):165-75.

20. Takahashi Y, et al. Thermal Deficit in Lumbar Radiculopathy. *Spine*. 1994. 1:19(21)2443-9;2449-50.

21. Nygaard OP and Mellgren SI. The function of sensory nerve fibers in lumbar radiculopathy. *Spine*. 1998. 23:3,348-352.

22. Sindrup SH, et al. Diagnostic yield by testing small fiber function in patients examined for polyneuropathy. *J Peripher Nerv Syst.* 2001.

23. Lang E, et al. Parameters of thick and thin nerve-fiber functions as predictors of pain in carpal tunnel syndrome. *Pain*. 1995. Mar;60(3):295-302.

24. Thimineur M. *Correlation of Quantitative Sensory Testing (QST) to Pain and Symptoms in Chronic Pain Patients*. American Pain Society, Poster. Oct. 1999.

25. Abraham C. Canadian M.D.'s locate the brain's pain cells. *Toronto Sun*, National News Section, Tuesday, April 20, 1999.

26. Becerra LR. Human brain activation under controlled thermal stimulation and habituation to noxious heat: an fMRI study. *Magn Reson Med*. 1999. May;41(5):1044-57.

27. Gelnar PA. A comparative fMRI study of cortical representations for thermal painful, vibrotactile, and motor performance tasks. *Neuroimage*. 1999. Oct;10(4):460-82.

28. Mailis A, et al. *FMRI in Unexplainable Widespread Somatosensory Deficits (WSDs) in Patients with Chronic Pain.* Poster, American Pain Society Annual Meeting, Oct 2000, Atlanta, Georgia.