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# Medication Treatment of Chronic Pain without Opioids

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## Abstract

Physicians often treat chronic pain the same way they treat acute pain. However, the neuroanatomical pathways, and neurosynaptic transmitters involved in transmitting the message of pain differs between acute and chronic pain. This distinction is described in the article. Moreover, determining the type of tissue damage is a more appropriate method of selecting a pharmacological agent than mere symptomatic treatment with narcotics.

**Keywords:** Acute pain; Chronic pain; Narcotics; Opioids; Pain

## Introduction

In light of the increasing use of opioids for control of pain, of all types, the drug seeking behavior of some segments of the population, and the small percentage of physicians who prescribe narcotics and opioids for unsubstantiated complaints of pain, the entire method of medication selection for pain has to be re-examined.

Pain is a subjective experience, and there is absolutely no way to reliably and consistently measure pain, other than "self-reporting" from a patient. However, saying a patient has "pain," is too broad a statement, akin to saying a patient has a car, which needs repair. A mechanic cannot repair a car without know what type of car it is, and what the problems the car has, anymore than a physician can help a patient without a proper diagnosis and understanding what type of tissue is damaged. This paper addressed a new conceptual framework for the pharmacological treatment of chronic pain.

There are four major components to the rational selection of medication, other than opioids, for pharmacological management of pain:

1) Assessing the Validity of Pain

2) Proper diagnosis is essential for the correct selection of medication

3) Recognizing that acute pain is not the same as chronic pain

4) Damage to different tissue types produce different types of pain, and each tissue type responds to different types of medications

### Assessing the Validity of Pain

Family physicians and Emergency Departments (ED) doctors are on the "front line" of pain assessment, since they usually see patients before other specialties. One research report evaluated 544 patients seen in two different emergency rooms by 38 different doctors. These doctors only had 34.4% to 48.2% accuracy in predicting drug seeking behavior [1] Factors which were used for predicting drug seeking behavior were 1) requesting narcotics by name of the drug, 2) more than twice the number of visits as the general emergency room population, 3) A totally subjective assessment that the patient had symptoms out of proportion to their physical examination [1]. The last assessment is so subjective as to be useless, which probably accounts for the poor predictive value of the assessment.

However, the best predictor of drug seeking behavior was the hospital site. One site had three times the level of drug seekers as the other site. The chief complaints of back pain, dental pain or headache were most associated with drug seeking behavior. Drug-seeking behavior was objectively defined as present when a patient had greater than or equal to 4 opioids prescriptions by greater than or equal to 4 providers in the 12 months before emergency department evaluation [1]. While the above methods of predicting drug seeking behavior had some success, they lack a refined approach to accessing patient symptoms, and focus more on behavioral and psychological components.

A group of doctors, most of who were on the staff of Johns Hopkins Hospital, developed a questionnaire focusing not on the issues of drug seeking behavior per se, but rather on the impact of pain on a patient's life. Patients are using the subjective complaint of pain as the reason to request narcotics. Therefore, a test which can determine if there is a valid, organic basis for the subjective complaint of pain would reduce any subjective errors and add a medical dimension to the evaluation.

The Pain Validity Test divides patients into two broad categories, 1) objective pain patient or 2) A subjective or exaggerating pain patient categories [2-8]. This questionnaire is called the Pain Validity Test. There are a number of articles, on a total of 794 patients, from various institutions, with multiple authors, researching this test. The test was developed by a

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retrospective analysis of these patients, pattern recognition, and then prospective testing using predictive analytic techniques. The Pain Validity Test could predict which patient would have medical test abnormalities with 94% to 95% accuracy and could predict which patients would not have any abnormalities with 85% to 100% accuracy [2-8]. These findings were independent of any preexisting or co-existing psychiatric disorder. The Pain Validity Test also has application in detecting drug seeking behavior or identifying patients who are faking and malingering in order to get opioids with 85%-100% accuracy [9]. The pain validity test is available from www.MarylandClinicalDiagnostics.com.

## Proper Diagnosis

A number of researchers have reported that 40% to 80% of chronic pain patients are misdiagnosed [10-14]. Victims of electrical shock are misdiagnosed 92% of the time, while patients are mistakenly told they have fibromyalgia, 97% of the time [15,16].

The Wall Street Journal cited 2013 research from a general medical practice, which found that physicians missed 68 diagnoses in 190 patients. The two major causes for this misdiagnosis rate were 1) doctors didn't take a complete medical history and 2) the doctors ordered the wrong tests [17].

As an example of "the wrong test" Jensen et al reviewed lumbar MRIs and found that 27 of 98 patients with no back pain, were told they had protruding disc (28% false positive rate) [18]. In another study, which compared 90 patients who had both an MRI and provocative discograms, Braithwaite found that 77% of patients, who had positive provocative discograms, had no changes in their MRI [19]. A group from Cornell, led by Sandhu studied 53 patients with severe neck pain using both MRI and provocative discograms. In the patients who have pain with a provocative discogram, 79.5% had no MRI changes [20]. Likewise, Johns Hopkins Hospital researchers showed that a regular CT missed pathology 56% of the time, compared to a 3D-CT test [21]. Hendler and his group studied patients with normal CT and MRI findings, who had been misdiagnosed as "psychogenic pain patients" The 3-D CT found pathology missed by the other two tests, and the diagnosis was changed from a psychiatric one to a medical one [22].

Since the average physician spends only 11 minutes taking a history from a patient, during which time he speaks 8 of the 11 minutes [23], it was apparent that a mechanism for obtaining a more complete history was needed. Researchers from Johns Hopkins Hospital developed an Internet based "expert system" for chronic pain patients, which duplicate a physician taking a careful and thorough history. The questionnaire consists of 72 questions, with 2008 possible answers, which takes 45 to 60 minutes for a patient to complete. The questionnaire, called the Diagnostic Paradigm, which is available in either English or Spanish, at www.MarylandClinicalDiagnostics.com, asks all the questions a physician would ask, if he spent an hour taking a careful history.

Once the website is accessed, it takes only 5 minutes for the staff member to set up a patient to take the test. After the patient finishes the questionnaire, the answers are scored, using a propriety scoring algorithm, which uses Bayesian logic. Within five minutes, diagnoses with a 96% correlation with diagnoses of Johns Hopkins Hospital doctors, are emailed to the treating doctor [24]. The results also include the Treatment Algorithm, which recommends the correct test to use for each diagnosis [14].

The Diagnostic Paradigm and Treatment Algorithm can predict intra-operative finding with 100% accuracy [25], The efficacy of this approach is shown by outcome studies, as well as outcome studies documenting consistent patient improvement after they have properly diagnosed and correctly tested and treating by following the recommendations of the Diagnostic Paradigm and Treatment Algorithm [8,13,14]. Once a patient is accurately diagnosed, and the source of the pain is identified, then selection of medication can directed to treating the type of tissue damage identified as the cause of the pain, instead of the mere symptomatic "treatment of pain with narcotics."

## Acute Pain Anatomy and Pharmacology

Acute pain is a type of pain which is expected to resolve once tissue damage is repaired. Anatomically, pharmacologically, and emotionally, acute pain differs from chronic pain. This distinction has critical clinical implications. Acute pain is due to damage to tissue, and the message of pain is carried to the spinal cord, where a synapse occurs, and then along the neo-spine-thalamic tract to the thalamus, where another synapse occurs and then on to the somatosensory cortex [26]. The neural stimulation must reach the cortex in order to be perceived as pain.

For most types of acute pain, i.e. short-term pathology, such as post-operative conditions, a broken bone, damaged ligaments or tendons, burns, trauma, gunshot wounds, knife wounds, displaced joints, etc., it is perfectly reasonable to use opioids to control the acute pain. Narcotic (opioid) medications mimic the action of naturally occurring enkephalin at the u1 and u2 morphine receptors in the brain to give pain relief.

Narcotics work on enkephalin receptors in brain, gut, spinal cord, heart, etc., such as K1 and K2, S1 and S2, which give psychosis, respiratory depression, and low testosterone [27-31]. Since one of the side effects of narcotics is euphoria and the other is adaptation, which leads to withdrawal symptoms, these medications are addicting. Part of this addiction mechanism is the receptor site upregulation, so a patient needs more over time to avoid withdrawal. Most acute pain can be controlled by narcotics, but they are less useful in neuropathic (nerve) pain, and chronic pain.

## Chronic Pain Anatomy and Pharmcology

Pain is the early warning system of the body. It tells the brain something is wrong. The message of chronic pain is the result of damage to tissue, and the damaged tissues send nerve signals to the spinal cord. The pain message synapses in the spinal cord and then travels to the brain using the palleo- or archio-spino thalamic tract, with synapses in the reticular activating system, the hypothalamus, the thalamus, and other structures. Then the pain messages converge on the somatosensory cortex [32,33].

This multi-synaptic pathway involves areas of the brain which control sleep and emotional features [34]. The chronic pain pathway differs from the acute pain pathway in several ways. It is a poly-synaptic pathway, and the pathway goes to different areas in the brain than the acute pain pathway [35].

## Different types of Tissue Damage

Another consideration often overlooked by clinicians is the origin of pain. Various tissues, when damaged, produce pain. The type of pain which is produced by a certain tissue is specific to that tissue, and often can assist in diagnosis. The type of tissue damaged

determines the type of message of pain which is sent to the brain. If a blood vessel is compressed, this can cause a throbbing pounding pain, while if there is a viral infection affecting the small C fibers; this causes a burning type of pain. It is important to ask the type of pain, to assist in diagnosis, and to help select the appropriate pharmacological agent.

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The message of chronic pain is transmitted from peripheral tissue damage, to the spinal cord, where a synapse occurs, and then it travels along the palleo or archio-spino thalamic tract, with synapses in the reticular activating system, the hypothalamus, the thalamus, and then the pain messages converge on the somatosensory cortex [32,33].

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Inherent to understanding all pharmacological activity is the understanding of the function of the synapse. The synapse affords a physician one way of modifying the perception of pain. These principles of synaptic modification can be applied to all aspects of pain modification, for various types of tissue damage.

1) **Primary Muscle Spasm:** Primary muscle spasm occurs when the striated muscle, which moves bones, is overstretched. This is typically seen in sports injuries. A parallel thread of actin and myosin constitutes muscle fibers called actinomyosin. There are neurosynaptic receptors in the muscle, which can be modified by muscle relaxing drugs like Zanaflex, Flexeril, or Dantrolin, or at a spinal cord level using Baclofen, on in the brain, like Diazepam, Baclofen and carisoprodol.

2) **Secondary Muscle Spasm:** This is the epiphenomenon which is seen when ligaments, which hold bones in place, are torn, and there is excessive movement between bones. At this stage, treating the muscle spasm is a futile exercise, since the pathology is the excessive movement, making the muscle fibers do the work of ligaments, which they were not designed to do, which causes protective spasm, so the muscle doesn't get overstretched or ruptured. Stabilization of the excessive motion is the treatment of choice in this instance.

1. **Vascular Spasm:** Vasospasm is the patho-physiological process behind classic migraine headaches. Unfortunately, 35%-70% of people told that they have migraine really have a mixed muscle tension-vascular compression headache. So, drugs which work on vasospasm will not be effective in these misdiagnosed headaches. For the true migraine without aura (formerly called common migraine), or migraine with aura (formerly called classic or complicated migraine), vasoactive drugs like Inderal, Nifedipine, or Imitrex relax the spasm. Raynauds is another example of a disease which has vasospasm as the basis of its pain production, and which responds to calcium channel locking agents such as verapamil and nifedipine. Other disorder such as Complex Regional Pain Syndrome (CRPS) has vasoconstriction caused by over-excitement of the sympathetic nerves, so that the vasoconstriction is a secondary result of sympathetic stimulation. In this instance, an alpha1 sympathetic inhibitor, such as Regitine is more appropriate than a vasoactive drug. As in the case of migraine headache, 71%-80% of people told they have CRPS actually have nerve entrapment, which would respond better to an anti-convulsant [35,36]. Again, this emphasizes the need for an accurate diagnosis before beginning treatment.

2. **Vascular Compression:** There is really no pharmacological basis to treatment for disorders like thoracic outlet syndrome. Only mechanical decompression treats the underlying problem, which has been advocated by a number of authors [37].

3. **Vascular Inflammation:** Temporal arteritis, or giant cell arteritis is an inflammation which requires large doses of steroids.

4. **Acute Joint Inflammation and Chronic Joint Inflammation:** A number of drugs have anti-inflammatory activity or inhibit prostaglandin synthesis. As a precautionary note, long-term or large doses are both hepatotoxic and nephrotoxic. Salicylates (e.g., aspirin) have antipyretic and analgesic effects as well as anticoagulant and anti-inflammatory actions. Theoretically, these actions result from the anti-prostaglandin activity, both centrally and peripherally. Unfortunately, these additional actions predispose this medication to produce gastritis and serious gastrointestinal problems, including bleeding ulcer, in susceptible individuals. Despite these problems, aspirin is still the cheapest and most readily available analgesic preparation. Nonsteroidal anti-inflammatory drugs (NSAIDs) have been well reviewed by Klipper and Kolodny. They list nine major categories. The most recent class of anti-inflammatory drugs is called cyclooxygenases, or COX inhibitors.

5. **Infection:** Diagnosis of this cause of pain is the single most important factor in treatment. Blood studies for sedimentation rate, C-reactive protein, and white blood cell counts are not adequate, since they miss the number of infections, including abscesses, and biofilm. The use of Indium 111 scans, and gallium scans augment the diagnostic process. Obviously, the treatment is an appropriate antibiotic, or in some instances, the use of several antibiotics simultaneously.

6. **Acute Bone Pathology:** Bone pain is very difficult to treat. When a patient has a broken bone, the physician is certainly

**Table 1:** Type of pain associated with type of tissue damage.

| **Methods to Asses Pain** | | | | | | |
|---|---|---|---|---|---|---|
| | Burning | Throbbing | Sharp | Dull | Aching | Spasm |
| **Constant** | This suggest nerve irritation- chemical, Metabolic, or viral | This suggest vascular compression-look for the source of the compression | This suggest entrapment of sensory nerves in the skin | This suggest a compression, tumor, deep bruise or infection get bone scan | Deep achy pain suggests bone bruise or fracture get bone scan | This suggest nerve entrapment or compression look for the source of compression |
| **Intermittent** | This would be associated with spasm of muscle or blood vessel treat those sources | This suggest vascular spasm use medications which reduce spasm like Imitrex | Seen in visceral spasm such as Crohn's disease use anti spasmotic | Pain only with use sprain or strain due to damage to tendon or ligament | This suggest inflammatory process use non-steroidal anti-inflammatory drugs | This suggests muscle spasm-use muscle relaxants |

Additionally, once the type of tissue damage is established, then the appropriate drugs within the categories mentioned above may be used.

justified in using narcotics. However, once the acute pain process has subsided (4-6 weeks), if there is still bone pain, then other sources, such as infection, mis-alignment, broken hardware, etc. should be explored.

7. **Ligament Damage:** Ligaments hold bones together. The acute phase, which should last no longer than 5-6 weeks, can be managed with external bracing, narcotics, and anti-inflammatory drugs. If pain with motion persists, then ligamentous evulsion, occult fractures, and other sources for pain need to be considered.

8. **Nerve Compression:** There is really no pharmacological basis to treatment for disorders like ulnar nerve compression or thoracic outlet syndrome. Only mechanical decompression treats the underlying problem. However, anti-convulsants such as Topamax and Lyrica may provide some relief until surgery. This same rationale applies to radiculoipathies, due to neural foraminal stenosis,

9. **Nerve Irritation:** Nerves can be irritated by entrapment, inflammation, or infections, such as herpetic infections, seen in herpes zoster or herpes simplex. A combination of anti-viral drugs, steroids, and anti-convulsants is far more effective than opioids or narcotics in the control of this pain.

The description of the type of pain may give important insight into the type of tissue which is damaged, and thus allow more rational selection of the type of medication best suited to control the pain. A table summarizing the clinical features of damage to various tissues is found below **(Table 1)**.

## Discussion

As Rhodes and his team have clearly documented, physicians are spending less and less time with their patients [23]. This truncated time leads to misdiagnosis, and the associated incorrect treatment of these patients [10-17]. The reduced time with a patient has led to a less than thoughtful pharmacological management of patients, with many doctors resorting to symptomatic treatment of both acute and chronic pain using narcotics. Accurate diagnosis improves the chance of identifying the type of tissue damage which produces the clinical manifestation of chronic pain [22,24]. This is best exemplified by the misdiagnosis rate of complex regional pain syndrome (CRPS), where 71%-80% of the patients actually had nerve entrapments. The correctly diagnosed nerve entrapments would be best treated with anticonvulsants and eventually peripheral nerve decompression, while the true CRPS patients are best treated with alpha1 blocking agents, sympathetic blocks, and eventually a sympathectomy. There is no role for narcotics for either diagnosis. Therefore, as precision in diagnosis increases, so should precision in pharmacological treatment [38,39].

## Conclusion

There are many types of acute and chronic pain, caused by a variety of tissue damage. By properly matching the correct medication for the correct tissue damage, there is an increased chance of improving control of chronic pain, without the need to use opioids.

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