June 2005

The Under-Treatment of Chronic Pain in the United States: A Theory of Inadequate Education

Darrin D'Agostino

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A Theory of Inadequate Education

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A Thesis
Submitted in Partial Fulfillment of the
Requirements for the Degree of
Master of Public Health
At the
University of Connecticut
2005
Final Approval Page

Master of Public Health Thesis

The Under-Treatment of Chronic Pain in the United States:
A Theory of Inadequate Education

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2005
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Chapter 1
Pain in Society

Introduction

Although chronic pain in the United States is well recognized, it is often under-treated and under-diagnosed for a variety of reasons. My experiences with patients who have chronic pain lead to the formulation of the main themes of this thesis. It has been my experience for the last seven years, that people with chronic pain are seeing numerous providers, receiving numerous medications, and are remaining in pain, ultimately becoming frustrated with the medical system and physicians in general. While I was attending classes for my public health degree, I realized that chronic pain, as a major public health issue, is not addressed adequately, nor is it given appropriate attention in our medical schools and residency programs. These doctors in training are not adequately prepared for their future careers and the treatment of chronic pain.

This manuscript will tie together many aspects of chronic pain, it’s causes, diagnosis and management, which I believe are affecting appropriate treatment strategies. I will also show that physicians have grown to fear using narcotics because of legal issues and state regulations, which attempt to decrease the illicit use of controlled substances. These regulations are adversely affecting chronic pain management. In addition, I will demonstrate how the lack of education of our young physicians is contributing to the inadequate treatment of pain, and will directly link this to the reservations older physicians have in prescribing controlled substances. Finally, I will show how the understanding of the pathophysiology of chronic pain can influence pain management. It
is through research focused on the specific mechanisms and physiologic changes that develop when painful stimuli are ever present.

The resources utilized for preparing this manuscript come from personal experience, interviews with other physicians treating pain, and literature searches for chronic pain. The literature searches focused on pathophysiology, diagnostic and treatment strategies, public health issues, law documents, and current Federal, State and local regulatory documents. In addition, the Internet was utilized to reference common materials available to the public relating to pain, its diagnosis, and treatment. Finally, numerous textbooks and primary literature were used to support the current knowledge base of the pathophysiology and biology of chronic pain, how it differs from acute pain, and how medications such as the opiates affect the pain sensing pathways in human beings.

Human Rights

Every person has the right to health. This is not a legal right but rather a human right. Although in the United States we have developed a medical system that grants the most access to medical care to privileged individuals, we are continually faced with the awesome task of providing care to those who are not privileged. Health is a fundamental human right, which it is the requisite entitlement for all other human rights. Every human being is entitled to maintain the highest possible standard of health that is conducive to living a life in dignity [1]. Internationally, pain is recognized as an impediment to health and dignity. Alleviating pain and helping to maintain dignity, especially during the terminal phases of illness, is recognized as a necessity [1].
Understanding this and knowing that it is proper to help relieve pain, it is hard to understand why more of an emphasis is not placed on the education of our medical students and residents in training regarding pain and its management.

Americans with Pain

In the United States the treatment of pain creates anxiety and frustration among physicians. The usual and customary approaches to managing low back pain, for instance, have proven themselves to be limited at best and debilitating at worst. Surgeries and surgical techniques have developed and have been refined over the years but are not the solution for all patients and often leads to additional pain due to altered mechanics [2,3]. With its many causes, the management of pain has been a nuisance to physicians because of the relatively limited tools, medicines, therapies and treatments available.

Over 75 million Americans suffer serious pain on a yearly basis. Of those in serious pain, annually 50 million endure serious chronic pain lasting 6 months or more [4]. Headache, low back pain, arthritis and other joint pain, and peripheral neuropathy are the most common forms of chronic pain and are the most common presenting complaints in a physician’s office [5]. Over 26 million adults experience frequent back pain and 2/3 of Americans will have back pain during their lifetime [6]. In the United States, 1 out of every 6 Americans suffers from arthritis [7].

Chronic pain has been recognized as a public health issue. A recent survey to see just who was stricken with chronic pain in the United States was performed and it was found that there was an increased burden of unrelieved pain in children, the elderly, minorities, and patients with active addiction or history of substance abuse, those with
developmental disabilities, and those with serious chronic diseases [8]. Of those experiencing pain, 61% are women and the majority of these people were 51 years of age or older. Seventy-two percent of American’s surveyed stated they have had pain for more than 3 years, which includes 34% who have had chronic pain for over 10 years. Seventy-six percent of people with chronic pain experience their pain daily. A staggering 48% of those who experienced pain daily say this pain is ever present. Fifty-nine percent of those patients with ever-present chronic pain say their pain is not under control [8].

Chronic Pain Impact on the Individual

Chronic pain impacts many aspects of a person’s life. Fifty-one percent of employed people who have pain, state that it adversely affects their productivity at work. Forty-one percent of these patients are unable to complete a full day’s work. This translates into lost productivity and increased expense for industry in the United States. In addition to lost productivity, 45% of those in chronic pain state their personal relationships suffer due to their condition. These relationships are with a spouse or partner, a child or grandchildren, or even with a close friend [8].

Quality of Life Impact

More than 50% of people in chronic pain are unable to perform normal activities of daily living. Seventy-five percent of people in pain state that their chronic pain impacts their sleep and their ability to play sports or exercise [8]. This has particular impact on younger patients with chronic pain in that the ensuing de-conditioning of the
musculoskeletal system puts them at risk for developing new and more extensive pain issues.

As stated above, chronic pain impacts women more than it does men. Seventy-three percent of women with pain state that it prevents them from doing household chores, as compared to 57% of men who state their household chores are affected. In addition, the emotional state of women is affected more than men with chronic pain. Seventy percent of women develop stress and 55% lose desire and motivation to perform activities of daily living, or pleasurable events. Thirty-nine percent have decreased coping ability, and 36% have decreased desire for sexual relationships [AA].

As you will see below, chronic pain does not affect adults only; there is now a new generation of children and adolescence who are affected by chronic pain. This will lead to an emerging pandemic when these individuals enter adulthood.

Pain Has Many Faces

There are many forms of chronic pain. Often the initial event that triggered the pain is remote and does not affect the course of treatment since the pain takes on a pathophysiologic process of its own. Chronic, non-malignant pain can develop from pain generating structures such as the musculoskeletal system, the neurologic system, or it can be idiopathic. Neuropathic pain can be central or peripheral depending on the site of injury causing the pain. Neurologic insults such as post-herpetic neuralgia or diabetic peripheral neuropathy can generate unremitting severe pain in the periphery while central neuropathic pain follows a central ischemic event in the brain [9].
Myofascial Pain syndromes are another major cause of chronic pain. Fibromyalgia is a generalized myofascial pain syndrome that is widespread and can be debilitating [9]. So unique is this syndrome that it is described in the literature as its own entity and is no longer considered a subset of myofascial pain syndromes [9]. Although the exact mechanism is not known, fibromyalgia is the subject of intense research and novel therapies. The hallmark of fibromyalgia is generalized allodynia (a condition in which ordinary, non-painful stimuli evoke pain) and hyperesthesia (a condition in which the body is much more sensitive than normal to stimulation). These characteristics tend to be the focus of therapeutic interventions [9]. Other myofascial pain syndromes can cause significant morbidity and often result from acute injury and repetitive motion strains [10].

All of these forms of pain are the subject of a large body of research and are adding to the knowledge base of pain medicine. One thing is certain; chronic pain can cause a significant amount of morbidity and mortality, which in and of itself is a public health concern [11].

Musculoskeletal Pain

Musculoskeletal problems can often lead to impairment or disability and weighs heavily on public health support systems. Often, an acute musculoskeletal injury commands immediate attention by a physician but it may be under-treated because both the physician and the patient are driven simply to decrease pain and inflammation, and not to address the underlying injury directly [12]. This approach indeed decreases the pain, but can also lead to early discontinuation of any therapy and thus incomplete
healing. When the drugs of choice are non-steroidal anti-inflammatory drugs (NSAIDs), the necessary inflammatory response needed to generate the repairative tissues is blocked. This can lead to re-injury and ultimately to increased pain. Arthritis pain is a prime example of this theory. When an arthritic knee is overused, it develops an inflammatory response. In the uncontrolled setting, this inflammation leads to a degree of disability. When anti-inflammatory medications are administered to the patient chronically, the inflammation decreases, but so does the healing potential of the knee. Arthritis is progressive and there are many factors leading to the development of this condition, but the acceleration and worsening of the arthritis is often driven by the medications used to decrease inflammation (Figure 1).

**Figure 1.**
NSAID induced chronic pain cycle

All ages are affected by pain. Teens and young adults are increasingly developing back, neck and shoulder pain. Prior to the 1980s, teens and young adults were not thought to be a major risk group for developing musculoskeletal pain. However, in a survey done in Finland in the 1980s, it was discovered that chronic back and/or neck pain was common among teens [13]. In fact, a Finnish population survey in 1991 found 15% of 12-18 year olds had pain in the neck or shoulder at least once a week, and 8% had pain
in the lower back [14]. Also, among Finnish 10-12 year olds, about 30% had musculoskeletal pain at least weekly [15]. It is more prevalent in girls than in boys and affects older groups of teens more commonly [15]. More recently, the use of backpacks by adolescents in the United States suggests that a major cause of this increase in musculoskeletal pain may be due to increased loads school-age adolescents are asked to carry [16].

Low back pain can be disabiling among adults and often leads to economic loss and financial strain on individuals and families [17]. The 1990’s saw a steady rise in the number of people experiencing back, neck, and shoulder pain. By the end of this decade there were more people with back and shoulder pain than in the preceding decade [15]. It can be expected that there will be a surge in degenerative musculoskeletal pain and disability in adults based on this information about teens and that this could represent a new disease burden on our youth [15].

Economic Impact

It is estimated that chronic pain, in it’s many forms, costs the United States approximately $90.7 billion per year [18, 19]. This is very difficult to calculate because of the many aspects of pain that will be discussed below. It is safe to say though, that the largest portion of the pain price tag is the lost productivity and missed workdays associated with pain. On average, people with back pain incur health care expenditures 60% higher than those individuals without back pain [19]. In addition, health care costs were higher per-capita in those people with back pain who were older, female, white, medically insured, or suffered from disc disorders [19].
A discussion about the public health ramifications of pain in its chronic state must address some basic groundwork and science. This author believes there are two generally accepted beliefs by physicians regarding pain treatment that interferes with the treatment of chronic pain. First, that chronic pain is simply long standing acute pain, and second, that chronic pain will respond to the same medications in the same way that acute pain will respond. A logical corollary is that if the same medications can be used, and that if the pain is simply long-standing acute pain, then prescribing medications would be long-standing and thus, many physicians do not want to get involved.

As will be discussed, the pathophysiology of chronic pain is different from acute pain. Based on this, it is reasonable to assume that the treatment of chronic pain must have different requirements. The mis-treatment of chronic pain is multifaceted and complex. But the basic reason is that a solid foundation is not laid in the early years of medical training. Medical schools and residency training programs do not do a good job in teaching students about pain and its treatment [20]. Because recently technology has been able to reach into the human body more deeply the understanding of chronic pain has grown. However, even with this knowledge growth, the dogma of treating chronic pain is slow to improve. In order to put this into perspective, we need to develop the foundation on which pain treatment must develop.
What is Pain

Acute pain plays a vital role in human survival. When acute, pain is a symptom or warning that must be heeded less grave consequences could follow. In one sense, pain is good and necessary as long as its presence is well defined with a beginning and an end. When these well-defined borders are compromised and the pain producing insult is not halted, pain becomes chronic, pathologic and, in some cases, debilitating. Chronic pain is no longer merely a symptom of a pathologic process but rather a chronic disease state thus mandating a change in diagnostic and treatment strategies [21]. There is no physiologic role or survival advantage to having chronic pain and therefore the goals of therapy must be aimed at the pain generating and maintaining process, not the remote initiating event. Simply masking the symptoms of the chronic pain disease does not alter its natural history and ultimately leads to treatment failure and dissatisfaction by both the physician and patient.

Pain is an “unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” [22]. This description of pain alludes to the vast nature of pain but also relates to the reader the emotional and cognitive aspects of pain and its effect on people. Pain is very subjective and for each individual the sensation of pain varies. When it is constant and chronic, the way pain is perceived changes. It is a conscious experience that is influenced by somatosensory and psychosocial factors. The perception can range from mild aches to complete disability based on a combination of the influencing stresses, both physical and emotional, and their
impact on the individual’s psychosocial foundation. Pain is transformed into the disease and has a combination of physical, psychological, social, economic, and spiritual effects on an individual [23].

Neurology of Pain

The sensation of pain travels via an incredibly sophisticated system of highly specialized tissue. Humans have the most highly developed and complicated nervous system in the animal kingdom. All bodily functions are under neurological control in one way or another [24]. With its complexity comes difficulty in diagnosis especially when different types of pain are present. Specialized nerve endings called primary afferent nociceptors are present where the sensation of pain is critical for maintaining homeostasis. In other words, the tissue that needs to be protected must have a sense organ that is able to detect noxious stimuli and thus allow the individual to respond to that stimulus. The most nociceptor rich tissue in the body is the skin since it is our most intimate interface with our environment; however, nociceptors are also found in subcutaneous tissue, periosteum, joints, muscles and visceral tissue [25].

Nociceptors are peripheral and are the free nerve endings of a sensory neuron with a cell body located in the dorsal root and trigeminal ganglia. When these receptors are activated by a noxious stimulus an impulse is sent to the spinal cord or brainstem nuclei predominantly via A-delta (myelinated and relatively fast) or C fibers (unmyelinated and are the large majority of peripheral nociceptors) axons. Nociceptors are depolarized by various stimuli--some by a specific type of stimulus such as high-threshold mechanoreceptors, while others by more than one type of stimulus such as the
polymodal nociceptor. In either case, this nociceptive information is then distributed to various cortical and subcortical structures of the brain. The result: conscious perception of pain and conscious and subconscious initiation of neuromodulatory, endocrine, and emotional responses [25]. When discussing pain that is generated from the bone it is critical to realize that the pain sensing organs of the bone are nociceptive afferent fibers that are most concentrated in the periosteum [26]. The periosteum is often the main source of pain caused by metastatic cancer, traumatic injury and even ligament or tendon injury, to name a few.

Pain arising in muscles, tendons, ligaments, and bones is detected by the free nerve endings imbedded in their connective tissue [27]. Joints have four types of sensory endings each of which are morphologically different and have unique physiologic responsiveness [27]. These cells are within and around the capsule of the joint and are responsible for detecting acceleration and deceleration. In addition, some of these cells within the ligaments respond to strain and allow for inhibition as a protective mechanism [28]. Finally, abundant in the synovial membrane, capsule and periarticular connective tissue are free nerve endings which are believed to respond to potentially injurious mechanical stresses and mediates pain in the diseased or traumatized joint [27]. Articular innervation is so important that it is the focus of Hilton’s Law which states that every peripheral nerve supplying a muscle sends a branch to the joint moved by that muscle and to the skin overlying the joint [27]. So when a joint is the source of pain all of its components, which are interconnected by their innervations, can generate pain to some degree.
Nociceptors fire in proportion to the amount of noxious stimuli they experience. When pain is prolonged, repeated and intense, and in the presence of damaged tissue or inflammation, the threshold for activating primary afferent nociceptors is lowered and the frequency of nociceptor firing is increased with relatively less noxious stimuli [29]. This process is called “sensitization” and is often mediated by bradykinin, some prostaglandins and leukotrienes [29]. In fact, tissue that is typically non-reactive to noxious stimuli can become intense sources of pain [29]. An important example of sensitized tissue is when a constant irritating and noxious stimuli is present at the viscera. The A-delta and C afferents that innervate the viscera are usually inactive and non-responsive to stimuli, but when sensitized they respond pathologically and can become a source of deep and debilitating pain [29]. It is important to realize that patients with chronic pain respond differently and with smaller amounts of stimuli, which often leads those patients to display characteristic “pain behavior” in an attempt to be pain liberated by physicians [30].

The main neurotransmitter used by nociceptors synapsing with the dorsal horn of the spinal cord is glutamate. Glutamate can bind to several different classes of receptors but plays a critical role in generating and maintaining chronic pain. Typically, the sensation of acute pain is mediated through AMPA (alpha-amino-3-hydroxy-5-methylisoxazole-4-propionic-acid) receptors. These are always exposed on afferent nerve terminals. These receptors, however, are not the key players in chronic pain. In contrast, the NMDA (N-methyl-D-aspartate) receptor is most involved in the sensation of chronic pain. This receptor lays dormant unless there has been a persistent or massive release of glutamate. Repeated activation of AMPA receptors dislodges magnesium ions that act
like plugs in the transmembrane sodium and calcium channels of the NMDA receptor [31]. This conformational change in the neuronal membrane makes these receptors susceptible to stimulation and is the primary step in central hypersensitization and marks the transition from acute to chronic pain [30,32].

Activation of NMDA receptors has a number of important consequences (see Table 1). Because activation causes spinal neurons carrying pain to be stimulated with less peripheral input (a phenomenon known as “windup”), less glutamate is required to transmit the pain signal, and therefore significantly more anti-nociceptive input is required to stop it [31]. Endorphins and other naturally occurring pain-relievers cannot keep up with the demand and essentially lose their effectiveness. So do exogenous opioids at usually prescribed dosages. The clinical implications are clear but underappreciated--inadequately treated pain is a much more important cause of opioid tolerance than use of opioids themselves.

### Table 1. Results and Responses to NMDA receptor activation

<table>
<thead>
<tr>
<th>Normal</th>
<th>Neuropathic</th>
<th>Inflammatory</th>
<th>Long-Term</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wind-up</td>
<td>Injury Discharge</td>
<td>Neuronal Responses</td>
<td>Gene-Induction</td>
</tr>
<tr>
<td>Reduced Opioid Effect</td>
<td>Hyperalgesia</td>
<td>Hyperalgesia</td>
<td>Novel Neurotransmission</td>
</tr>
<tr>
<td></td>
<td>Allodynia</td>
<td>Reduced Opioid Effect (time dependent)</td>
<td>Cell Death</td>
</tr>
<tr>
<td></td>
<td>Reduced Opioid Effect</td>
<td></td>
<td>Pain Memory</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Reduced Opioid Effect</td>
<td></td>
</tr>
</tbody>
</table>

Adapted from Brookhoff, 2000 and Dickerson, 1994.
Healing

The biochemical basis of healing has not changed over the eons because it is an efficient, complicated and magnificent process. Healing of injured tissue is complicated. Once an animal is injured, multiple responses are induced and a symphony of cells, proteins, cytokines, growth factors and neurohumoral factors begin the process of healing. Interestingly, inflammation is necessary to induce healing and is the basic physiologic process that is common to all wounds [33]. Once started, this process has essentially three phases that overlap and share common mediators. One of the major goals of healing is to lay a new foundation of connective tissue and allow the maturation of this tissue into a well-formed network of linked proteins that have a solid matrix and increased tensile strength. Regardless of the tissue involved, the same process occurs with the resultant differentiation of tissue dependant upon the foundation to which it is attached and the forces applied to it. There are four divisions of healing that are generally described: Inflammation, Epithelialization, Fibroplasia and Maturation [34]. Often, epithelialization and fibroplasias are grouped into the “proliferative” phase since it is during this period that epithelial cells and fibroblasts propagate. It is also during this phase that the most important substance is produced, collagen (Figure 2).

In the inflammatory phase, vasoconstriction initially occurs for hemostasis and platelets aggregate to the wound site. Mononuclear leukocytes begin to accumulate and eventually differentiate into macrophages [35,36,37]. During this phase, mast cells degranulate and release histamine, among other mediators, which causes edema and more importantly, cellular migration. The resulting chemotaxis is driven by cytokines and growth factors. Among them are the interleukines, interferons, tumor necrosis factor,
platelet derived growth factor (PDGF), and transforming growth factors (TGF) [37].
PDGF released at the wound site appears to be the primary wound hormone and has both
chemotactic and mitogenic activity toward fibroblasts and smooth muscle cells [33].
Finally, small vessels become permeable to molecular and cellular mediators. Clinically,
this is identified by the accumulation of edema, swelling and pain [34]. Macrophages
peak at approximately three days, which coincides with the peak of the swelling and pain
that a patient will experience after wounding.

The proliferation phase begins approximately 4 days after wounding and actively
promotes healing for approximately 42 days. It is marked by the increase of three
specific cell lines and follows the peak of macrophage migration and differentiation.
Fibroblasts, epithelial cells and endothelial cells are the main players during this phase.
Fibroblasts are “summoned” to the wound in a multitude of ways but most importantly by
chemotactic and growth factors liberated by the macrophage and local cells. The wound
is less edematous at this point and the main activity is the deposition of collagen by
fibroblasts [33]. It is critical to allow the first two phases of wound healing to occur. To
decrease the pain people experience after injury and wounding, physicians often prescribe
medications (i.e. NSAIDs, steroids, even ice to some degree) that interfere with these
crucial stages thus interfering with the deposition of collagen. Because of its importance
in healing and thus pain, collagen, its structure, and biosynthesis will be discussed below.

The third stage of healing, maturation, begins about 3 weeks after wounding and
continues for upwards of three years (although the majority of maturation occurs by nine
months in adults) [33]. This phase is responsible for the maturation and remodeling of
connective tissue that is continually being laid down during the proliferation phase. The
proliferation and maturation stages overlap dramatically. In fact, biochemically many of
the cytokines and growth factors overlap and induce responses in a variety of cells at any
given time during the healing of a wound [37].

The process by which collagen matures and stabilizes by intermolecular cross-
linking is called remodeling. It is also during this third phase of healing that wound
tensile strength increases dramatically and, if graphed, is represented by a sinusoid curve
that plateaus below the original tissue’s tensile strength [38]. It is important to realize
that the wound’s tensile strength is not solely due to collagen synthesis or its quantity. It
may be related to the type of collagen that is produced or to its final form [38]. For
example, during granulation of a skin wound, the collagen that is laid down resembles
type III collagen, which is characteristic of embryonic collagen. During maturation, this
type III collagen is replaced by type I, the usual collagen found in skin [38]. Thus,
maturation of the wound by intermolecular cross-linking helps to differentiate the
collagen matrix and increases the tensile strength of the wound [38]. Once inflammation
is induced, particularly at the ligaments or tendons (any connective tissue in theory), the
healing of the incompetent tissue ensues and eventually, through physiologic forces (see
“connective tissue” below) organizes into structurally normal, non-pathologic connective
tissue [39].
Figure 2. Timing of Healing.

Relative amounts and timing of two key cells in healing with the resultant collagen accumulation in time. Growth factors and cytokines specific for the cell are represented (not in order of importance or relative concentrations) in the area under the curve.

Connective Tissue

Connective tissue is made up of macromolecules with collagen being the most abundant. It is ubiquitous and can be found in most organs and tissues of the body [40]. These macromolecules are comprised of at least 19 different types of collagen, fibrous proteins (elastin and fibrillin), and a series of proteoglycans. In recent years, researchers
have found other molecules in this matrix but have only partially defined their roles in connective tissue [40].

Collagen is the most abundant protein in the animal world and provides the very structure to which all cells interact. As mentioned above there are many forms of collagen, however, not all have known functions [38]. Type I is primarily found in skin (80%), bone (90%), tendons and ligaments, and most organs. Type II is found in cartilage (50%) and the vitreous humor of the eye. Type III is found in blood vessels, the uterus and skin (10%) [38]. These first three types are known as the fibrillar or interstitial collagens and can form tough dense structures. Types IV – XI are amorphous, do not form fibrils, and are found in interstitial tissue and basement membranes [38](Table 2). Fibril assembly is fascinating. The collagen that forms these fibrils is long and rod-like owing to its triple helix conformation. The triple helical formation occurs because of the molecular structure of the component three chains. Every third amino acid is glycine, the smallest amino acid. This chain can be designated by the formula (-gly-X-Y-)333 since each sequence is about 1000 amino acids long. When three chains are near each other they form the triple helix since the glycine amino acid sterically limits the potential binding spaces of the molecules. The remaining amino acids (X and Y) are mainly proline and hydroxyproline, which add stability and strength to the triple helix. These chains are bound to other chains spontaneously due to hydrophobic and charged regions along the surface of the molecules, thus forming into large collagen fibrils [40]. The self-assembly of the collagen fibrils takes place in the extracellular space, in particular, at the sight of a wound or injury.
Table 2. Major Types of Collagen

<table>
<thead>
<tr>
<th>Type</th>
<th>Characteristics</th>
<th>Distribution</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Bundled fibers</td>
<td>Skin (90%), Bone, Tendons, Ligaments</td>
<td>Structure, strength, integrity of tissue</td>
</tr>
<tr>
<td></td>
<td>High tensile strength</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>Thin fibrils, structural</td>
<td>Cartilage, vitreous humor</td>
<td>Shock absorption, joint mobility</td>
</tr>
<tr>
<td>III</td>
<td>Thin fibrils, pliable</td>
<td>Blood vessels, uterus, skin (10%)</td>
<td>Allows mobility and distensibility of vessels</td>
</tr>
<tr>
<td>IV</td>
<td>Amorphous</td>
<td>All basement membranes, basal lamina</td>
<td>Filtration, mess-like scaffolding</td>
</tr>
<tr>
<td>V</td>
<td>Amorphous/fine fibrils</td>
<td>Interstitial tissues (2%-5%), blood vessels</td>
<td>Cytoskeleton of cells, similar to type III</td>
</tr>
</tbody>
</table>

Fibroblasts are the producers of what will eventually become collagen matrix. While in the fibroblast, the proα chain, procollagen, is more soluble and is synthesized by ribosomes [40]. This chain comes off of the ribosome and moves into the rough endoplasmic reticulum and undergoes biochemical modification. At this point it has an extra length of polypeptides at either end of the chains (these promote solubility) [38]. From here, the chains move to the golgi apparatus and are excreted from the cell while a procollagen peptidase clips the polypeptides off of the procollagen molecule. This extruded molecule is insoluble in the extracellular space and is now called collagen [41]. In the extracellular space the collagen begins to form fibrils, which in turn begin to line up and form fibers. This process is called cross-link formation and is regulated by the enzyme lysyl oxidase [41]. It is here that collagen gains its structural integrity and strength. “On a per weight basis, the strength of collagen approaches the tensile strength of steel!” [41]. As collagen begins its cross linking, it also looses water. It becomes a
white semi-crystalline material that is firm, similar to the texture of ligaments and tendons. As the water is displaced by protein-protein hydrogen bonds, the collagen takes up less space and contracts [42].

Scar collagen, which fills the void left by trauma (intended as in surgery or accidental), does not regain the same strength as the collagen of the original tissue [33,38]. In fact, it may only achieve 70%-80% of the original strength [38,43]. After injury, the body tries to reestablish highly organized tissue with normal strength through an ongoing battle between the degradation and the production/remodeling of collagen. There is an equilibrium that develops and anything that interferes with production, remodeling, or maturation will offset the balance and shift the process toward degradation [41]. If this happens, the wound becomes weak and unstable. Proper nutrition and avoiding medications that inhibit the production of proteins become important to proper healing and remodeling in time [41].

Structure and Function

Ligaments and Tendons are highly organized bundles of protein. The collagen in ligaments is arranged in parallel, oblique, or spiral orientations as an adaptation to specific forces and restrictions on joint mobility [44]. Tendons are bundles of collagen fibers that connect muscle to bone and transmit tensile forces produced during muscle activity through the enthesis (osseo-tendinous junction or fibro-osseous junction) to the bone. These attachments vary in shape based on the muscle’s purpose [44]. This strong attachment is accomplished by decussating and perforating Sharpey’s fibers and creates an attachment that histologically has four zones: tendon zone, fibrocartilage zone,
mineralized fibrocartilage zone, and lamellar bone [44,45]. Within this attachment there is a high concentration of nociceptors and blood vessels, which perforate the transition fibers from the tendon or ligament at the attachment of the bone. In fact, the tendons and ligaments proper have relatively few nociceptors compared to their attachments at the enthesis [27]. When injured, this is the area that inflammation and pain is produced and is also the place where healing can occur.

Sources of Pain

Pain can originate from many structures and in many places but when it originates from the musculoskeletal system specific lesions can often be identified. Pain generating structures in the musculoskeletal system are fascia, ligaments, tendons (including their muscles), enthesis, intervertebral discs and the joints [44]. Fascia is an interesting and all-encompassing tissue that is critical for the normal physiologic function on the musculoskeletal system and deserves some attention.

Fascia is connective tissue that is everywhere in the body. It covers, supports and lubricates the organs and muscles [46].

"The fascia is the major connector between the ectodermal derivatives of the outer body and the endodermal derivatives of the inner body. It contains and maintains the internal environment, the ECF, and orchestrates homeostasis. No disease escapes notice in the fascia and no cure occurs without its assistance!" [47]

Since the fascia is so important to homeostasis, it would make sense that an alteration in body mechanics and stresses on tissue would alter the healing process. It is known that
tissue organizes and then re-organizes in response to the stresses placed upon it. An example of this is Osgood-Schlatter disease and the remodeling of bone while under stress. The transmission of forces through the fascia guides the repair process. “The linear nature of the healing collagen is dictated by the distribution of fibrin matrix in response to tension in the tendon” [44]. It becomes essential, therefore, to introduce movement into traumatized tissue in order to establish the correct blue-print for matrix formation, repair, and to re-establish normal physiology [44]. A formal review of fascia and its essential role in homeostasis is beyond the scope of this article but it is prudent to realize that including this connective tissue in the healing and repairative plan will greatly increase the success of the treatments, and will also help to re-establish homeostasis.

The ligaments maintain stability of a joint and, when sprained due to sudden shearing forces, generate pain due to disruption of the enthesis [44,48]. Tendons secure muscle to bone and when this attachment is compromised (as in a strain) inflammation and pain develops [44,49]. Enthesopathies develop due to poorly organized and degenerated tissue at the enthesis (osseo-tendinous junction)[45,50]. Tendinosis and ligamentosis (non-inflammatory conditions) are essentially a failure of cell matrix adaptation due to excessive load and tissue hypoxia [44,50]. This wound is often mistaken for tendonitis or ligamentitis and treated with anti-inflammatory medications that fail since the requisite inflammation for these medications to work is not present [50]. Ligament laxity, whether post-traumatic or congenital, often leads to painful hypermobility [44,51]. It is this specific reason that may people, once injured, never fully return to their pre-injury, pain status. Interestingly, this concept is not taught in medical school. In fact, this is a new and developing field of musculoskeletal medicine that seeks
to focus on the origin of the pain and not in the resultant sensation of the injury [45]. It should be noted that the sensation of pain due to musculoskeletal injury is what brings patients to see the doctor. This is addressed most often in the traditional ways…rest, ice, compression and elevation (know as R.I.C.E. therapy) with or without a pain medication (non-steroidal anti-inflammatory medications, narcotics, etc.). This acute phase of treatment is often repeated over the course of the injury well into its chronic stages. It has been shown in recent literature that treating the pain from these injuries, once they are chronic, by focusing on the inflammation is not effective [26] and, as was demonstrated above, by stopping inflammation there is the risk that the injury might not heal completely.

As has already been discussed, a major driving force, which prevents physicians from treating a patient’s pain more aggressively and appropriately, is the inadequate use and fear of prescribing narcotics.
Chapter 3
How Pain Affects Us

Interpretation of Pain

The human body makes its own pain medication. These chemicals block pain by inhibiting the transmission of pain through the spine and also by blocking the activation of the “pain“ receptors in the brain. Injuries in the body trigger a complex and fascinating cascade of events that translates into the perception of pain. The signal that initiates the cascade is inflammation due to the tissue damage of the injury. The inflammatory mediators and growth factors (see Table 3) trigger pain signals that transmit an impulse electrically to the brain via unmyelinated nerve fibers (C-fibers) called nociceptors. These C-fibers synapse in the dorsal horn of the spinal cord with the spinothalamic tract to carry information to the cerebral cortex. It is here, in the cerebral cortex, that pain is perceived, interpreted, and localized. It is here, in the central nervous system, that narcotic based medications work.

<table>
<thead>
<tr>
<th>PDGF</th>
<th>Platelet derived growth factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>TGF-β</td>
<td>Transforming growth factor-β</td>
</tr>
<tr>
<td>TGF-α</td>
<td>Transforming growth factor-α</td>
</tr>
<tr>
<td>FGF</td>
<td>Fibroblast growth factor (acidic, basic)</td>
</tr>
<tr>
<td>KGF</td>
<td>Keratinocyte growth factors</td>
</tr>
<tr>
<td>EGF</td>
<td>Epidermal growth factor</td>
</tr>
<tr>
<td>IGF-1</td>
<td>Insulin-like growth factor-1</td>
</tr>
<tr>
<td>VEGF</td>
<td>Vascular Endothelial Growth Factor</td>
</tr>
</tbody>
</table>
The Anti-Pain System

Often not thought of, but equally as important is the anti-nociceptive system that allows us to function even though we are in pain. Once pain signals arrive in the brain, they stimulate the release of endorphins in the periaquiductal gray matter and enkephalins in the nucleus raphe magnus of the brainstem. Endorphins inhibit the propagation of pain signals by binding the Mu-receptors on the post-synaptic terminals of the nociceptors and also post-synaptically on the dorsal horn. The enkephalins bind to delta-receptors on inhibitory interneurons in the substantia gelatinosa of the dorsal horn. This in turn causes a release of gamma-aminobutyric acid (GABA), among other chemicals, that moderate the flow of pain signals in the dorsal horn [32]. Dynorphins are chemicals released by the spinal interneurons, which activate kappa-opioid receptors. These activated receptors lead to closure of the N-type calcium channels in the spinal cord cells that normally relay the pain signals to the brain [32]. This complex mechanisms to counter the sensation of pain is absolutely necessary to human survival. Imagine a minor injury, such as a paper cut or scraped knee, that never stops hurting, eventually leading to total disability. The human race would not have survived.

Pain Begets Pain

Once the pain cascade is initiated, the pain sensing system becomes more sensitive; thus it is easier to start and maintain the painful sensations. Enkephalins are produced when nociceptors are active. While these nerves are transmitting pain, the enkephalins bind to the presynaptic delta-receptors, which are found on vesicles containing neurotransmitters. Once the neurotransmitters are released, the delta receptors
are incorporated into the presynaptic cell membrane and augment the pain transmitting ability and efficiency of the nociceptive fibers [32].

The physiology of chronic pain is not a variation of acute pain. There is a physiochemical change that makes the neural pathway hypersensitive to painful stimulation and resistant to anti-nociceptive input. When thought about in these terms, there are two possible pathways to chronic pain. The first is a direct route, which essentially stimulates the pain sensing fibers and does not cease, thus overwhelming the pain sensing areas of the brain. The second way is to alter or impair the anti-nociceptive system in such a way as to decrease or inhibit its ability to function normally. It is this latter theory that is currently being explored in the pathophysiology of fibromyalgia [9,32].
Chapter 4
Barriers to Treatment

Medication Barriers

The above physiology and neurology review sets the stage for physicians and the perceived barriers inhibiting the treatment of chronic pain. It is believed in medicine that patients with chronic pain always keep coming back and never get better. In the past, the science of pain was poorly understood and this comment developed as a result of the lack of treatment options except for opioids. Opioids have been available for physicians to prescribe to their patients as early as 3400 BC in lower Mesopotamia. First cultivated from Papaver Somniferum (the opium poppy), opium was used for centuries to treat many illnesses and diseases. The Sumerians referred to it as “Hul Gil” (or “joy plant”) in 3000 BC. In 460 BC Hippocrates acknowledged opium’s use as a narcotic and styptic in treating internal diseases, diseases of women and epidemics, essentially for its awesome pain relieving properties [52]. Since then, opium and its derivatives have seen many uses and mis-uses, both medicinally and recreationally. It is the extraordinary history of the opioid medications that contributes to their cautious use by physicians.

Despite good intentions and genuine concern for patients' comfort on the part of physicians, research on pain therapy over the past 20 years suggest that many patients do not receive adequate pain relief. In 1973, Marks and Sachar documented the under-treatment of pain in hospitalized medical in-patients and since this time, these findings have remained consistent [53,54]. Interestingly though, according to pain experts, 70% - 90% of people in acute or chronic pain could have adequate relief with the use of non-steroidal anti-inflammatory and narcotic medications [55]. There are common
misconceptions about treating pain with narcotics that need modification. The most common misconception is wrapped around a concept known as addiction.

Terminology Barriers

Addiction is a compulsive disorder in which an individual becomes preoccupied with obtaining and using a substance. Continued use of the substance could result in a decreased quality of life. Addiction can also be described as a primary, chronic, neurobiologic disease. There are genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterized by behaviors that include the following: impaired control over drug use, craving, compulsive use, and continued use despite harm. Physical dependence and tolerance are normal physiological consequences of extended narcotic therapy for pain and are not the same as addiction [30].

Tolerance is the development of a reduced effect of a narcotic with continued, chronic use. This is a physiologic state resulting from regular use of a drug and leads to the need to increase dosage to produce the desired pain relieving effect. Tolerance may or may not be evident during opioid treatment and does not equate with addiction [56].

Dependence is a physical state that develops with long-term use of narcotics. This is an adaptation of human physiology manifesting itself when the dose of a narcotic is rapidly reduced or stopped abruptly. This “withdrawal” is not addiction, but a very real physical dependence upon the medication [30].
Access Barriers

Access to professional services, prescription drugs, and medical equipment is usually necessary for effective pain care [57]. The lack of reimbursement influences the way in which pain is treated, where it is treated, and the necessary supportive care that is available [58]. Interestingly, for those who are insured, reimbursement policies may favor the use of more expensive pain management modalities over less expensive ones. Medicare, for example, does not reimburse for outpatient oral medications (including narcotics) but will reimburse for pain management in an inpatient facility. Thus, "a person may well have reimbursement for the $4,000.00 cost of patient controlled analgesia (PCA) morphine but will have no coverage for $100.00 of oral morphine solution" [59]. Clinicians should consider a patient's ability to pay for treatment. The cost of medications and other treatments may overburden a patient with limited financial resources and result in compromises between compliance with the prescribed regimen and other financial responsibilities [60]. Costs of analgesic drugs, for example, including many that are equally effective for pain management, vary dramatically [61].
The Opium Concern

“…when diverted from the legitimate distribution system, the non-medical use of controlled substances can lead to serious public health problems…” [62].

As already mentioned, opium and its derivatives, also known as opiates, have been used for centuries to relieve pain and suffering. Because of their addictive potential, opiates have been the focus of law enforcement agencies for decades. In fact, opium and its derivatives were the focus of the first conference for drug control held in Shanghai in 1909. This conference, known as the Opium Commission Forum, was attended by 13 countries. Its purpose was to establish guidelines for controlling the growing opium market. Escalating addiction problems in Far Eastern countries and the rapid development of the opium trade led to the first Drug Control Treaty signed in The Hague in 1912. The focus of this treaty was to simply limit the manufacture and trade of opium for solely medical purposes [63].

During the International Opium Convention of 1925, a statistical system of monitoring the production, manufacture, trade, and distribution of opioid drugs was developed with a Central board to oversee its activity. By the 1931 gathering of this convention, the participating governments were required to supply annual estimates of their opiate needs and their potential production based specifically on, and limited to, medical and scientific need [63].

Why do physician’s under-prescribe opiates and controlled substances? This question has multiple answers, but boils down to this: Are physicians under-prescribing
because of lack of knowledge or fear of regulatory oversight? Could both factors be the case?

In every modern country there is a need to protect the public from harm. Laws develop in countries to police, regulate and defend its citizens. In the United States, particularly focused on public health, a three-tiered foundation for our modern drug laws developed from international treaties, federal laws and state laws. The primary goal of these laws is to balance appropriate medical use of controlled substances with the illicit diversion of these drugs [62].

International Treaties

Internationally, the principal treaties recognize that many controlled substances are indispensable to public health and that their availability for legitimate medical and scientific purposes must be ensured [64,65]. Most governments of the world agree with these treaties [66]. In some countries, laws have become so strict, that judicial, appropriate use of opioid medications is curtailed and in some cases restricted due to the laws that developed to protect against diversion [67].

Federal Laws

The Federal laws in the United States adequately balance diversion and appropriate medical use. The Federal Food, Drug, and Cosmetic Act of 1962 gave the Food and Drug Administration (FDA) the power to approved opioids, stimulants, and sedative hypnotic as safe and effective for medical use and commercial marketing. This act did not restrict physicians from prescribing medications to either labeled indications
or recommended doses [68]. In fact, “...a physician may prescribe it (medication) for uses, in treatment regimens, or in patient populations that are not included in the approved labeling” [69]. The federal anti-drug efforts developed to allow physicians to still have control over treating their patients. “Appropriate medical practice and patient interest require that physicians be free to administer drugs according to their best knowledge and judgment” [70].

“New uses for drugs are often discovered, reported in medical journals and at medical meetings, and subsequently may be widely used by the medical profession... When physicians go beyond the directions given in the package insert it does not mean they are acting illegally or unethically, and Congress does not intend to empower the FDA to interfere with medical practice by limiting the ability of physicians to prescribe according to their best judgment” [71].

In summary, when physician go beyond the packet insert, they are not acting illegally or unethically and Congress will not interfere with the practice of medicine. The practice of medicine is deferred to the states as long as the state laws do not conflict with federal law [71].

Controlled Substances Act

The Controlled Substances Act (CSA) of 1970 parallels International treaties in that it attempts to balance illicit diversion with appropriate medical use. The CSA specifically states that legitimate medical use is “…necessary to maintain the health and general welfare of the American People” [72]. It is the CSA that allows for the scheduling of medications based on their abuse potential. The scheduling of medications
is an attempt to monitor medication production and prescribing habits of physicians. Medications are categorized in any one of five schedules (categories). Schedule II medications have the highest potential for abuse while schedule V medications have the least. Schedule I medications are reserved for research and scientific purposes only. Worried that excessive production of controlled substances would increase diversion and illicit use, the CSA gave authority to set production quotas for many of the opioids, sedative hypnotics and stimulants to the Drug Enforcement Agency (DEA). These quotas must accommodate legitimate medical and scientific needs [72].

Uniformed Controlled Substances Act and State Law

The states regulate medical practice, not the federal government. This authority is based on the police power in state constitutions and it underlies the medical practice acts that are designed to protect the public health and safety [73].

The state laws, like the federal laws, prohibit the non-medical use of controlled substances. However, state laws do not clearly recognize the public health benefit of controlled substances or the need to balance their availability for medical purposes. In fact, most state laws interfere with the prescribing of controlled substances [62]. The model for most state laws is the Uniformed Controlled Substances Act (UCSA) of 1970. This is a federally influenced act to help unify the out-dated and often oppressive older state laws and to help the states achieve a more appropriate balance between licit and illicit controlled substance use. Instead, the UCSA simply mentioned that states could include an advisory committee to oversee the state regulatory agencies. In addition, there
is no mention of ensuring availability of medication for professional use nor is there a
definition of “addict,” thus leaving the individual states to define this.

Federally, an addict is one who is a danger to society and to whom narcotics can
only be prescribed by specially registered treatment programs. A physician may not
prescribe opioids to an addict unless they are for pain. Once the states were allowed to
define addict, many confused addict with patients who are dependent on narcotics (see
above), thus limiting (not eliminating) the physicians’ ability to prescribe opioid
medications to those in pain [74]. Although many states adopted the UCSA, many did
not repeal their existing laws, thus creating (in many cases) a combination of antiquated
laws with new, confusing laws that influence the prescribing and manufacturing of
controlled substances.

Multiple Copy Prescription Program

Although controlled substance prescriptions and manufacture are monitored, one
state’s novel program, implemented in 1913 in New York, directly affects a physician’s
ability to prescribe controlled substances. The multiple copy prescription program
(MCPP), or “triplicates,” was developed specifically to monitor the prescribing and
dispensing of narcotics. Since this time, 16 additional states have developed monitoring
programs (whether “triplicate” or “duplicate” prescriptions or electronic) (see Table 4).
The DEA believes the MCPP is one of the best ways to control opioid diversion. With its
implementation, Schedule II prescriptions generally decrease by 50%, the states
consumption of controlled substances decreases and there is a decrease in the number of
Table 4. States Currently Monitoring Controlled Substance Prescriptions

<table>
<thead>
<tr>
<th>State</th>
<th>Program</th>
<th>Year Enacted</th>
<th>Schedules Covered</th>
</tr>
</thead>
<tbody>
<tr>
<td>California</td>
<td>Triplicate / Electronic</td>
<td>1940</td>
<td>Schedule II</td>
</tr>
<tr>
<td>Hawaii</td>
<td>Duplicate / Electronic</td>
<td>1943</td>
<td>Schedule II and Hydrocodone</td>
</tr>
<tr>
<td>Idaho</td>
<td>Duplicate / Electronic</td>
<td>1967</td>
<td>Schedules II, III, IV</td>
</tr>
<tr>
<td>Illinois</td>
<td>Triplicate</td>
<td>1961</td>
<td>Schedule II</td>
</tr>
<tr>
<td>Indiana</td>
<td>Electronic</td>
<td>1995</td>
<td>Schedules II</td>
</tr>
<tr>
<td>Kentucky</td>
<td>Electronic</td>
<td>1998</td>
<td>Schedules II, III, IV</td>
</tr>
<tr>
<td>Massachusetts</td>
<td>Electronic</td>
<td>1992</td>
<td>Schedule II</td>
</tr>
<tr>
<td>Michigan</td>
<td>Single Copy / Electronic</td>
<td>1989</td>
<td>Schedule II</td>
</tr>
<tr>
<td>Nevada</td>
<td>Electronic</td>
<td>1997</td>
<td>Schedule II, III, IV</td>
</tr>
<tr>
<td>New Mexico</td>
<td>Electronic</td>
<td>1994</td>
<td>Schedule II</td>
</tr>
<tr>
<td>New York</td>
<td>Triplicate</td>
<td>1913-15, 1972</td>
<td>Schedule II and Benzodiazepines</td>
</tr>
<tr>
<td>Oklahoma</td>
<td>Electronic</td>
<td>1990</td>
<td>Schedule II</td>
</tr>
<tr>
<td>Rhode Island</td>
<td>Electronic</td>
<td>1979</td>
<td>Schedule II, III, Needles and Syringes</td>
</tr>
<tr>
<td>Texas</td>
<td>Triplicate / Electronic</td>
<td>1985</td>
<td>Schedule II</td>
</tr>
<tr>
<td>Utah</td>
<td>Electronic</td>
<td>1995</td>
<td>Schedules II, III, IV, V</td>
</tr>
<tr>
<td>Washington</td>
<td>Triplicate</td>
<td>1989</td>
<td>N/A-Punitive</td>
</tr>
<tr>
<td>West Virginia</td>
<td>Electronic</td>
<td>1995</td>
<td>Schedule II</td>
</tr>
</tbody>
</table>

physician requests for triplicate forms [75]. Studies have suggested that for physicians who treat cancer pain, these decreases are largely due to a reluctance to prescribe secondary to excessive state monitoring of Schedule II prescriptions [76]. The MCPP programs can, in fact, preferentially influence the use of weaker opiates in terminally ill patients when stronger medications would be appropriate [77].
The current playing field for treating chronic pain with controlled substances is fraught with obstacles. Although the regulation of medical practice is the states’ responsibility, international, federal and state laws are at play when controlled substances are prescribed. Although there are no consistent or unified laws from state to state, there is evidence that too much monitoring of the prescribing habits of physicians directly influences patient care. Ultimately, the quest for appropriate balance between protecting public health by limiting diversion of controlled substances and preserving the physician’s ability to treat patients remains elusive. As our understanding of the biology of pain increases so does public demand for improved pain treatment. Perhaps, with appropriate education and more unified state laws, this elusive balance can be attained.
Chapter 6
Education

Medical Schools and Physician Training

When faced with a patient in pain, most physicians will under-prescribe narcotic medications either because they lack knowledge about how to use them or because they are afraid to use them [78]. Physicians generally have not been taught in their medical schools or residencies the specifics and subtleties of pain medicine. It was recognized in 1985 that medical schools were sorely lacking education on pain control, and the International Association for the Study of Pain developed a model curriculum for medical schools they believed would better prepare student physicians for treating this pandemic problem [79]. Interestingly, this curriculum is still appropriate today even when scientific advances are factored into the education; however, it is not being used in medical schools [80]. Currently, in the United States, there are no medical schools that have incorporated a specific curriculum on pain. Little is being taught about pain or pain management, and information about pain is poorly integrated into the 4-year curriculum [81]. When polled, practicing physicians state they had poor and inadequate training in pain medicine [82]. In Canada, medical schools devote an average of 11 hours of instruction to palliative care and cancer pain control [83,84]. A survey of 106 medical students completing a third-year clerkship in Arizona, suggests that 57 (54%) felt they were poorly equipped to deal with terminally ill patients with regards to their pain and palliative care issues; upon graduation form medical school [85]. Medical education can actually foster the mistreatment of pain because the lack of knowledge and the
preconceived notions about pain and the negative opinions about pain medications impair prescribing [86].

Resident Physicians

Since there is very little taught about pain in medical school, most resident physicians are ill prepared for the appropriate treatment of pain. Most patients are treated for acute pain in the hospital setting. Too often though, long-term treatment of chronic pain is sorely lacking, usually due to the fear of addicting a patient. It has been estimated that less than one percent of patients who are started on narcotics in the hospital during an acute stay will become addicted [87]. Opiophobia is a term that is used to describe a well-documented medical syndrome that is fed by fear, superstition, and the war on drugs [87]. Physicians in training are particularly susceptible to opiophobia because they often do not have role models in the medical system that can appropriately educate them. When doctors suffer from opiophobia, patients suffer from pain.

A Model Curriculum:

A pain curriculum must include some basic components. Medical students, residents and attending physicians must be able to recognize pain, define its impact on the patient, understand the normal pain transmitting physiology and the pathophysiology of chronic pain. A curriculum should also prepare the students to be able to develop a plan to treat the pain. Finally, this curriculum must also teach the students how to help a patient maintain dignity during and throughout the treatment of their pain. In order to accomplish these goals the institution utilizing an educational curriculum must be
prepared to “practice what it preaches.” This would require physicians to learn and practice pain medicine. Often, patients in pain need psychosocial, economic and spiritual assistance as well as physical and medical treatment. These components of management are often the most difficult to orchestrate and can be the aspects of medical care that create obstacles for the development of a pain medicine program (see “Barriers to Care” above).

A chronic pain curriculum should educate the students in many different areas of medicine. The interconnection of the physical, psychological, social and spiritual aspects of a person is never more pronounced than when he or she is in pain. Therefore, a pain curriculum should incorporate all of these components. The outline below presents a sample chronic pain curriculum:

Outline of Chronic Pain Curriculum:

**Introduction**
- Pain as public health issue
- Epidemiology of pain
- Impact of pain on society
- Economic impact of pain

**Definitions**
- Acute vs. Chronic pain
- Pain terminology

**Basic Science**
- Neuroanatomy
- Normal pain physiology
- Pathophysiology of chronic pain
- Anthropologic basis of pain

**Clinical Science**
- Current evaluation tools
Clinical Presentation
Patients and their varied presentations of pain

Ethical and medico-legal Issues
Physician’s obligation to treat
Impact on Healthcare system
Use of opioids
   The “Controlled Substance Contract”
   Balance appropriate use with diversion
Pain research in humans
Disability determination
Pain and opiate dependence

Management
Goals of treatment
   Appropriate and realistic
   Patient centered NOT physician centered
Expectations of medication treatment

Special chronic pain circumstances
Cancer pain
Neuropathic pain
Psychological (idiopathic) pain

Treatment
What’s available
Pharmacologic
   Opioids
   Adjuvative treatment
      Complimentary therapies
   Neuroleptics
   Antidepressants
   NSAIDs
Future trends
Chapter 7
Conclusion

The United States has a growing epidemic that began in antiquity. Pain, in its purest form, is most probably the strongest survival sensation higher order animals have developed. Acute pain is necessary for survival but chronic pain, to date, has not been shown to have any survival advantage.

There are physiologic changes in the pain sensing system that develop with prolonged (or intense) acute pain. These neuroanatomical transformations make the transmission of pain easier and more efficient, thus fewer stimuli are needed to create pain [31,32]. Why is this change in sensation needed when pain is chronic? How can this be reversed? Medical science has not been able to answer these questions, but as research on pain progresses, so needs the education of physicians to progress. Education on pain and its management is lacking in medical schools. This deficit has been recognized for many years, yet no formal programs have been added to the curricula of any medical school [79]. Residencies have suffered the consequences of this lack of education. Many of the preconceived biases concerning narcotics influence the practice of medicine and add barriers to the treatment of pain. The attending physicians who teach residents and students tend to under treat pain in the hospital. Possible reasons for this include lack of experience with opioid medications, fears of side effects, medicolegal issues, and the inability of physicians to heal the underlying chronic disease [87].

Disease management and the ability to care for all aspects of health is a popular and proven method of managing chronic diseases. Chronic pain becomes an entity unto itself and should be treated as a chronic, self-sustaining and progressive disease.
Everyone has a right to be healthy. Generally, health care providers believe this to be true. Although human rights may differ from legal rights, it is generally accepted that if a person wished to be healthy, society will accept this and every effort should be made to help a person attain health. This dictum, however, is not followed when chronic pain is the cause of ill health.

The public health issues surrounding chronic pain are vast and reach many aspects of society. The state and federal governments have a duty to protect public safety. But at what cost? The regulatory agencies that are sworn to protect the public often develop barriers to patient care that restrict and often inhibit the treatment of patients with narcotics. The media reports the addiction of public figures partially for sensationalism, which primes the lay-person with mis-information about the medications that might be the most appropriate to treat their pain.

This paper reviewed the issues I believe are most important in reforming the inadequate treatment of chronic pain in the United States. The cost of chronic pain to society is awesome and is driven by inadequate management of its symptoms and its altered physiology. The misconception that chronic pain should be treated like acute pain is fostered by the lack of education of our young physicians in training and the fears of prosecution by our more experienced physician trainers. These fears are based in laws and regulations that attempt to balance diversion and illicit use with appropriate, licit medical application. Most of the states that have monitoring programs for the prescribing of controlled substances also have physicians who feel these programs are restricting them from treating chronic pain appropriately. Understanding the pathophysiology of chronic pain can allay much of the physicians fear and worry about prescribing controlled...
medications. Recent research focusing on specific pathophysiologic changes that occur when pain is not controlled, is increasing our knowledge base and will also aid in the development of new medications targeting these changes. Educating student physicians in medical school with specific curricula designed to incorporate the current pertinent scientific literature into the issues surrounding pain treatment will be the most effective way to ensure adequate pain treatment.

The medical understanding of chronic pain is growing as we look deeper into the physiology and chemistry of man. Identifying the mechanisms that fuel disease can take the mysticism out of the diagnosis and treatment of poorly defined illness. Although chronic pain has been a chronic disease for as long as humans have roamed the earth, the source of its mysterious natural history and unrelenting tenacity remains hidden. This creates obstacles that prevent physicians from learning about pain and treating patients appropriately.
References


56. The Use of Opioids for the Treatment of Chronic Pain A consensus statement from the American Academy of Pain Medicine and the American Pain Society. Approved by the AAPM Board of Directors on June 29, 1996 Approved by the APS Executive Committee on August 20, 1996.


