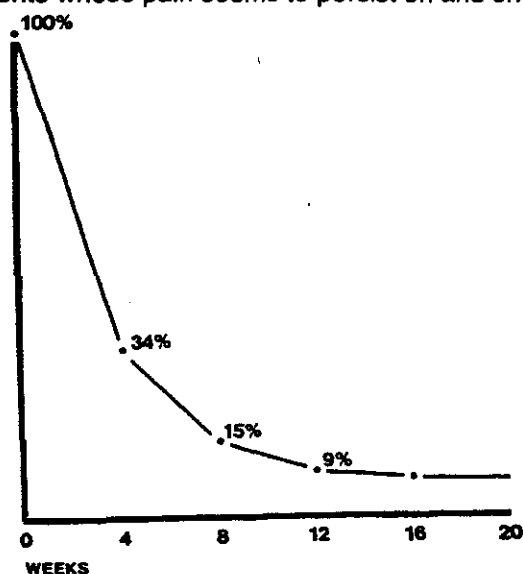


Pain and Misperceptions in Neuropathways

C.Chan Gunn, MD

What is pain? Everyone knows what the sensation of pain is, but its definition is not at all simple. Many of us simply treat pain without bothering with its definition, yet we are convinced that we have excellent results. How can this be explained? The fortunate part of treating pain is that the great majority of patients we treat recover relatively quickly. In fact, over 90% recover within eight weeks and it does not seem to matter what type of treatment is given, the body has a great capacity to heal itself. The problem begins, when, after several weeks have gone by, after we have tried all forms of treatment, there are still some patients whose pain seems to persist on and on—



THE NATURAL HISTORY OF HEALING

The dictionary gives several meanings to the word. There is the archaic definition, meaning punishment: "Upon pain of death thou shalt not....." Even today, when pain is mentioned, there is still a deep down, subconscious feeling that there must be a guilty reason for it and that the patient must "suffer", which is another meaning given to the word. Yet another meaning is that of hardship and toil - "he took pains to accomplish this".

The definition used by the International Association for the Study of Pain is: "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described by the patient in terms of such damage". This definition can be misleading because pain is not just one, but at least three distinct entities. Furthermore, pain, the central perception of noxious input, can arise from non-painful signals misperceived as painful ones. Pain can even arise when there is no external input.

Nociception

For many years it was thought that excess intensity of stimulation onto any of the five senses would cause pain. Today, this intensity theory of pain has given way to that of specificity, meaning pain is a sensation unto itself, with its own specific receptors or nociceptors.

Let's briefly review how pain perception works in the nervous system by using a simple analogy. Imagine a tall building with a central tower and wings. In each wing there are two fire wardens whose specific job is to bring reports on the outbreak of a fire (pain signals) to the Central Tower (spinal cord) and thence to management (brain).

Suppose the wardens have discovered a fire in a wing of the building. One of the wardens, old Charlie (representing thin, slow, Type C nerve fibers), shuffles slowly towards the Central Tower. At the same time, young Adam, the other fire warden (representing faster, A-Delta fibers) strides briskly towards the the Central Tower. Adam brings his message from skin and mucous membrane, and Charlie from deep tissues as well. In the body, there are many more Charlies than Adams. At the entrance gate to the Tower (the dorsal horn) there is a guard called Tom (the Transmission cell), who passes information to others messengers inside the Tower by writing the message on a piece of paper (Substance P). Tom is a busy person since he is required to pass information from both wardens as well as from other messengers carrying non-painful information (such as touch, pressure and muscle tension). Many of the other messengers are bigger and swifter, and if too many of them arrive at the gate at the same time, Tom is unable to give his attention to the fire wardens. (This is the basis of the well-known Gate Theory of

Melzack and Wall - when there is simultaneous input of non-noxious and noxious information, the faster and larger fibers get their messages through the gate first, hindering the pain messages. This explains why rubbing the painful area reduces the hurt.)

Once past Tom, Charlie's message is handed to Charlie II in the Central Tower, who immediately climbs the stairs to the next floor. There, he passes the message on to Charlie III, who, in turn, climbs to the next floor; and so the message is passed on, floor by floor, until it arrives at the brain itself.

On the way up, at each floor, Charlie announces his message to the entire floor, alerting all the other wardens, including those who regulate blood flow (vasomotor), sweating (sudomotor), and "goose-bumps" (pilomotor). The alarm can spread to the other side of the body, and occasionally may be relayed to a distant location as "referred pain".

Charlies are part of a primitive signalling system, the only one present in reptiles. Their message gets only as far as the floor below the penthouse, reaching the reptilian and old mammalian brains (limbic system), because Charlie's system was developed before the top-floor penthouse, or thinking brain had evolved. The older brains are the emotion-controlling centers which regulate our glandular system, as well as the entire autonomic system. The commotion created by Charlie's message often causes anxiety and switches on the emergency systems for the body's response of "fight or flight".

Adam's route is a more recent evolutionary development. It is quicker and more efficient. For instance, when you step on a nail, you not only feel pain, but you can also localize it. Adam's message is likewise passed to Tom, who relays it to Adam II, inside the Tower (spinal cord). Adam II, however, is smarter than Charlie II; instead of climbing the stairs, he jumps into the elevator and zooms directly to the Penthouse (conscious brain). There, he passes the message to Adam III, who runs down the hall to deliver the message to the map room (sensory cortex) localizing the pain. Since there are only three Adams involved, this system is faster. You locate the pain, before you realize it is painful: "Ouch there" comes before "ouch".

Fire wardens in general are consistent in their alertness. Accordingly, the peripheral threshold of pain does not vary from one person to another. A pin-prick should be felt as a pinprick by everyone, but an individual's interpretation of pain in the brain may vary: one man's pin-prick may be another man's stab. A "high threshold for pain" means that you can cope well with it mentally.

The central tower also has an inner stairwell. Charlies travelling via this inner stairwell may meet staff in the inner rooms (the peri-aqueductal region of the midbrain) who have cooler heads. They often decide to play down the alarm and do so by sending inhibitory messages down to Tom via the inner stairwell (the Descending Fibers System). This makes Tom a busy person indeed, since in addition to all his other duties, he has to obey inhibitory commands to ignore incoming pain messages.

To recap, pain receptors send messages to the brain via two main tracts. One tract, the neospinothalamic tract (Adam or A-delta) is newer, faster and more efficient, requiring only three relays. Adams are situated as a veneer on the surface of the body (skin and mucous membrane) and they function as a frontline defence that reacts immediately to pain, or threatened pain. Nociception mobilizes protection to counteract or to escape from the cause of injury. Adams' message (for example, a slap on the face) is usually fleeting, and rarely gives rise to lasting pain.

Inflammation Pain

Unlike a slap on the face, a blow given forcefully likely results in pain which persists for many days. The reason is that tissue cells are damaged, releasing intracellular chemical contents (such as Histamine, Serotonin, Bradykinin and Hydrogen ions) that lead to local inflammation. Inflammation is the response of tissue to injury or infection and is the vital prelude to repair processes. The hallmarks of inflammation are easily recognized: redness, swelling, increased local temperature, and of course, pain. The released substances inflame Charlies, who are the prime messengers of inflammatory pain signals.

"Acute" pain becomes "chronic" when ample time has been allowed for inflammation to subside and wounds to heal. At this stage, the patient is

more concerned with caring for the injury than its cause, and may be dominated by anxiety. Anguish turns into frustration and depression when it proves difficult for the condition to be accurately diagnosed or effectively treated. Standard diagnostic techniques and laboratory tests are not helpful. The patient focuses more and more on the condition, and less and less on surroundings. The search for treatment may dominate the patient's life. The word "psycho-somatic" may insinuate itself into your mind, and if compensation is involved, the ugly suspicion of malingering may arise.

"Acute" and "Chronic" pain

These terms are imprecise and do not define the underlying pain condition. "Acute" simply means "coming sharply to a crisis", and one thinks of diseases that arise suddenly and are, hopefully, self-limited. Acute tonsillitis, for example, is a sudden inflammation of the tonsils.

"Chronic" pain does not indicate the pathology involved. Pain can become intractable and persist far beyond the usual time for healing if any of the following situations is present.

(1) Steady, ongoing nociception or inflammation; but a constant source of tissue damage or inflammation is usually quickly found and treated.

(2) Psychogenic factors, which are outside the scope of this lecture.

(3) In the absence of injury or inflammation, the most likely cause is some malfunction or disorder in the nervous system. This usually causes the pain sensory system to become overly sensitive and misperceive non-painful signals as pain. This third category of pain involving unhealthy nerves is often misunderstood because medical diagnosis traditionally presumes that pain is a signal of tissue injury conveyed to the CNS via a healthy nervous system.

Examination typically fails to reveal a source of pain, and the astonishing reason is that there is no pain source in the generally accepted sense of the word -- the following anecdote may explain this paradox.

Our house had been burgled and we decided to install a burglar alarm. The experts we called in installed an elaborate system. There were pressure-sensitive pads under the carpet, infra-red visual sensors in the library, temperature-sensitive

detectors in the living room, and so on. Activating any one of these would cause a siren to sound, and a message to be relayed by phone to the police station. In effect, the experts had created a sensory system not unlike the nociceptive system in the body. The detectors are like nociceptors. The siren is like a cry of pain. The telephone lines are like nerves. The policeman at the station is like the central nervous system. In the very first month after the installation, there were three alarms and the police were quick to respond each time. However, all were false alarms. Finally, when I discussed the situation with the police, I was told that alarms are mostly false. It is the installation that is usually at fault. An alarm system can malfunction and become too sensitive, thus overreacting to normal inputs. Instead of the weight of a man's step on the pad, a cat can trip the alarm. Instead of the body temperature of an intruder, the setting sun can activate the heat detector. Sometimes, the alarm system can activate itself without any apparent cause.

This gave me an insight into the nature of pain when there is no apparent pain source. Is it possible for an abnormal nervous system to be up to tricks and produce pain when there is no noxious input? If so, then the search for a tangible source of noxious input (just like the search for a burglar) is pointless.

The smart policeman also put me on the right path. To diagnose and remedy the alarm problem, we would require the services of an alarm system expert. In pain, the corollary is obvious: an overly sensitive nervous system requires desensitization. Physiologists recognise that a malfunctioning or neuropathic nerve can become overly sensitive and generate abnormal impulses -- the technical term for an overly sensitive structures is Supersensitivity, and its appropriate treatment is desensitization.

To understand how this type of pain, neuropathic pain, can come about, we must examine three key factors -- Neuropathy, Prespodylosis, and Cannon's Law of Denervation.

Neuropathy.

Degeneration is a normal and inevitable process, and the nervous system is the most vulnerable

system because nerve cells lose virtually all their cellular replicative properties during youth. Healing in nerves, is slow and patchy. It is like a growing child who is given new clothes as he grows out of them; but when he has reached his full-grown size, he has to make do, for the rest of his life, with old clothes that are patched up and again and again. A malfunctioning nerve is a very common condition. A nerve can malfunction even before there is structural damage: this condition is known as neuropathy.

Prespondylosis.

Another inevitable consequence of degeneration is the gradual disintegration of the intervertebral disc and surrounding tissues or Spondylosis. Spondylosis can irritate the nerve root, and cause malfunction in the structures innervated by the nerve. Spondylosis is usually unsuspected unless there is associated pain. I have named the silent stage of spondylosis, when there can be abnormal function but no pain or other symptoms, "Prespondylosis".

There are hundreds of causes of neuropathy besides wear and tear: injury, infection, general metabolic diseases (such as, diabetes mellitus or thyroid disease), vitamin and trace element deficiencies, environmental pollutants including chemicals and radiation, and carcinoma.

Cannon's Law of Denervation.

Would you fly in a plane if you were told that the designer of the plane is unaware of the universal Law of Gravity? Of course not, yet many professionals who treat pain are aware of Cannon's universal Law of Denervation. This law deserves to be quoted as originally stated by Cannon and Rosenblueth:

"When in a series of efferent neurons a unit is destroyed, an increased irritability to chemical agents develops in the isolated structure or structures, the effect being maximal in the part directly denervated."

Simply put, when a nerve link to a part of the body fails, that part of the body becomes highly irritable and extremely excitable. Cannon used the term "supersensitivity" because the sensitivity in denervated structures increases not just by a small

amount but sometimes by over 1000 times. Supersensitivity can occur in every part of the body including skeletal muscle, smooth muscle, spinal neurons, sympathetic ganglia, adrenal glands, sweat glands, and even brain cells. Supersensitive structures overreact to a wide variety of inputs including stretch and pressure. Supersensitive receptors may explain why some individuals can feel barometric changes and are able to predict rain.

Contracture, Spasm and Muscle Shortening

The most significant structure to be affected by supersensitivity in relation to pain is striated muscle. In a supersensitive muscle, the neurotransmitter acetylcholine acts, not only on motor end-plates, but over the entire surface of the muscle fiber. Normally, acetylcholine is released in small measured amounts, and after performing its function, is immediately destroyed by Acetylcholine Esterase. In neuropathy, the production of acetylcholine esterase is reduced therefore, the entire muscle responds abnormally: contraction is prolonged and exaggerated.

Denervation also causes "territorial invasion". Every gardener knows what this means -- when a bed of roses dies, the weeds move in to take over. Whenever muscle cells lose their nerve supply, adjacent surviving nerve axons send sprouts to invade the deprived sector and take over, enlarging their territory. Sprouting distorts the normal pattern of muscle contraction (and are seen in electromyography as "Giant waves").

In neuropathy, the sodium pump does not function properly and this upsets the composition and electrical properties of individual muscle cells. Individual fibers may then generate spontaneous, asynchronous contractions known as Fibrillations. It is like children at school: when the teacher is out of the room, the fun begins

Abnormalities also occur in neurons. A supersensitive nerve fiber is sensitive to chemical transmitters at every point along its entire length instead of just at the terminal. As in muscle fibers, denervation induces sprouting in adjacent neurons and they become more receptive to foreign innervation. Thus, muscles and nerves may accept contacts from many other types of nerves,

including autonomic fibers and even sensory nerve fibers. Short circuits or "Ephapses" may occur. Sometimes abnormal contacts between autonomic nerves which control vasoconstriction and other sensory nerves may give rise to Reflex Sympathetic Dystrophy or Causalgia.

All these abnormal changes create chaos. Instead of muscles contracting and relaxing properly, with all muscle fibers acting in unison as in a "contraction", different fibers contract individually and without coordination. In the early stages, there may be twitches. Later, the condition becomes a "Contracture", when there is a chronic shortened state, and parts of the muscle may be felt as tender, ropey strands. Contracture may lead to fibrous changes, and when it is associated with pain, it is sometimes labelled as "Fibrositis" or "Fibromyalgia".

You can "see" and "touch" this type of pain once you are aware of its pathology. The subtle signs are to be found within the distribution of the nerve and involves all its components: motor, sensory and autonomic.

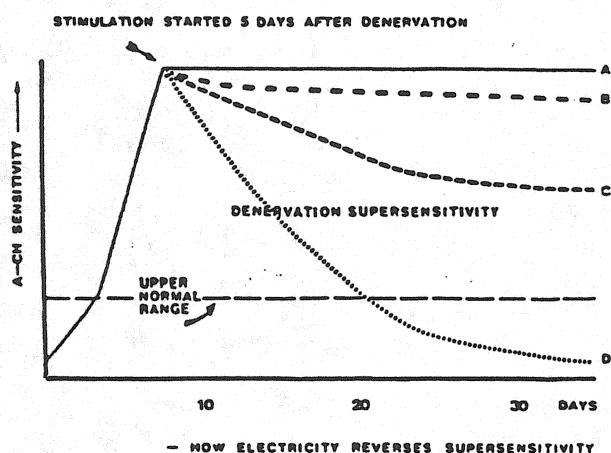
The Trophic Factor The welfare of every part of the body needs a vital factor known as the Trophic Factor delivered by the nerve. When a part of the body is deprived of the trophic factor, it "a-trophies". In neuropathy, the delivery of the factor is impeded. Lomo has demonstrated that supersensitivity and the other abnormal features of neuropathy can be reversed by direct electrical stimulation. In effect, Lomo showed that the trophic factor is energy in the form of electricity.

It is relevant to note that all physical methods of treatment are forms of energy which ultimately stimulate the body. If your shoulder aches, your natural reaction is to massage it. You are giving an input of mechanical energy which is sensed by specific tactile and pressure receptors. Other forms of mechanical energy are exercise, traction and, of course; manipulation. These are sensed mainly by muscle spindles and Golgi organs. Temperature receptors can be stimulated with thermal energy - eg, hot or cold packs. Other forms of energy are radio waves, electromagnetism and laser beams. But all local treatments are effective only if the nerve is still functioning. A stimulus is sensed by receptors, transduced into an electrical signal and

sent to the spinal cord. It is the reflex electrical impulse bouncing back from the cord to the affected structure that stimulates.

Unfortunately, physical treatments all have a severe limitation -- they are passive modalities, and when treatment is stopped, the extrinsic source of energy ceases. They are temporary substitutes for the body's own bio-energy, and like giving insulin to a diabetic, it does not solve the problem.

There is, however, one ideal source of energy. It is the body's own healing force which is easily tapped. Galvani, in a series of experiments which marked the beginning of electrophysiology, demonstrated in 1797 the existence of electricity in tissues. He was able to detect the electrical potential following injury and called it the "Current of Injury". This intrinsic source of energy, the primary agent in promoting relief and healing, is easily achieved by making minute injuries with a fine needle as in acupuncture. Unlike extrinsic sources of energy, the stimulation remains in effect for days, until the miniature wounds heal.



Needle therapy has another unique benefit: it heals by releasing the Platelet-derived growth factor (PDGF) from blood which induces cells to proliferate. In effect, blood is a healing agent, bringing to damaged cells a gene-factor they require to multiply. There is no other treatment I know of which does this.