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American Medical Association Journal of Ethics May 2013, Volume 15, Number 5: 401-402.

FROM THE EDITOR Ethical Perspectives on Pain

In the residents' lounge at the University of Kentucky, there is a scrap of paper posted on the wall with a haiku scribbled on it: "Drug-seeking patients / You will get NONE of your candy / When I am on call." It's unknown how long the sign has been up, but concerns about pain and pain relief have a long standing in medicine. Evidence of fossilized opium has been found in the remains of our earliest hominid ancestors, and narcotics are mentioned liberally throughout the Homeric epics. In our own day and age, more than 100 million Americans experience the debilitations of chronic pain. So, when confronted with such a massive problem, why all the cynicism?

Part of this lies in the mysterious and ambiguous nature of pain. We inherit the word "pain" from the Romans, who viewed it as a punishment for moral failure. Over the years, we have deemphasized that aspect in favor of more scientific explanations. In 1975, the International Association for the Study of Pain finally defined pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" [1]. Despite this consensus, the biology of pain remains poorly understood, and options for the treatment of pain remain frustratingly inadequate.

This issue of *Virtual Mentor* highlights the ethical dilemmas that clinicians face when treating patients who experience significant pain. Our authors hail from diverse professional backgrounds; they are legal experts, psychiatrists, family medicine practitioners, and hospital administrators. They bring their individual perspectives to explore and help resolve ethical dilemmas in pain management.

Broadly speaking, the issue is dominated by three themes: (1) the differing perceptions of pain, (2) the inadequacy of current management strategies, and (3) the societal need for responsible pain management.

The first theme explores the subjective nature of pain. Three authors write principally from the perspective of the patient. In our medical humanities section, Fernando Antelo, MD, shares the experiences of the renowned Mexican painter Frida Kahlo, whose works illustrate the profound physical and emotional pains that dominated her life. Likewise, Gillian Bendelow, PhD, speaks in her medicine and society article about the need to humanize pain and think of it as more than just the result of altered neurophysiological processes. This emphasis on incorporating biopsychosocial approaches is also highlighted in the policy forum section by Ronald Wyatt, MD, where he notes how culture and ethnicity influence the perception of pain. Other authors suggest ways to reduce discord between patients and physicians over perceptions of pain. In the journal discussion section, Robert Learch, DO, and Jeremy Cumberledge, MD, systematically examine the roots of inequity in pain management and advocate for individualized approaches. David Borsook, MD, PhD, calls for more objective measurements of pain in the state of the art and science section. And in the medical education feature, Nalini Vadivelu, MD, Sukanya Mitra, MD, and Roberta Hines, MD, emphasize the importance of incorporating pain management into undergraduate medical education.

A large portion of this issue is devoted to ethical dilemmas in pain management. The inadequacies of current treatment are the focus of three articles. Craig T. Hartrick, MD, overviews the profile of opioids in the treatment of chronic pain in his state of the art and science piece. In the first of three case commentaries, Jack M. Berger, MS, MD, PhD, and Nalini Vadivelu, MD, provide a framework for negotiating tough situations in which pain relief may inadvertently shorten a patient's life. And Igor Grant, MD, makes his case for the legalization of marijuana for the relief of chronic pain in an op-ed.

Finally, this issue concerns itself with larger societal concerns about pain and pain management. Since at least the nineteenth century, the widespread use and abuse of opiates has been identified as a public health problem. In the health law section, Valarie Blake, JD, MA, provides updates on federal and state legislation designed to curtail prescription drug abuse and diversion. Kristy Deep, MD, MA, also writes about the diversion and misuse of opioids from her perspective as a physician who employs narcotic contracts. And Pamela L. Pentin, JD, MD, explains the difficulties emergency department physicians face in distinguishing pain crises from drug-seeking behavior.

Pain is a perplexing symptom that physicians have difficulty addressing and treating, in both its acute and chronic forms. Sadly, its nebulous nature lends itself to either underestimation or overtreatment, both of which pose significant ethical dilemmas. It is unlikely that we find an ideal solution in the near future, but perhaps through introspection and reflection in forums such as *Virtual Mentor* we will discover insights that help us better serve our patients.

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American Medical Association Journal of Ethics May 2013, Volume 15, Number 5: 403-409.

ETHICS CASE Common Misconceptions about Opioid Use for Pain Management at the End of Life

Commentary by Jack M. Berger, MS, MD, PhD, and Nalini Vadivelu, MD

Dr. Cohen practices internal medicine at a small community hospital in Nebraska. He recently admitted Mr. Lopez for rib and back pain, found, upon x-ray, to be due to pathological fractures. Mr. Lopez, 72, had a history of metastatic squamous cell lung cancer that had progressed despite two cycles of chemotherapy. Prior to admission, he had been on palliative chemotherapy and oxycodone, which provided imperfect relief of his day-to-day cancer-related pain.

When Dr. Cohen entered the room, he found Mr. Lopez wincing in pain. Though he was on high dose opiates, he continued to ask for more. Seeing Mr. Lopez's intense pain, Dr. Cohen wrote an order to increase the amount of his medication.

Later in the day, Mr. Lopez's nurse told Dr. Cohen that Mr. Lopez had started to get increasingly drowsy. Dr. Cohen went to check and found Mr. Lopez somnolent but arousable and oriented to time, place, and location. Looking at the cardiac monitor, he saw that Mr. Lopez's respiratory rate had decreased and wrote a new order to return to the previous dose of pain medication.

Within the next 4 hours, Mr. Lopez was breathing well, but once more in extreme discomfort. Dr. Cohen went to the bedside to talk with Mr. Lopez about why he had reduced the pain medication to the current level. When Mr. Lopez responded, his speech was labored. He said the pain was intolerable and that he couldn't "take any more."

Dr. Cohen explained again the danger of lowering Mr. Lopez's respiration, but Mr. Lopez said, "You don't understand this, this...I can't take it. I would rather be dead."

Commentary

Weiss et al. report that the number of seriously ill patients who experience "substantial" pain ranges from 36 to 75 percent [1]. Addressing pain early in patients who are seriously ill such as patients with cancer could improve their quality of life [2]. Opioids are one of the most common medications given for pain control, but an inaccurate assessment of their dangers can lead to an irrational fear of opioid use among patients and physicians alike [3]. Much of inadequate pain management, particularly in end-of-life care, can be traced to lack of knowledge on the part of physicians. We will address four common misconceptions about opioid use for pain management at the end of life: (1) that dying patients' unconsciousness is necessarily unnatural and problematic; (2) that it is necessarily wrong to help with pain at the cost of some consciousness or length of life; (3) that there are legal restrictions on doing so, and (4) that managing a patient's pain necessarily entails making a tradeoff about consciousness or length of life.

Need Patients Be Kept Conscious at the End of Life?

First, we will address misconceptions about loss of consciousness at the end of life. As P.A.J. Hardy has written,

The use of an opiate antagonist in potentially fatal circumstances demands an answer to the question: *is such treatment humane*? If endorphin release during extreme stress has evolved to provide analgesia and detachment, are doctors to dictate that such effects are to be denied in a last ditch attempt to maintain vital functions which are becoming resistant to conventional support, only to leave the moribund more aware of their circumstances [4]?

Let's say, for example, that death is imminent for a patient with nasopharyngeal cancer that has spread to encompass his entire nasopharynx and face. If, after more than 2 weeks of receiving 300 mg per day of intravenous (IV) morphine, the patient slowly loses consciousness, should the doctors turn off the morphine infusion to test whether the morphine was the cause of the change in mental status? Absolutely not [5]. Discontinuing an ongoing opioid infusion in a terminal patient who slowly loses consciousness can intensify the patient's already moderate-to-severe pain [6].

But importantly, the painkillers may not be the reason for the unconsciousness. Metabolic encephalopathy, infection, and brain metastases are more commonly the cause of altered mental status than opioid overdose in patients with chronic cancer pain [7], especially patients who have been on stable or slowly increasing doses of opioids [8].

Is It Wrong to Alleviate Terminally Ill Patients' Pain If Doing So Reduces Consciousness or Length of Life?

Another common misconception about pain relief at the end of life is that it is necessarily wrong to help with pain at the cost of some consciousness or length of life. To provide another example, let's say that a physician is managing an end-stage AIDS patient who has a do-not-resuscitate (DNR) order and a documented pain score of 6 out of 10 (10 representing the worst possible pain imaginable) despite receiving 3 mg/hour IV morphine infusion. If the physician is concerned that the morphine is hastening death, need he or she reduce the dose, thereby intensifying the patient's already severe-to-moderate pain?

In end-of-life care and pain management, as in medicine generally, there are four guiding ethical principles that govern our decision making and care of patients [9-12]: nonmaleficence (minimize harm), beneficence (do good if you can), patient autonomy (respect the patient as a person), and justice (fair distribution of available

resources). In implementing the four principles of ethical medical care, the physician has to contend with three sets of conflicting goals:

- Benefiting the patient and minimizing the burden of doing so
- Striving to preserve life and providing comfort in dying
- Meeting individual needs and those of society

In cases such as this, we are dealing with the first two sets of goals. The principle of double effect, initially developed in the Catholic tradition from the thirteenth-century teachings of Thomas Aquinas, states that an action that has two effects, one good and one bad, is permissible if five conditions are met [13]:

- 1. The act itself is good or at least morally neutral, e.g., giving morphine to relieve pain.
- 2. Only the good effect (relieving pain) and not the bad effect (ending the patient's life) is *intended*.
- 3. The good effect is not achieved *through* the bad effect (pain relief does not depend on hastening death).
- 4. There is no alternative way to attain the good effect (pain relief); if there were, that would be the appropriate course of action.
- 5. There is a proportionately grave reason for running the risk such as pain so intense that it could cause severe hemodynamic consequences like respiratory depression, myocardial infarction, or stroke.

The main point of the principle is that the *intention* of the caregiver is what matters. In certain respects the principle *reverses the order of nonmaleficence and beneficence*—that is, it gives primacy to doing good in spite of the risk of causing harm. According to this viewpoint, it is not morally wrong to alleviate the patient's pain, using whatever doses of opioids are necessary, at the cost of some consciousness or length of life [14, 15]. It does not, however, alter the role of respect for autonomy—the patient or surrogate decision maker should be informed of the various options and their probable effects and choose freely among them.

As we have said elsewhere, we think a principal reason that double effect doctrine continues to be an area of lively debate in bioethics is the ambiguous intentions of caregivers in treating patients at the end of life [15]. For example, even when a physician has no desire to hasten a patient's death, the death of the patient may nevertheless be seen as a good or desirable outcome [14, 15]. However, there is a distinct difference between giving a poison with the intention to end the patient's life and giving medication to relieve pain or reduce suffering when that medication may have adverse effects leading to the patient's death [14].

In applying the principle of double effect to this therapy, the rate of administration or the dose of administration should not be changed abruptly or even decreased to a previous level if that previous level did not alleviate the pain and suffering, and the patient, understanding the consequences, has indicated that he or she prefers to prioritize pain relief. If there is no other way to relieve the patient's suffering, the doses of the opioids necessary to relieve pain produce deep sedation are permissible [14].

This seems to be the case with Mr. Lopez. It appears that he would rather risk a somewhat earlier death than be conscious and in agony. If this is so, it is therefore incumbent upon his physician to confirm Mr. Lopez's consent for possibly life-limiting pain relief and then increase his opioid again until Mr. Lopez is comfortable or unconscious. His physician must also obtain informed consent for implementing a DNR order status from Mr. Lopez. This treatment, like all treatments, is only acceptable because the patient wills it. To sum up, clinicians should never withhold needed pain medications from terminally ill patients for fear of hastening their death, if they have received informed consent from the patient to increase the dose.

Are There Legal Restrictions on This Kind of Pain Management?

Physicians may also believe that they are legally prohibited from alleviating pain to this degree. This is untrue. The 1993 California Medical Board Statement on the Prescribing of Controlled Substances indicated that, when there is legitimate medical need, physicians should not be reluctant to prescribe controlled substances used for medical purposes, even those with high potential for abuse and dependence [16]. The Federal Controlled Substances Act (CSA), too, does *not* regulate medical treatment decisions such as the selection or quantity of prescribed drugs [17].

More specifically, the U.S. Supreme Court addressed pain management for the terminally ill in the 1990s [17]. The court drew a distinction between using drugs to terminate life and adequate pain and symptom management, as reported in the *New England Journal of Medicine* in 1997: "a Court majority effectively required all states to ensure that their laws do not obstruct the provision of adequate palliative care, especially for the alleviation of pain and other physical symptoms of people facing death" [18]. Similarly, the New York State Task Force on Life and the Law declared in 1994 that "it is widely recognized that the provision of pain medication is ethically and professionally acceptable even when the treatment may hasten the patient's death if the medication is intended to alleviate pain and severe discomfort, and not to cause death" [7], citing guidance from the American Medical Association's Council on Ethical and Judicial Affairs as well as Catholic and Jewish bioethical analysis.

Model guidelines for the use of controlled substances for the treatment of pain developed jointly by the DEA and Federation of State Medical Boards of the United States cite widespread undertreatment of pain in end-of-life care and now include language stating that the adopting body "will consider inappropriate treatment, including the undertreatment of pain, a departure from an acceptable standard of practice" [5]. End-of-life cancer pain management also need not carry with it the usual fear of being sued for injury or addiction caused by prescriptions of opioids.

Will This Tradeoff Even Occur?

The last misconception we will address is the belief that giving patients such doses of opioids will necessarily reduce consciousness or shorten life. This may not be the case. In a retrospective study of 238 patients, Thorn and Sykes found that there was no difference in survival between patients requiring escalating doses of opioids and patients on stable doses [19]. This would seem to suggest that the use of opioids for pain control at the end of life does not even need justification with the principle of double effect [19].

Concluding Remarks

It is our job as compassionate and professional physicians to "do the kind thing, and do it first," as William Osler told us so many years ago [20]. And it behooves all physicians who are privileged to care for patients at the terminal stages of life to be aware of the doctrine of double effect as well as its legal and social ramifications and to know data that clearly show that palliative sedation applied appropriately has no life-shortening effect [21]. In the case of Mr. Lopez, our conclusion is clearly that Dr. Cohen should increase his opioid again until Mr. Lopez is "comfortable" or loses consciousness.

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ETHICS CASE Drug Seeking or Pain Crisis? Responsible Prescribing of Opioids in the Emergency Department

Commentary by Pamela L. Pentin, JD, MD

Dr. Jones is an emergency room physician in Baltimore. Late one afternoon, he sees a young woman named Marie who has come to the ER because of extreme abdominal and knee pain over the past 12 hours. Marie says that she is in great distress and rates her pain at a 10 out of 10. She says that the pain resembles that of her previous sickle cell crises and that only Dilaudid helped. She points to her abdomen and both of her knees as the sites of pain and refuses to allow Dr. Jones to touch them. Dr. Jones observes no overt swelling or redness.

Looking at her chart, Dr. Jones sees a long list of emergency department visits and admissions over the past 2 years. Marie, 25, has a diagnosis of sickle cell disease. On most ER visits, the peripheral blood smear reports were inconclusive for vaso-occlusive crisis. Notes from her hematologist comment that she is habitually noncompliant and that they have considered consulting psychiatry to help address her persistent chronic pain.

As he is leafing through the file, Dr. Jones is interrupted by his colleague, Dr. Kapoor, who recognizes the patient's name and quips, "Good luck with her—she's a pro at getting drugs."

When Dr. Jones reenters the room, Marie is tearfully pleading for pain relief.

Commentary

Between 1999 and the present, there has been a 300 percent increase in the prescribing of opiates in the U.S. The misuse and abuse of prescription painkillers results in approximately 500,000 emergency department visits annually [1]. In 2008 more than 36,000 Americans died from drug overdoses, most of them caused by prescription opiates [2]. More than 12 million Americans admitted using prescription opiates recreationally in 2010 [3].

How did this dilemma come about? My take is that we created it. We believed ourselves to be well-meaning, most of us having sworn to do our utmost to relieve suffering. Yet in an effort to do just that, we now find ourselves pawns in the play of a health care system in which pain complaints are managed with opiates despite enormous risks to the patient and a numerical pain scale rating carries more weight than a patient's level of function or even consciousness; a system in which a patient complaint of poorly managed pain quickly reaches the highest level of institutional administration, and nonpractitioners tell us how to practice medicine. We joke with colleagues about "frequent flyers" for pain medications in the emergency department (ED), but we then let those patients convince us to prescribe the opiates we know will not really help them. We prescribe "a few" tablets to move patients out of our EDs, thinking that we are somehow doing less harm than prescribing "a lot" of opiates.

We had the best of intentions. In 1997, a collaborative project was initiated to integrate pain assessment and management into the standards of the Joint Commission on Accreditation of Healthcare Organizations (now the Joint Commission) [4]. High levels of uncontrolled pain were felt to be a public health problem, with significant physiological, psychological and financial adverse consequences to the patient and society. Patients' "right" to have their pain managed adequately was recognized. After review by many experts and committees, JCAHO pain standards were published in 2000, effective in 2001, requiring pain assessment and management at every initial patient visit. Pain became the fifth vital sign.

The JCAHO pain standards were a remarkable innovation in compassionate patient care. But our knee-jerk response to them was misguided. As a group, we rushed to meet those standards at almost any cost. I can still hear my then-institution's administrators when these standards first appeared, arbitrarily requiring every patient who rated their pain at 4/10 or higher, to be stopped at the exit door until their pain was better managed. Nutritionists were obliged to walk their stable, functional patients with arthritis to the ED for evaluation because their pain rating that day happened to be a "5."

Around the same time as the JCAHO pain standards appeared, the pharmaceutical industry formulated new, long-acting opiates. In the absence of other effective treatments for nonmalignant pain, opiates initially studied and widely adopted for the management of cancer pain filled the void. Once thought "unattractive" to addicts because of its time-released coating, OxyContin was formulated in much higher doses than previous immediate-release opiates, the idea being that it would provide smooth, long-lasting pain relief. But people found ways to crush the pills to snort or inject the oxycodone within. OxyContin in particular was heavily marketed to physicians in rural areas who had patients with severe pain, but little training in pain management or the recognition of addiction and few resources to deal with that addiction when it occurred [5]. Hence was born "hillbilly heroin," and with it a population of prescription opiate-seeking patients. By 2001 OxyContin was the bestselling name-brand opiate analgesic in the country [6].

In 2003, the FDA cited the manufacturer of OxyContin twice for misleading promotional advertisements to physicians, underplaying the addictive risks of the drug. In 2007, three executives of the company pled guilty to charges of misleading the public about the drug's safety and risk of abuse [7]. But the deed was done and the landscape was forever changed. (Incidentally, the misrepresentation of opiate safety by manufacturers is nothing new. Recall the early days of the twentieth

century when the manufacturer of heroin marketed it as a safe, nonaddictive cough suppressant in substitution for the more "addictive" morphine [8].)

The era of long-acting high dose opiates, and ensuing prescription opiate addiction, had arrived. Patient addicts quickly learned the diagnoses that could not be definitively confirmed or ruled out by examinations or test results but that precipitated rapid pain management with opiates. Patient addicts also learned that physicians had no "dipstick" to assess their pain and that their subjective reports had to be accepted. It was quite simple to claim an allergy to, or lack of relief from, nonopiate analgesics. "Headache," "backache," and "dental pain," are now common complaints used by drug seekers in emergency departments and urgent care clinics because the underlying etiology for the pain is often difficult to objectively confirm [9].

Even patients with quite legitimate pain sometimes exaggerate their pain for reasons of anxiety or pseudoaddiction. In pseudoaddiction, patients may amplify reports of pain for iatrogenic reasons, because their previous reports of very real pain were not believed and they fear that pain returning. Many of us have cared for patients who incoherently mumble a pain rating of "it's a 10, doc" as they drift into a deeply narcotized sleep. How many of us have stayed the hand of a well-meaning colleague from administering even more opiates to a sleeping "10 out of 10"?

So how do we balance the needs of patients who legitimately suffer from pain against the risks of the opiate addictions that we as practitioners have helped to create? We must start using the safety nets available to us, we must insist that our patients become our partners in their care, and we must say "no" to opiates when the risk of harm to the patient and the community exceeds the benefit to the patient.

Web-based prescription monitoring programs (PMPs) or legislation to enable them now exist in 48 states and 1 territory, allowing us to assess who else is prescribing scheduled drugs to the patients we see. Though it takes a few extra minutes of our time and the security requirements of some PMP websites make navigation slow, it is incumbent upon us to devote that extra effort to protecting our patients and the public. The information I glean from my state's PMP never ceases to surprise.

Once we recognize from the PMP a pattern of aberrant behavior, like frequent ED visits or other doctor-shopping, it is incumbent upon us to speak with our practitioner and pharmacist colleagues about shared patients at risk. Respect for privacy does not bar communication with other practitioners when the purpose is to protect the safety of the patient or the public. And there are clearly times, as with prescription forgery or theft, when the risk of harm to the patient or community outweighs any breach of confidentiality, and a call to the police is in order. I would rather face a judge to explain my decision to violate privilege than attend the funeral of a patient who has overdosed on opiates I prescribed.

The advent of the electronic medical record (EMR) has improved communication among health care professionals immensely, but as the old adage says: "garbage in, garbage out." If we do not carefully document what we learn about our patients, our efforts will be fruitless. We must feel empowered to enter terms such as "addiction," "substance abuse," "dependence," and "doctor shopping" in bold type, underlined with flashing lights if necessary, and descriptions of relevant behavior on EMR problem lists. And we who have access to these information-laden EMRs must take the time to actually read the entries and act accordingly.

Medical care of all types, including the management of pain, is a partnership between patient and physician. Controlled substance agreements are built upon this principle. In exchange for management of their pain with opiates, many such agreements appropriately require patients to be partners in their own care by seeing only one practitioner, using only one pharmacy, taking their medication as prescribed, and avoiding other substances of abuse or sharing medication. The provision of urine or blood samples to screen for substances of abuse and ensure a patient is taking medication as prescribed is another component of the care partnership. Agreements can also be used to ensure use of essential components of pain management, such as behavioral interventions and physical therapy, which may reduce a patient's reliance on opiates and other drugs.

In essence, we, the medical community, created patients like Marie. We swore to do our best to relieve her suffering. But we then compelled her to report her pain as a number, we taught her the number to report to trigger the flow of opiates, and we reinforced our teaching by opening the opiate faucet whenever she uttered the threshold number. We allowed pharmaceutical manufacturers to flood the market with new opiates for Marie and to mislead her and us about their safety and their risk of addiction. A critical lack of pain management resources for Marie and others, especially those who live in rural America, and our own lack of training to recognize and manage addiction, prompted us to prescribe more and more opiates to her.

Marie may have real, terrible sickle cell disease. But it is time to look beyond the surface of cases like Marie's. She must be a partner in her own care. For a patient with previous drug-seeking behavior and questionable reliability, a refusal to allow full physical examination or blood draws should be deemed a refusal of care and precipitate a polite decline to prescribe opiates. Urine toxicology screening may yield critical information for decision making and should be employed early and often. Test results unsupportive of a vaso-occlusive crisis in Marie's case should be reviewed with hematology colleagues before opiates are administered—acetaminophen and nonsteroidal anti-inflammatories can be used in the interim. A psychosocial inventory should be administered, yes, even in the ED, to determine whether Marie has other reasons, such as anxiety, depression, or life events, for coming to the ED seeking opiates.

It's also time to assess pain based upon function rather than a numerical score, even in the ED. Reports from triage staff that, for example, Marie was seen ambulating comfortably and eating a hot dog before checking in to the ED should be given high credibility.

Use of electronic media, in all its facets, should be undertaken by ED staff to ensure the safety of prescribing opiates to Marie, and when EMRs are not available paper records should be requested by fax on an accelerated basis. Review of the records of other practitioners who have seen her, queries of state PMP websites and calls to her PCP and her pharmacist are all in order before administering opiates which may not be clinically indicated. Controlled substance contracts often set forth a plan for pain crises, and these should also be consulted by practitioners before acting whenever possible.

It is time to take back the management of pain with opiates from JCAHO, from administrators, and from the pharmaceutical industry and place it where it belongs in the hands of cautious and well-informed practitioners. And sometimes the right thing to do to is just to say "no."

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ETHICS CASE Use of Narcotics Contracts Commentary by Kristy Deep, MD, MA

Brad was a 53-year-old postal worker who moved from Lansing, Michigan, to Tucson, Arizona. He had been relatively healthy since quitting drinking at 48. Due to his prior alcohol abuse, however, he had developed chronic pancreatitis, which caused him debilitating abdominal pain. He had modified his diet and had been taking pancreatic enzyme supplements faithfully for some time but needed longacting daily morphine to carry on his normal work activities at the post office.

To continue his care in Tucson, Brad went to a primary care clinic, where he was seen by Dr. Lee. Dr. Lee had long experience in prescribing opioid medications and required all his patients to sign opioid treatment contracts, which explicitly state the risks and benefits of treatment, prohibited behaviors, and criteria for termination of treatment.

A resident physician in Dr. Lee's clinic approached Brad to discuss the terms by which he could continue to receive his prescriptions for long-acting morphine from Dr. Lee. As the resident explained the contract, Brad got increasingly upset. Finally he said, "Stop. Why are you treating me like a criminal when I have a legitimate medical condition?"

The resident physician saw his point. She wondered whether this contract had been offered in good faith and whether it was Dr. Lee's way of managing legal risks or discouraging patients he didn't want to treat. If the latter, it seemed to manage risk at the expense of the patient-physician relationship. The resident didn't know what to say to Brad.

Commentary

Managing chronic nonmalignant pain is an important aspect of primary care. Approximately 75 million Americans experience chronic or recurrent pain. The pharmacologic treatment options, and the evidence to support their use, vary with the underlying condition; a large number of patients receive opioids to treat their chronic nonmalignant pain. As with all therapies there are risks and benefits—and the risks of prescription opiates have received a considerable amount of attention in the medical profession, lay press, and from regulatory agencies. These include abuse, diversion (selling to others), addiction, and lethal overdose.

Alarmingly, the majority of nonmedical users of prescription drugs report that they get the medication from a friend or relative, and the majority of time that person is

being prescribed the medication by one doctor [1]. Seeing the consequences of such prescription drug abuse exacts a toll on well-meaning clinicians who prescribe pain medications with the goal of relieving suffering and improving a patient's quality of life. We now find ourselves in a world in which a patient's complaint of uncontrolled pain cannot always be taken at face value. The threat of a patient's misrepresenting his or her symptoms to obtain a drug of abuse is real.

Enter the narcotics contract. A narcotics contract is a treatment agreement signed by the patient and clinician that sets out the expectations for a patient using these high-risk medications. Common contract elements include:

- informing the patient of the risk of opioid tolerance and physiologic dependence,
- requiring that only one doctor prescribe and one pharmacy dispense the drug,
- stating that lost or stolen prescriptions will not be replaced,
- prohibiting dose or frequency increases by the patient,
- use of prescription drug monitoring programs (databases that report all controlled substance prescriptions filled by that patient), and
- assessments of compliance—e.g., random pill counts and urine drug screens in the prescriber's office

One could certainly agree with Brad—these contracts may seem to presume guilt and potentially threaten the nature of the patient-doctor relationship. So do the benefits of such arrangements outweigh the possible costs?

Do Narcotics Contracts Make Opiate Prescribing Safer?

Unfortunately, there is little data to answer this question. A systematic review of 11 studies of opiate treatment agreements found only weak evidence of a reduction in opiate misuse [2]. It should be noted that these studies were methodologically poor. Routine use of prescription drug monitoring programs, only one element of narcotics contracts, has been correlated with reduced opiate sales but not a reduction in abuse [3, 4].

For the sake of argument, let's assume that narcotics contracts and the processes they entail (identifying aberrant behavior, random urine drug tests, and pill counts) are effective in identifying abusers and diverters and will reduce inappropriate prescription drug use. This potentially benefits the patient and society. If the patient is abusing, the source of harmful drugs will be curtailed, perhaps lowering the risk for unintentional overdose. At the community level, disrupting the pipeline of prescription drugs to nonmedical users may also be of benefit. These assumptions of benefit will allow us to examine the ethical questions raised by these contracts.

Do the Potential Benefits of Safer Prescribing Outweigh the Potential Burdens to the Patient or the Patient-Doctor Relationship?

The impact of narcotics contracts on the patient-doctor relationship has not been extensively studied. Many patients are aware of the recent increases in prescription drug abuse and recognize the importance of preventing abuse and diversion. If framed as a tool to ensure safety for both the individual patient and society, contracts may be viewed as acceptable even by patients who are at very low risk for abuse.

While these contracts are often formatted like informed consent documents, one must wonder whether a patient's need for effective analgesia introduces an element of coercion. Perhaps a patient would agree to any requirements, no matter how burdensome, to obtain needed medication. The resident in this case scenario wonders whether the contract arises from a need to manage legal risks. While there is a possibility of physician liability in cases of prescription drug overdose, the ability of narcotics contracts to mitigate those risks has not been evaluated.

Perhaps the greatest potential harm in the use of narcotics contracts is the inherent message to the patient that he or she can't be trusted. Does a contract then fundamentally alter the fiduciary nature of the relationship between the doctor and patient? While the documents may contain language about shared goals, the bottom line is that the patient wants a medication that is perceived to be of benefit. The physician has the power to provide it but also may dictate the terms of provision. Physicians may frame the use of these contracts as tools to ensure patients' safety when taking a high-risk medication, but we do not use similar contracts for other medications that pose substantive risks to patients. Consider warfarin, for example. If the patient fails to undergo routine lab checks or takes too much, he or she could experience life-threatening bleeding. However, we do not terminate treatment for patients who have difficulty maintaining adherence. Clearly the nature of the medication involved—specifically the potential for abuse by the patient—is a key factor in deciding to utilize treatment contracts.

But should the "nature" of the patient be a key factor as well? Judging a patient's risk for drug abuse based on age, ethnicity, socioeconomic status, or appearance would be inaccurate and unjust. There are a number of short questionnaires and risk assessment models that can be used to estimate a patient's risk for prescription drug abuse [5]. Alternatively, a physician may decide to simply employ such contracts with all patients to avoid any sort of "judgment" about an individual. This approach could alleviate an individual patient's concern about being singled out as a potential drug abuser, but some patients may still have a response similar to Brad's.

Do Narcotics Contracts Place Patients at Risk for Unjustified Termination of Opiate Analgesia?

The apparent violation of opiate contracts may occur for reasons other than abuse or diversion. A patient who has real pain may be denied effective analgesia if the terms of the contract are violated for other reasons. One's pain medication could inadvertently fall into the toilet. A patient could experience a severe pain crisis on a weekend and need to take extra doses of pain medication to avoid a trip to an emergency room—and as a result have an inaccurate pill count. As a result, the widespread use and enforcement of narcotics contracts may place some patients with low risk of abuse at elevated risk for undertreated pain. Physicians ought to exercise some degree of flexibility in addressing "violations" of such contracts.

Conclusions

When considering both the potential benefits and burdens of narcotics contracts, one can conclude that using them for patients at high risk for abuse or diversion is justified. The alternatives to narcotics contract use could be either physicians continuing to prescribe with no procedural safeguards to reduce abuse *or* refusing to prescribe opiates at all. The consequences of both are worse than those of using contracts. As with many clinical decisions, physicians ought to consider the individual risks and benefits rather than automate an intervention that could lead to patient harm. Screening all patients using evidence-based tools to estimate risk, then requiring contracts for high-risk patients, seems a reasonable approach that is justified by the current state of the science.

In the case of our patient Brad, assessing his risk of abuse and, if it is high, communicating that this contract-based approach is designed to ensure his safety may help ameliorate the concerns he expresses in the visit.

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MEDICAL EDUCATION

Undergraduate Medical Education on Pain Management across the Globe Nalini Vadivelu, MD, Sukanya Mitra, MD, MAMS, and Roberta L. Hines, MD

Introduction and an Appeal

Pain is common, easily recognized, and largely treatable, and, despite this, pain is often inadequately assessed and managed in clinical practice [1-5]. Inadequately managed pain is a worldwide problem that leads to significant suffering, dysfunction and disability, loss in job productivity, and an increasing health care burden [1-3]. Adequate pain management is now recognized as a patient/human right [6].

An essential cause of suboptimal pain recognition, assessment, and treatment is inadequate education of health care practitioners. This is of particular concern because patients with pain are most likely to visit their primary care or general physicians first. In other words, we are failing to teach a large percentage of doctors who are the first line of patient care. The failure to do so during residency training has particularly notable consequences.

This failure should not be attributed to the lack of guidelines or clinical and research studies. In fact, there are numerous guidelines and a robust body of literature on how pain management should be taught and implemented. For example, a detailed "core professional curriculum" for teaching about all aspects of pain, developed by the International Association for the Study of Pain (IASP), has been available for the past 25 years [7], with the latest (third) version published in 2005 [8]. Guidelines to ensure that hospital staff are adequately trained to manage acute pain were issued by the Joint Commission on Accreditation on Healthcare Organizations (now the Joint Commission) more than a decade ago [9]. Thus, inadequate pain management is rooted not in a lack of guidance but in the deficiencies in our current methods of pain education [10].

We addressed this issue in a recent publication on acute pain education and management [11]. In that piece, we argued that improved medical education is the key to solving the problem of inadequate acute pain management. Residency is the seminal period during which attitudes toward pain are conceived and nurtured. Instilling an early understanding of and empathy for pain during residency will greatly enhance the chances that future practitioners will be more willing and able to treat pain. This understanding, coupled with the knowledge and skills required for assessment and management of acute pain, will round out all three domains of medical education: cognitive, psychomotor, and affective. In this article we seek to expand upon the early discussions of acute and chronic pain and focus on the broader area of pain education. We make the appeal that such education should start early into the career of the undergraduate medical student, whose mind is more receptive and impressionable [11]. We also believe that such education should be integrated in the general medical curriculum from the first through the final years to ensure the broadest reach possible at both the national and the international levels.

We contrast our approach with those aimed at developing pain medicine as a dedicated specialty. While there is no doubt that such emphasis and approaches are required (and, indeed, being followed in some countries), our point is that a more broad-based and early introduction to pain education is likely to yield richer dividends. Utilizing this approach, common pain conditions can be effectively managed in primary or secondary health care settings, thus freeing up valuable time, limited manpower, and even more limited resources to manage the complex pain conditions at the tertiary care level.

Pain Education: A Bird's-Eye View of the Global Situation

Recently we examined pain education from a global perspective by reviewing the varying degrees of information available from several developed and developing countries: the U.S., Canada, the United Kingdom, Finland, Australia, New Zealand, and India [11]. Our results showed that, despite marked variations across countries, the overall picture was one of inadequacy and dissatisfaction on the part of practitioners. For example, until recently only 3 percent of medical schools in the United States had any part of their curricula specifically dedicated to pain education [12]. In a 2009-2010 survey of 117 medical schools in the U.S. and Canada, the situation appeared much better: 80 percent of U.S. medical schools and 92 percent of Canadian medical schools required at least one pain session in their curricula. The actual content, style, and format of the education, however, were found to be "limited, variable, and often fragmentary" [13]. On closer scrutiny it was discerned that many topics of the IASP core curriculum were not even addressed [13]. Findings with similar results have been reported from Finland, Australia, and New Zealand, and the United Kingdom [14-17].

The recently published results of a comprehensive survey conducted by the Special Interest Group on Pain Education of the British Pain Society are eye-opening [18]. In this survey of 19 higher education institutions affiliated with 11 universities offering 108 undergraduate programs in a wide range of medical and related disciplines across the U.K., it was found that pain education comprised less than 1 percent of the university-based teaching for health care professionals. The average pain-related content comprised only 12 hours. Of note, more coverage of pain-related topics was provided in physiotherapy and veterinary science programs than in medical science. Only 11 programs (less than 15 percent) offered a specific pain teaching module. The original report finally concluded that "the amount of pain education in the curricula of healthcare professionals is woefully inadequate given the burden of pain in the general population in the UK" [17].

The emphasis on integrating pain education into the medical school curriculum has been studied significantly less in developing countries than in the developed world. In a recent preliminary, impression-based survey of medical centers, one each from 7 developing countries (India, China, Indonesia, Philippines, Thailand, Nigeria, and Guatemala), it was felt by all respondents but those in Thailand that there was "no" or "some" availability of education in acute pain management in medical, nursing, or pharmacy schools [19]. Pain was felt to be adequately managed in only 30 to 50 percent of patients. Indeed, all respondents agreed that "pain control is not given priority." Of note, "concerns about addiction (even for Acute Pain)" was mentioned as a barrier to opioid use in severe acute pain management [19]. Additionally, the IASP conducted a survey in its chapters in the developing countries in 2005 [20]. More than 90 percent of the respondents agreed that pain recognition and management was a significant issue in their populations. Furthermore, results from the survey revealed that, although up to 50 percent of respondents had, as undergraduates, attended formal courses relating to pain, more than 90 percent stated that the level of education they received was not sufficient to cover their needs at the time they entered clinical practice.

Ways Forward: Learning Lessons from Existing and Innovative Programs

The most desirable way to advance pain education is to encourage its integration in the regular medical school curriculum. Some institutions have begun to do this, although in most situations there is a lack of coordination between the preclinical and clinical curricula [21, 22]. Pain as a topic is often relegated to brief lectures or seminars at most institutions. There are several reasons for this, including attitudes of the program administrators but also the real constraint on time in an ever-expanding medical curriculum that forces prioritization of themes and topics to be covered during medical school.

Despite these limitations, it is encouraging that even brief study can still produce positive effects. Even a 6-hour course for first-year medical students that combined written materials on behavioral, social, and biological aspects of pain with clinical observations of an acute and chronic pain treatment team produced a greater recognition of pain as a real and complex entity and a stronger belief that working with pain patients is rewarding [23].

When even less time is available, the role of bedside instruction assumes particular significance. For example, fourth-year medical students randomly assigned to a 1-hour lecture on regional anesthesia plus a 1-hour bedside teaching session scored significantly better on an objective structured clinical examination than those assigned to a 2-hour classroom-based structured course alone [24]. A recent report from the Johns Hopkins University School of Medicine demonstrated the utility and feasibility of a short (18 hours over 4 consecutive days) pain education program for first-year medical students. This program combined core curriculum knowledge on pain with affective and attitudinal development in an innovative way [25]. The program consisted of 4 didactic lectures, 3 learning "labs," 3 team-based learning

exercises, and 3 small-group teaching sessions. Overall, the students gave positive feedback on their training and expressed enhanced interest in pain medicine.

In Canada, the University of Toronto Centre for the Study of Pain has offered an interfaculty, interprofessional pain curriculum (IPC) since 2002 [26, 27]. In this 5-day offering, a 20-hour integrated pain course was provided by six health science departments—dentistry, medicine, nursing, pharmacy, physical therapy, and occupational therapy—to some of their second- or third-year students. Evaluation of the program revealed that it not only produced significant improvements in pain knowledge and beliefs, but also generated a high degree of student satisfaction with both the process and content of teaching [26]. Recently, the same group published on an interactive multimedia pain education program focusing on cognitive (knowledge-based) as well as reflective (affective, experiential, and attitudinal) aspects of pain evaluation and management [28].

The Developing Countries Working Group of the IASP has been supporting several educational initiatives specifically for developing countries for a decade now by giving grants for educational programs (74 grants to members from 34 countries) and establishing clinical training centers [29].

Conclusion

A recent editorial by John D. Loeser, MD, former president and founding member of the IASP, identified "inadequate education of primary care providers about pain and how to treat it" as one of five major crises in pain management today [30]. To effectively address this problem, basic pain education should be made a mandatory and integral part of medical school curricula in developed and developing countries alike. A small but growing number of such educational efforts are taking place, mostly in developed countries, as briefly reviewed above. Now is the time to rigorously evaluate these programs to probe their effectiveness [31] and expand upon their evidence base so it can be effectively used in political and advocacy campaigns to further expand pain education offerings worldwide. As a recent editorial put it [32], "education...education...education" in the area of pain should be our motto now.

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THE CODE SAYS

The AMA Code of Medical Ethics' Opinion on Sedation at the End of Life

Opinion 2.201 - Sedation to Unconsciousness in End-of-Life Care

The duty to relieve pain and suffering is central to the physician's role as healer and is an obligation physicians have to their patients. Palliative sedation to unconsciousness is the administration of sedative medication to the point of unconsciousness in a terminally ill patient. It is an intervention of last resort to reduce severe, refractory pain or other distressing clinical symptoms that do not respond to aggressive symptom-specific palliation. It is an accepted and appropriate component of end-of-life care under specific, relatively rare circumstances. When symptoms cannot be diminished through all other means of palliation, including symptom-specific treatments, it is the ethical obligation of a physician to offer palliative sedation to unconsciousness as an option for the relief of intractable symptoms. When considering the use of palliative sedation, the following ethical guidelines are recommended:

(1) Patients may be offered palliative sedation to unconsciousness when they are in the final stages of terminal illness. The rationale for all palliative care measures should be documented in the medical record.

(2) Palliative sedation to unconsciousness may be considered for those terminally ill patients whose clinical symptoms have been unresponsive to aggressive, symptom-specific treatments.

(3) Physicians should ensure that the patient and/or the patient's surrogate have given informed consent for palliative sedation to unconsciousness.

(4) Physicians should consult with a multidisciplinary team, if available, including an expert in the field of palliative care, to ensure that symptom-specific treatments have been sufficiently employed and that palliative sedation to unconsciousness is now the most appropriate course of treatment.

(5) Physicians should discuss with their patients considering palliative sedation the care plan relative to degree and length (intermittent or constant) of sedation, and the specific expectations for continuing, withdrawing, or withholding future life-sustaining treatments.

(6) Once palliative sedation is begun, a process must be implemented to monitor for appropriate care.

(7) Palliative sedation is not an appropriate response to suffering that is primarily existential, defined as the experience of agony and distress that may arise from such issues as death anxiety, isolation and loss of control. Existential suffering is better addressed by other interventions. For example, palliative sedation is not the way to address suffering created by social isolation and loneliness; such suffering should be addressed by providing the patient with needed social support.

(8) Palliative sedation must never be used to intentionally cause a patient's death.

Issued November 2008 based on the report "Sedation to Unconsciousness in End-of-Life Care," adopted June 2008.

Related in VM

Common Misconceptions about Opioid Use for Pain Management at the End of Life, May 2013

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JOURNAL DISCUSSION

Physicians' Responsibility to Understand Patients' Pain Robert Learch, DO, and Jeremy Cumberledge, MD

Crowley-Matoka M, Saha S, Dobscha SK, et al. Problems of quality and equity in pain management. *Pain Med.* 2009;10(7):1312-1324.

Pain has risen to epidemic levels in the United States, and how we as physicians manage it best has become a widely debated issue. More than 100 million American adults suffer from chronic pain [1], the financial implications of which are astounding. It is estimated that the direct cost of pain treatment is around \$300 billion dollars annually. That is more than treatment for cancer and diabetes combined [2]. Joint pain alone is responsible for 12.5 million emergency department and clinic visits annually [1]. While pain management has become an issue that physicians deal with on a daily basis, there is not yet consensus on how best to address it. In "Problems of Quality and Equity in Pain Management," Crowley-Matoka et al. identify three elements of biomedical culture that contribute to the current problems in managing pain: (1) mind-body dualism; (2) a distinction between disease and illness; and (3) bias toward cure rather than care [3].

The principle of mind-body dualism—viewing body and mind as being separate [4, 5]—as well as the favoring of objective over subjective data are certainly pervasive and cause damaging inequities in our current medical culture. The situation stems, in large part, from an unclear understanding of the pathophysiology of pain and how social, cultural, and psychological factors affect it. The authors note that mind-body dualism may be at least partly responsible for the fundamental structure of modern medical knowledge—diseases of the mind and body are taught separately in the classroom and treated individually in the clinical setting. The current biomedical model inclines physicians to label the easily measurable findings related to pain as "real" and to treat them more proactively. Alternatively, in the absence of objective findings, physicians are more likely to doubt the authenticity of reported pain and the potential for lack of proper treatment increases. The nature of pain involves both mind and body.

There are some signs that point to change from the classic biomedical model of medicine to a biopsychosocial model with increased use of psychotropic medications, specifically antidepressants and atypical antipsychotics [6, 7]. It is not outside the realm of possibility that improvements such as these could correlate with advances in the awareness and treatment of chronic pain as we learn more about how pain uniquely affects both the mind and body together, and not at all separately.

The contrast between disease and illness implies a separation of the two, as though they reside at opposite ends of a continuum. Crowley-Matoka and colleagues note that it is easy for physicians to identify diseases, represented by a collection of exam findings, lab results, and other tangible objective information. Patients, however, experience "illness," which is not limited to objective findings but encompasses psychosocial effects of being unwell in the setting of a patient's culture. It is the summation of these factors that ultimately affects their lives, manifested as pain or any number of physical or mental ills. The disease model of medicine is insufficient because it places an inappropriately high value on classic presentations of particular diseases. When the patient fits the criteria for diagnosis, they are enthusiastically treated, and physicians are satisfied by a job well done. Conversely, patients who do not precisely fit a discrete syndrome may be inadequately treated or disregarded completely. Correcting the "disease-vs.-illness" approach involves understanding patients as a whole, and not just diagnosing and treating their disease or pain. This understanding comes at a cost, however, since physicians must overcome the tendency to view patients in pain or with atypical presentation of illness as frustrating or difficult [8, 9]. Instead they must commit themselves to considering and understanding the often unpleasant social situations of their patients.

The bias toward cure and away from care can also be viewed as a continuum, the pendulum having swung far toward cure with rapid advances in biotechnology and in the availability of novel treatments for a number of ailments [10, 11]. Pain management lags behind other treatable ailments in this sense. Opioids have become a mainstay in the treatment of chronic pain, though the data is severely lacking to guide our management [12]. We tend to focus on "curing" and yet we know little about how to diagnose pain and have comparatively few tools to manage it. Before there were treatments for many diseases, a culture of caring for patients prevailed because there frankly was no way to cure them. With the advent of these curative measures, physicians are now pushed to be efficient in "curing" and often are not able to spend the time required to understand their patients' situations and diagnoses [13]. We assert that if chronic pain cannot be cured, we must at least seek to care for patients in the same way we did before so many "cures" came along.

Crowley-Matoka et al. report that the characteristics of modern biomedicine manifest themselves in inadequacies in three phases of clinical pain management. First, the communication of pain between patients and physicians may suffer because of the current model. The fact that complex illnesses like chronic pain syndromes cannot be easily measured or classified may result in physician reluctance to address them. When social or cultural differences are present, the communication breaks down further. Physicians can view pain management as frustrating or difficult, which may limit their commitment of time and effort to communicating with these patients [3].

Assessment and management of pain are flawed under the current biomedical model, and this error has significant social and cultural ramifications. Physicians and patients commonly identify with very different culture groups. Though some group overlap may exist, membership related to socioeconomic status, education, and ethnicity often does not. Our inability or potential unwillingness to recognize that a patient's illness occurs within social context can lead to mislabeling difficulties in treatment as misunderstandings with the patients themselves [3]. The harsh reality is that mislabeling these problems can affect the quality of medical care. Recognizing this should call us to reflect and introspect about how we as individual physicians approach patients from different cultures, ethnicities, and socioeconomic backgrounds.

We agree with Crowley-Matoka et al. that there is a weakness in the current biomedical culture and there are a number of factors that contribute to our problems. These factors may include, but are not limited to, our patients' personal or cultural views toward illness, the business of health care under which we all operate, and our own personal opinions about the ideal of health and wellness. As the leaders in the health care arena and the "healers" of our day, physicians must take the reins to ensure equity for our patients' sake. If we can begin to analyze our actions and motives and honestly assess how we approach these patients, perhaps we will drive the transformation of our biomedical culture. Individuals can navigate between cultures and cultures themselves can change over time [14]. It is past time for a shift towards a biopsychosocial orientation to pain, and we are the physicians who are called to see that through.

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STATE OF THE ART AND SCIENCE Long-Term Opioid Treatment Craig T. Hartrick, MD

For many physicians the prospect of opioid prescription evokes a visceral reaction that is perhaps unique among medications. While other commonly prescribed medications that do not induce such feelings may be arguably more toxic or have narrower therapeutic indices (e.g. insulin or digoxin), the risks associated with longterm opioid use for pain from conditions other than cancer should not be underestimated. The development of tolerance, the potential for abuse and misuse, and a lack of understanding as to the indications for use all contribute to physician angst. Over the last 2 decades, changing perspectives in the U.S. regarding opioid prescription have followed advances in basic science, as well as hard-learned clinical experience.

Tolerance

The development of physiologic tolerance can be expected following repeated exposure to exogenous agents that occupy receptor sites normally responsive to endogenous substances. The body attempts to maintain homeostasis by reducing the number and sensitivity of receptors. In the case of opioids given for analgesia, muopioid receptors (so named for their prototypical agonist, morphine: mu) that normally respond to endogenous endorphins become phosphorylated, making them less responsive. Ultimately they are internalized by endocytosis, decreasing their number and the physiologic response to the exogenous opioid. The natural tendency of clinicians, then, is to increase the dose, hoping to achieve the response that was previously experienced. Unfortunately, the success of such a dose escalation strategy may be hindered by the repetition of the physiological reaction. This response is unpredictable and varies considerably by person [1].

Tolerance can develop surprisingly rapidly, even in cases of acute pain; clinical evidence of tolerance can be seen within just a few weeks. Moreover, the apparent need to maintain long-term opioid therapy following an acute injury is not a rare phenomenon. While the severity of injury and anticipated duration of rehabilitation are important factors in the transition to chronic pain, they may account for only half the expected variability in the need for long-term opioid therapy [2]. Affective pain components, self-perceived risk of addiction, prior opioid exposure, and genetic and other influences may all play prominent roles. Most importantly, the development of tolerance is by no means equivalent to addiction. Dose escalation due to tolerance is common and not necessarily directly related to the development of an obsession for the procurement and compulsive use of the drug, hallmarks of addiction.

Addiction, Abuse, and Misuse

The distinction between tolerance and addiction should be emphasized; most opioidtolerant patients do not exhibit signs of addiction. Once again, individual variability characterizes the development of addiction, making outcome prediction difficult [3], but some features are associated with increased risk for addiction: increasing dose requirement, younger age, preexisting mental health disorders, and prior substance abuse [4]. Significantly, aberrant behaviors have been observed in nearly a quarter of patients taking opioids for noncancer low back pain in the U.S. [5]. The current widespread use of opioids for chronic noncancer pain created a need for vigilance in identifying patients who are abusing (unlawful use or use despite harm to the user) or misusing (use other than as prescribed) opioid medication.

Fear of Tolerance and Addiction

The unpredictability of patients' responses to opioid treatment fuels the fear of iatrogenically induced addiction, which historically has caused doctors to limit openended opioid prescriptions for patients with noncancer pain. Yet the undertreatment of pain is itself detrimental and in fact can lead to pseudoaddiction. Patients subjected to perpetual undermedication continually request dose escalation due to poor analgesic effect. Or, fearing addiction, they avoid taking the prescribed medication on a time-contingent basis [6], instead holding off until the pain is intolerable, then having difficulty "catching up" to the pain. Thus both physicians and patients contribute to this pseudoaddiction effect.

In response to the undertreatment of pain, the American Pain Society (APS) issued a 1997 statement encouraging judicious use of opioids and even suggesting that tolerance was rare [7]. Over the next decade it became apparent that the pendulum, particularly in the U.S., had swung too far and that tolerance is natural, common, and necessary to consider. The recommendations from the APS have subsequently been revised to reflect the clinical importance and frequency of tolerance development to opioid therapy [8].

Indications

Identifying patients who may be appropriate candidates for long-term opioid treatment goes beyond screening for addiction and abuse potential. Some pain states are relatively less responsive to opioids. This lack of efficacy results in relative undertreatment, which can lead to dose escalation. Phenotypic switching from opioid-predominant mechanisms to noradrenergic predominance has been observed preclinically following nerve injury [9]. This may contribute to the long-held impression that neuropathic pain responds poorly to monotherapy with mu-agonist opioids. On the other hand, combination therapy, in which opioids are combined with agents that have complementary, nonopioid-mediated mechanisms of action, especially anticonvulsants or antidepressants, has been useful in some neuropathic pain states [10].

Recent Developments

Targeting multiple receptors. Some opioids have additive or even synergistic effects because they combine nonopioid-mediated pain pathway activity with mu-opioid agonism: a dual mode of action in a single drug. One advantage of such drugs is the avoidance of drug-drug interactions (DDI). Methadone, in addition to having mu-opioid agonist effects, interacts with other receptors as well, including the N-methyl-D-aspartate (NMDA) receptors on ionotropic calcium channels. While this effect may make it a relatively better opioid choice for neuropathic pain than pure mu-opioid agonists, its long and variable elimination half-life, especially in the elderly—as well as other challenges, such as QTc prolongation and CYP3A4 metabolism—make it difficult to titrate safely. A somewhat newer agent, tapentadol, exhibits both mu-opioid agonism and synergistic norepinephrine reuptake inhibition in a single molecule with a low potential for DDI [11]. An extended-release preparation is available and approved for chronic use.

Newer formulations. The recommendations for using long-acting opioid formulations in chronic noncancer pain are controversial. While having to take medication only once or twice daily would be expected to improve compliance, the overall results on outcomes when compared to less expensive short-acting immediate release preparations remain a subject of debate. The major advantage of the long-acting formulations may lie in improvement in quality-of-life measures [12]. Transdermal delivery systems can provide less dramatic swings in blood levels, reducing euphoric effects and providing sustained analgesic levels of opioid [13].

Opioid formulations that include opioid antagonists induce withdrawal when oral tablets are misused by being taken intravenously. These formulations have been only partially successful in reducing abuse liability. The combination of buprenorphine with naloxone is a notable exception and is used to treat opioid addiction. The partial agonist, buprenorphine, which is less efficacious at the mu-opioid receptor than pure agonists such as morphine, reduces cravings without inducing withdrawal or appreciable euphoria.

Rotation and combination. Patients taking opioids even for a few weeks can not only become tolerant but can suffer withdrawal as well, though they are clearly not addicted. In an effort to deal with increasing tolerance with long-term opioid use, opioid rotation has been widely recommended and practiced clinically. While there is little evidence to support this practice [14], one can hypothesize that switching from one opioid to another might exploit subtle differences in opioid receptor subtype activation patterns [15]. Even though the mu-opioid receptor is encoded by a single gene, alternative splicing results in multiple variations in the intracellular portion of the receptor. This results in considerable variety in activation patterns and may provide a scientific rationale for both opioid rotation and the synergistic combination of two opioids given concurrently.

Conclusion

Future developments in opioid management can be expected as we learn more about the basic science of opioid analgesia generally and effective methods of glial cell modulation specifically. The development of tolerance, opioid-induced hyperalgesia, and perhaps even addiction share a common factor: altered central immune signaling [1]. By increasing knowledge about analgesia and glial cell modulation we may be able to demystify opioid management of chronic noncancer pain, lessen the stigma associated with opioid medication use, improve patient selection, and, ultimately, improve patient outcomes.

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Virtual Mentor

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STATE OF THE ART AND SCIENCE

Objectifying Chronic Pain: From the Patient to Diagnostic Metrics David Borsook, MD, PhD

Introduction

A 2012 article in *The Lancet* reported that four pain conditions ranked among the top 16 clinical afflictions affecting the world's population [1]. Chronic pain has reached epidemic proportions in the United States, burdening the country, the people affected, and their families with medical costs, social isolation, and lost working hours [2]. With an aging population this burden will only get worse unless there are breakthroughs in medications and other treatments for chronic pain. At this time studies of effectiveness for chronic pain treatments suggest that 30 percent of patients have better results with some drugs than with placebos, which themselves tend to decrease pain by 20-30 percent. Currently, pharmacological pain treatment takes a trial-and-error approach; we treat on an ad hoc rotational system, starting with one drug and adding or replacing a drug on best-guess basis because we do not have specific diagnostic measures to pinpoint the cause of pain and few, if any, robust treatment approaches. We need a more objective, individualized process. So how can this change?

Why Is It So Hard to Objectify Pain?

Nearly 100 million patients in the U.S. suffer from chronic pain. Chronic pain problems increase with age, and the U.S., as with other Western societies, is facing an increasingly large older population. All clinically active physicians will treat or interact with patients with chronic pain. Current approaches use a relatively simple metric—the 11-point pain scale (0 = no pain; 10 = maximal pain). But this does not capture the nature of chronic pain: *a sensory and emotional response to an actual or perceived bodily threat that lasts for more than 3 months* [3].

First, subjective responses, particularly for small differences, are notoriously difficult to evaluate, in part because pain means something different to each individual, in part because pain varies over time, and in part because pain is a complex experience that is also dependent on context, previous experience, social situation, psychological state, and so on. Second, the patient lives with chronic pain day in and day out, so capturing a chronic pain patient's "state" as either a single measure or a measure over time is difficult. Third, no common diagnostic metric such as an EKG or blood tests for myocardial infarction exists.

Think about trying to describe a chronic pain process. The pain varies over time; pain is frequently comorbid with depression and anxiety (including posttraumatic stress disorder—PTSD); indeed it may induce these conditions in patients who were

never depressed. Pain is a reward-deficit syndrome. Emotional, cognitive, and interoceptive (internal physiological status of self) components of pain are copresent. Even inattention and changes in perception of size are subtle but clear changes that are well described in chronic pain. Pain contributes to social isolation. Whatever its etiology, e.g., traumatic (e.g., postsurgical neuropathy), idiopathic (e.g., fibromyalgia), endocrine-related (e.g., diabetic neuropathy), due to an inborn error of metabolism (e.g., Fabry's Disease), infection-related (e.g., post herpetic neuralgia), channelopathy-related (e.g., hemiplegic migraine, erythromelalgia), or other, chronic pain is a behavior and affects the brain and our response to the disease and its treatment.

Objective Metrics: From Genes to the Brain Systems

Technology is introducing several approaches to predicting the likelihood of chronic pain, measuring pain signals, and predicting response to analgesics. When patients are about to undergo surgery, diagnosis or prediction of the probability of chronic postsurgical neuropathic pain can be made using genetic [4], psychological [5], and imaging [6] measures.

Advances in nuclear magnetic resonance and functional activity measures allow brain pain signals to be visualized. Recent work has provided evidence that measures of brain structure and functional activity can define a pain state and predict disease chronification in conditions such as back pain [6] and perhaps migraine [7]. Some techniques have allowed for prediction of analgesic drug effects [8, 9].

These approaches are becoming more standardized, and routine use in clinical practice may not be far off. Specifically, the evolution of a brain biomarker for chronic pain (disease and analgesic effects) would seem to be well within grasp. If successful, these developments will contribute to transforming the poor state of chronic pain treatment. Brain imaging is one of many ongoing research areas that have radically changed our notion of chronic pain conditions. Other approaches to measures of brain systems in chronic pain include near-infrared spectroscopy (NIRS) and EEG methods that determine alterations in cortical changes. The latter have the benefit of being performed in the clinic and being cheaper.

Adapting to the Clinic

What would the characteristics of an objective measure or pain-metric be? A number of desired characteristics are obvious: (1) it should have high specificity and sensitivity; (2) it should be easy to implement—including testing procedures and evaluation processes (i.e., analysis, interpretation); and (3) the cost-benefit comparison should be clear. Simple approaches such as a questionnaire or a blood test are obviously preferable to complex methods like imaging. The more portable approaches noted above (NIRS, EEG) may be more cost-effective, but NMR imaging may acquire data faster and does not need application of specialized head caps for placement of electrodes or NIRS emitters and receivers.

Conclusions

We currently have no simple test of any kind that tells us whether someone has pain. Furthermore, we have few if any treatments that are highly effective in most patients with chronic pain [10]. Thus, the continued clinical challenge is to do the best we can for the individual patient using a therapeutic armamentarium that is by and large deficient or the efficacy of which is unclear.

If pain assessment based simply on the subjective rating worked well, we would probably have a more rational approach to treatment of our patients than the hit-andmiss approach that is generally practiced. Technology-based studies like those described above have not been replicated and validated sufficiently [11-14]. Most of them focused on cohorts of subjects and did not evaluate changes at the individual level. Nevertheless, there is reason to be optimistic that brain imaging can contribute to the overall evaluation of pain. The imaging field is in its infancy but the trend is towards metrics for individualized brain measures for pain and, for that matter, for other diseases that affect the brain, akin to the use of anatomical MRIs that is predicted to be part of routine clinical practice [13].

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HEALTH LAW Fighting Prescription Drug Abuse with Federal and State Law

Valarie Blake, JD, MA

Prescription drug abuse is an epidemic in the United States that has been the subject of ongoing legislative control since the 1970s. The pharmaceutical dispensing of opioids increased 48 percent between 2000 and 2009 [1], and prescription drugs play a significant role in unintentional death: accidental poisoning is second only to car accidents, and prescription drugs are the leading cause of it, above both cocaine and heroin [2]. Among teens, prescription drug abuse is exceeded only by marijuana use [1]. Physicians, the guardians of prescription drugs, play a key role in limiting their misuse and diversion. This article will review federal and state legislation that targets prescription drug abuse, including legislation aimed at prescribers and dispensers of controlled substances.

Federal Programs and Laws

Federal drug regulation began early in the twentieth century with opiate regulation in the 1910s [3] and the 1919 Volstead Act (prohibition of alcohol) which remained in effect into the 1930s [4]. Passage of the most comprehensive federal drug law, the Controlled Substances Act, came in 1970, putting in place a single system for regulating psychotropic and narcotic drugs [5] and establishing the legal framework that secured the 1973 creation of the Drug Enforcement Administration (DEA) [6]. Today a sizeable government program with 5,000 special agents and a budget of \$2.02 billion, the DEA is the primary agency charged with policing the issuance and dispensing of controlled substances, including prescription drugs [7].

DEA regulations apply to manufacturers, dispensers, and distributors of controlled substances, but this article focuses mainly on implications for physicians and their practice. Physicians must be registered with the DEA to prescribe controlled substances (or in very rare cases, receive an exemption from registration), which is predicated on their obtaining proper state licensing [8]. Registration must be renewed every 3 years, and the physician must be registered in every state in which he or she dispenses controlled substances [8].

Regulation enforcing the Controlled Substance Act further stipulates that there be a legitimate medical purpose for prescriptions, the practitioner must be acting in the usual course of practice, and that only a pharmacist can legitimately fill a prescription [9]. All prescriptions have to be signed and dated on the day of prescribing (which makes pre-signing blank prescription pads illegal) [9]. Practitioners can prescribe up to a 90-day supply of a controlled substance, but only with certain precautions (e.g., written instructions on the prescription about the

earliest date on which it can be refilled) [10]. There are limits on the number of refills for certain classes, called schedules, of highly addictive substances like opioids [11]. There are additional regulations for e-prescriptions (online prescriptions) to minimize chance of fraud or abuse [12], and registrants have to notify the DEA, in writing, of any significant loss or theft of a controlled substance [13].

Penalties for violating various aspects of the law can include jail time, fines, and loss of DEA licensure (and thus loss of ability to prescribe some or all controlled substances). Physicians may lose their DEA registration if they lose their license to practice medicine in the state, and, moreover, the DEA itself can investigate, and participate in the arrest and prosecution of, physicians who violate controlled substance laws. Example cases can be found on the DEA web site [14].

The Food and Drug Administration (FDA) has also taken measures to address the growing problem of prescription drug abuse. The Food and Drug Administration Amendments Act of 2007 granted the agency the authority to require companies to develop a risk evaluations and mitigation strategy (REMS) when the potential risks of a drug outweigh the benefits [15]. Extended-release or long-acting opioids currently have a REMS to manage the risk of accidental or intentional misuse and the risks to patients who are prescribed these drugs but do not need them. The strategy mainly requires sponsors of opioids to foot the bill for educating prescribers and patients on the risk of opioid mismanagement and proper prescribing, storage, and disposal practices [15]. At the same time, the FDA will monitor patient access to these drugs to ensure that patients receive proper pain management (and that the REMS does not dampen proper prescribing of controlled substances) [15].

President Obama has been active on this issue, launching an ongoing campaign to combat prescription drug abuse [1]. In addition to calling for a REMS for opioids, the campaign promotes youth and parent education, encourages research on patterns of abuse and successful abuse deterrents, increases tracking and monitoring of controlled substances, supports better resources for proper medication disposal, and provides increased resources to law enforcement to target improper prescribing practices and pill mills (clinics and physicians that prescribe controlled substances irresponsibly) [1].

Most recently, the Senate Finance Committee has begun investigating medical groups, physicians, and bioethicists who have advocated for increased use of narcotic and opioid painkillers to determine whether they received compensation or had inappropriate ties with drug manufacturers like Purdue Pharma and Johnson & Johnson [16].

State Regulatory Approaches

Like the federal government, states have increased regulation of prescription drug use and abuse since the 1970s, and legislation in this area continues to develop.

Most states have general prohibitions against the obtaining of drugs through fraud, deceit, or misrepresentation that date back as far as the Uniform Narcotic Drug Act of 1932 and the Controlled Substances Act of 1970 [17]. These are broad prohibitions intended to cover a range of bad actors—patients, physicians, or persons selling drugs for profit [17]. In addition to bans and penalties for fraud, at least 43 states have prescription drug monitoring programs (PDMPs), most funded by the federal government's Department of Justice, that monitor who is writing and filling prescriptions in an effort to flag fraudulent activity [18]. There are also wide-ranging regulations that attempt to put legal limits on the amount of controlled substance prescribed, dispensed, or refilled. Examples include limits on number of refills, limits on the quantity of pills dispersed in one refill, limits on how long after a drug has been prescribed it can filled, and limits on the types of personnel who can dispense certain quantities of drugs [19].

Some state laws target abuse and diversion by restricting behaviors like intentionally withholding information from physicians and doctor shopping, in which patients seek prescriptions from different clinicians [17]. Some states require that patients show an ID to fill prescriptions [20]. A small number of states (Alaska, Maryland, New Mexico, and Washington) have some sort of immunity from prosecution or reduced sentencing for people who seek emergency help for an overdose (either for themselves or for another) [21].

Other laws apply specifically to physicians. A large majority of states require physicians to conduct a physical exam, take a patient history, or both to ensure medical need before prescribing controlled substances [22]. Some states require physicians to use tamper-resistant prescription pads with features like watermarks, serial numbers or logos, or chemically resistant paper that make it more difficult to forge or falsify prescriptions [23]. And some states, like Florida, Louisiana, and Texas, create special rules and burdens for pain clinics that may include special registration, state inspections and investigations of complaints, and requirement that the pain clinic be owned and operated by a practitioner certified in pain management who does not have a record of felonies or disciplinary action for improper prescribing [24].

State medical boards also play a key role with physician behavior. The Federation of State Medical Boards' model policy to guide state medical boards in their review of physicians' pain management practices recommends: proper medical evaluation of a patient including a history and physical; a written treatment plan that clearly states the objectives of treatment; a discussion of the risks and benefits of treatment with the patient, including patient responsibilities like urine drug screening, reasons why therapy might be discontinued, and limits on refills; periodic review of efficacy and consideration of other treatment modalities; clear documentation in medical records; and compliance with applicable state and federal law [25].

Regulations at the state level change frequently, and more bills are continuously being introduced to target this epidemic. A review of latest developments can be found at the National Conference of State Legislatures web site [26].

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POLICY FORUM Pain and Ethnicity Ronald Wyatt, MD, MHA

It is estimated that more than 116 million Americans suffer from chronic pain, which costs \$560 to \$635 billion annually in medical treatment and lost productivity [1]. Although pain is a widespread problem, studies have found that chronic disease, psychological distress, Medicaid insurance, and lower education levels are associated with higher incidences of severe pain [2]. Undertreating pain can lead to adverse outcomes, including elevated heart rates after surgery and increased risk of myocardial infarction, ischemic stroke, and bleeding events as a result of elevated systemic vascular resistance and elevated levels of catecholamines [2]. Other consequences of uncontrolled pain include reduced mobility, loss of strength, sleep disturbances, immune system impairment, increased susceptibility to disease, and medication dependence [3].

Despite the availability of effective pharmacologic and nonpharmacologic interventions and methods to manage pain, there is a significant gap between the evaluation and treatment of pain in white people and its evaluation and treatment in African American and Hispanic people [4]. Differences in pain treatment may be due to differences in needs—e.g., resulting from genetic differences—or to inequities—unfair differences in access or opportunity, e.g., unavailability of opioids in a neighborhood [2]. Another cause of differences in treatment may be a lack of awareness among clinicians and trainees of evidence-based guidelines.

Defining Pain

The American Academy of Pain Medicine classifies pain as acute or chronic. In acute pain, a "one-to-one relationship exists between injury and pain," and the "pain is frequently short-lived and self-limiting" [5]. However, the pain "can become persistent and intractable if the underlying disease process or injury is chronic or incurable, or if the activation of pain is unavoidable, as in pain caused by movement or weight bearing in injuries of the spine or in diseases such as arthritis" [5]. Chronic pain is defined as pain that persists longer than three months [5]. Pain can be managed with a range or combination of treatments such as nonsteroidal anti-inflammatories (NSAIDs) and other nonopioid medications, physical therapy, psychological interventions, alternative medicine, referral to a specialist, or opioids.

Pharmacogenomics and Pain

A review of the literature on the influence of race or ethnicity on the pharmacokinetics of analgesics found that there may be differences in bioavailability, hepatic metabolism, renal secretion, protein binding, and distribution [6]. For this reason, a patient's genetic makeup should be considered when prescribing medications that are known to be affected by genetic factors [6]. Research in the area is limited, but pharmacokinetic studies of codeine have demonstrated that 10 percent of the white population and 0.5 percent of the African American and Asian populations obtain no pain relief from codeine due to the lack of an enzyme needed for metabolism of codeine to morphine [6]. However, although pharmacogenomics has the potential to identify a particular analgesic that may not work in certain populations, more research is needed.

Social and Economic Conditions and Pain

Pain and its treatment are strongly influenced by race and ethnicity as well as by the social and economic conditions in which people work and live [4]. Reviews of literature on race and pain found that:

Race influences the experience of pain and of seeking treatment.

- In a population-based survey, 27 percent of African Americans and 28 percent of Hispanics over the age of 50 reported having severe pain most of the time; only 17 percent of non-Hispanic whites did [7].
- African Americans were found to have lower pain thresholds than whites for cold, heat, pressure, and ischemia [4]. Most studies showed no racial differences in pain intensity ratings, although African Americans described comparable pain intensity as a more unpleasant sensation than did whites [4]. Racial disparities in reports of pain unpleasantness differed by condition [4].
- African Americans were more likely than non-Hispanic whites to underreport pain unpleasantness in the clinical setting, especially in the presence of physicians who were perceived as having "higher social status" [4].
- African Americans were more likely to attribute pain to personal inadequacies and to use "passive" coping strategies, such as prayer, than were non-Hispanic whites [4].

White people are more likely to endanger themselves with the misuse of drugs.

- African Americans and Hispanics were more afraid than were non-Hispanic whites of opioid addiction [4].
- African Americans and Hispanics were less likely than white people to misuse prescription opioids [4].
- The overall rate of drug-related deaths was highest among non-Hispanic white people [4].

Despite this, whites receive more and better pain treatment than African Americans and Hispanics.

- African Americans and Hispanics were less likely than white patients to receive any pain medication and more likely to receive lower doses of pain medication, despite higher pain scores [4].
- They had their pain needs met less frequently in hospice care than did non-Hispanic whites [4].

- They were more likely to wait longer to receive pain medications in the emergency department than whites [4].
- Several studies of patients with low back pain found that African Americans reported greater pain and higher levels of disability than whites but were rated by their clinicians as having less severe pain [8].
- African American and Hispanic veterans with osteoarthritis—particularly African Americans—received fewer days' supply of a nonsteroidal anti-inflammatory drug than white veterans did [8].
- "Minority" and low-income children were less likely to have oral pain assessed and treated appropriately, especially if they had Medicaid insurance coverage [8]. For example, Hispanic children received 30 percent less opioid analgesia after tonsillectomies or adenoidectomies than white children [4].

These findings suggest that clinicians incorrectly believe that Hispanic and African American patients are more likely to abuse drugs than whites and therefore should have less access to them, when in fact they are *less* likely to do so, and that Hispanic and African American patients experience less severe pain than whites, when in fact they report comparable pain. The findings suggest, in other words, that variations in treatment are based on misconceptions rather than evidence.

Sickle Cell and Pain Management

Sickle cell diseases (SCDs) are an example of how biological differences and social inequities come together to create a "perfect storm" of inappropriate pain management. The spectrum of SCDs affects more than 100,000 people, predominantly young African Americans from urban areas, in the United States [6]. About one in every 300-400 African Americans born will have SCD; among Hispanics, the rate is approximately one out of every 36,000 and, among whites, roughly one out of 41,647 [3]. The fact that SCD is most prevalent among urban members of "minority" groups may result in discrimination by health care staff and miscommunication between patients and their clinicians [9].

The presentation of SCD is variable so it can be challenging for clinicians to determine whether a patient is experiencing a true pain episode or engaging in drug-seeking behavior. In SCD, pain may be the only symptom; there may be no pertinent laboratory or physical findings.

Guidelines for pain management in SCD include prompt initiation of parenteral opioids, use of effective opioid doses, repeat opioid doses at frequent intervals, and individualization of treatment based on prior opioid response histories [10]. Though cognitive behavioral therapy can be a useful long-term strategy [11], there is no evidence that adjuvant therapies such as heating pads and nonsteroidal anti-inflammatory agents are beneficial in the inpatient setting [12]. Patients with SCD may know which analgesics are most likely to be beneficial to them. What 7-22 percent of physicians, residents, nurses, and medical students considered drugseeking behavior [13]—requesting particular opioids, rather than an openness to

trying various methods including nonopioid treatment—is appropriate patient behavior in the case of sickle cell disease.

Furthermore, a survey found that less than 4 percent of sickle cell patients met the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria for substance dependence [14]. Large academic centers have estimated the proportion of adults with SCD abusing opioids to be in the range of 0 to 9 percent—less than the rate in the general population (estimated to be 6 to 9 percent) [15, 16]. If clinicians were better informed about condition-specific appropriate behavior for patients with sickle cell diseases, pain associated with it would be managed better and with less suspicion.

Adequate Pain Assessment and Management

Possible barriers to equitable pain management include [8]:

Health care-specific inequalities.

- Inadequate knowledge and education on the part of clinicians.
- Overreliance on pain scales in clinical assessment, as opposed to exploring the pain in a more multifaceted way, including its characteristics and symptoms, its impact on the patient's social and physical function and quality of life, and the patient's perception of it.
- Conscious or unconscious negative racial attitudes and stereotyping that affect clinical decision-making despite evidence-based guidelines.
- Lack of cultural sensitivity or competence.

Larger social inequalities that affect health.

- Unequally distributed insurance coverage and underinsurance.
- Limited access due to geography (e.g., segregated communities that have poor access to pharmacies).
- Insufficient health literacy.
- Insufficient advocacy from pain organizations for nondiscriminatory assessment and treatment.

Addressing such a multifactorial phenomenon will require a multipronged approach. Clearly, improving cultural sensitivity and competence is key. Mossey [4] recommends addressing the presence of bias and discrimination directly and at the level of the individual: empowering individuals to report pain accurately, encouraging physicians to examine their own cultural beliefs and stereotypical perceptions, and modifying counterproductive beliefs and attitudes regarding pain. The Institute of Medicine (IOM) advocates for improving and increasing education and training of health care professionals on these topics.

Evidence-based treatment approaches that are culturally sensitive are also recommended. The IOM recommends revising reimbursement policies to promote evidence-based pain management [1]. Anderson and colleagues [8] suggest employing cultural leverage—briefly, tailoring interventions to patients' cultures; recruiting individuals from the community who have training and knowledge of pain management to assist in counseling patients; and relying more on face-to-face interventions than computer-based or automated intervention, unless cultural leverage indicates otherwise.

Several significant organizations have called for increasing and improving the data available about pain and pain treatment. In 2010, The Joint Commission released requirements for the collection of data on all patients' race, ethnicity, and language as a means to identify potential disparities in care and to improve patient-clinician communication [17]. In the 2011 report *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education and Research*, the Institute of Medicine cited the lack of data on the scope of pain among some racial and ethnic groups and emphasized the need for better data collection on subpopulations at risk [1].

Conclusion

Pain control is a quality-of-life and quality-of-care issue. Although the effective treatment of pain is a professional responsibility of all healing professionals and health care organizations, there is overwhelming evidence that the management of pain in the United States is inequitable. Additional research and urgent action are needed to achieve the goal of eliminating disparities in pain management. By acknowledging gaps in pain management and actively seeking improvement, the imperative to deliver equitable care can be met.

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MEDICINE AND SOCIETY Chronic Pain Patients and the Biomedical Model of Pain Gillian Bendelow, PhD

Treating or alleviating pain is a primary role of medicine. What actually constitutes pain is subjective, value-laden, and difficult to define objectively and empirically, relying as the definition does on bodily signs and language, both of which are culturally embedded and subject to multiple interpretations. Biomedical theories of pain concentrate upon its neurophysiological aspects in both diagnosis and treatment. Hence, scientific medicine reduces the experience of pain to an elaborate broadcasting system of nerve signals, rather than seeing it as molded and shaped by the person who is experiencing it and his or her particular sociocultural context. The biomedical concept of pain is unsophisticated and oversimplified, often resulting in physicians' doubting the veracity of patients' reports of pain and the marginalization of such patients. We must incorporate engagement with the social and emotional context into medical understanding and treatments of pain to fully encompass its complex nature.

Pain in Biomedicine

The long-dominant conceptualization of pain has focused upon *sensation*, with the subsequent inference that it is able to be rationally and objectively measured. Biomedical practice traditionally assessed the nociceptive—"sensing harmful stimuli"—aspects of pain and employed the acute-chronic differentiation which did not necessarily take emotional aspects of pain into account. The observable links between test-confirmed physical disorders and expressions of pain are more obvious. On the other hand, one of the most complex and difficult types of pain to treat is *idiopathic* pain—that is, pain for which there is no observable or confirmable physical pathology. Often termed *chronic pain syndrome* and subsumed under the label of medically unexplained symptoms (MUS), these are illnesses or syndromes that cannot be defined in terms of organic pathology and are given low clinical importance. Frustrated by the seemingly intractable nature of idiopathic pain, practitioners often describe sufferers as "frequent fliers" or "heartsink" patients, further adding to their marginalization [1].

Other Concepts of Pain

As well as being a medical "problem," pain is not solely a creation of our anatomy and physiology but, in lay terms, is an everyday experience, emerging at "the intersection of bodies, minds and cultures" [2]. Moreover, defining pain is a semantic problem; in any language there may be wide variations in interpretation and meanings. Dictionary definitions of pain refer to any or all of the following:

PAIN [from the Latin poena, meaning penalty or punishment]

- 1. An unpleasant feeling caused by injury or disease of the body.
- 2. Mental suffering.
- 3. [old use] punishment e.g. on pain of death. [3]

In ancient Greece, the word used most often for physical pain was *algos*, which derives from roots indicating neglect of love. Another such word *akos*, literally meaning "psychic pain" from which we derive the English "ache" [4]. Implicit in these meanings is a much broader understanding of the multilayered cause and nature of pain—e.g., neglect of love can be the source of *algos*—than the narrowly defined Cartesian proposition which inevitably acts to divorce mental from physical states and tends to attribute single symptoms to single causes.

Indeed, the notion of that pain has a substantial emotional component, literally the obverse of pleasure, is much older than that of pain being a physiological sensation and can be traced back to Plato's (429-347 BCE) deliberations of extremes and opposites in the *World of Forms*. Plato declares pleasure and pain to be the twin passions of the soul, the results of the interactions between earth, air, fire and water [5]. Aristotle (384-322 BCE) developed the pain and pleasure principles further, describing them as basic moral drives guiding human action, and believed the pain experience to be negative passion which had to conquered by reason. He believed that pain was conveyed by the blood to the heart, yet excluded it from his classification of the five senses, instead preferring to describe it as "a quale [meaning "emotional quality"] of the soul; a state of feeling and the epitome of unpleasantness" [6]. Western literature, theology, and philosophy abound with considerations of the nature and purpose of pain (among many others, see Tillich and Kierkegaard [7, 8]), and the pleasure-pain dichotomy is constantly evoked and reinforced as in this passage from Montaigne:

Our well being is only freedom from pain, That is why the philosophical school which has given the greatest importance to pleasure has also reduced it to mere absence of pain. Not to suffer is the greatest good man can hope for... [9].

Conflict and Synthesis

The critique of the limitations of biomedicine has emerged from within medicine by those working in the area of pain, most notably pioneers like Melzack and Wall [10, 11] and Bonica [12]. Developments such as the widespread acceptance of Melzack and Wall's gate-control theory of pain and the influence of the hospice movement have shifted the pain paradigm, increasing the emphasis upon cultural and psychological components and the need for a multidisciplinary approach.

Social science perspectives, in particular the sociological literature on chronic illness, offer a rich framework for understanding the experience of chronic pain by focusing on the *person* who is experiencing the pain. Using a focus on the person, as advocated by Dame Cicely Saunders [13], one of the founders of the hospice movement, rather than measuring so-called objective symptoms allows us to encompass more easily the full notion of pain, which includes psychological,

spiritual, interpersonal, and even financial aspects of chronic pain, as well as its physical aspects.

When the pain experience is considered in this light, concepts such as biographic disruption, narrative reconstruction, and illness adjustment [14-17] are valuable and have been adopted by enlightened practitioners. In relation to adjustment to chronic pain, Kotarba [18] charted the process of becoming a "pain-afflicted" person, in order to trace the continuity of personal identity. Using pain biographies he identified three stages in this process. First, there is the "onset" stage, which is perceived to be transitory and able to be dealt with by diagnosis and treatment. Here, pain is diagnosed as "real" by physicians, having a physiological basis. The second stage concerns what Kotarba terms the "emergence of doubt." At this stage, treatment may not work, there is an increase in specialist consultations, but patients still feel in control in seeking the best care available. Finally, Kotarba terms the third stage the "chronic pain experience." Following the shortcomings of treatment, the patient, at this stage, may return to the lay frame of reference and seek help within the "chronic pain subculture" [19].

Beliefs about pain have been shown to have an important effect on compliance with physical treatment interventions [20]. While, at a theoretical level, modern health care practice may acknowledge the holistic, multifaceted nature of pain, attempts to transcend mind-body dualism in practice have been controversial and difficult, especially in the case of chronic pain.

How Pain Is Treated Today

Pain clinics or pain centers are institutions developed specifically for the treatment of chronic pain syndromes (pain with no demonstrable cause was rarely treated before the 1970s.) The concept of having special institutions for treating pain originated with John Bonica, an anesthetist in the U.S. who recommended in *The Management* of Pain [12] that the understanding and treatment of pain would be best achieved through cooperation among different disciplines. The first pain clinic was set up in the U.S. in 1961 by specialists from thirteen different disciplines aiming to collaborate in a nonhierarchical manner. The subsequently developed pain centers throughout North America and Europe are characterized by diversity in provision, resources, organization of work, medical specialities, working principles, and therapies. They can be private organizations or affiliated with medical schools, university departments, or hospitals. A cross-sectional survey of pain centers in the U.S. [21] found wide variations in the treatment modalities offered, types of pain conditions treated, populations served, patient selection criteria, and diagnostic and etiologic frames of reference. First, they found multidisciplinary, comprehensive pain centers dedicated to all kinds of pain problems and offering a wide range of treatment modalities. Secondly, there were syndrome-oriented centers that treated only one kind of pain problem (e.g., headache or back pain). Finally, there were modality-orientated treatment centers that offered only one type of treatment modality (e.g., analgesic nerve blocks) [22].

Gradually, a refocusing on the sociocultural aspects of the pain experience using illness narratives and phenomenological accounts has influenced treatment in many contemporary pain clinics across the U.S. and Europe. Vrancken [23] reviewed the theory and practice of academic pain centers in the Netherlands, and identified five broad approaches to both theoretical and practical aspects of pain: namely somatico-technical, dualistic body-orientated, behaviourist, phenomenological, and consciousness. These approaches range from the use of traditional biomedical techniques such as nerve blocks, at one end of the spectrum, to interventions more orientated to managing chronic pain, rather than trying to find a cure. More recently, pain practitioners in the U.K. are encouraged by the National Institute for Clinical Guidance to use mind-body techniques, including cognitive behavioural therapy (CBT), mindfulness, and acupuncture, for idiopathic low back pain [24].

Conclusion

The phenomenon of chronic pain provides us with one of the clearest examples of the need to adopt integrative models of health care that take into account the relationship, not only between mind and body, but among mind, body, and society. The key to eliminating the stigma and marginalization experienced by many chronic pain patients is physicians' acknowledgement that pain is "real." This is still the most important aspect in the treatment of chronic pain [20].

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American Medical Association Journal of Ethics May 2013, Volume 15, Number 5: 460-465.

IMAGES OF HEALING AND LEARNING Pain and the Paintbrush: The Life and Art of Frida Kahlo Fernando Antelo, MD

Pain is a prevalent symptom that causes patients to seek medical advice. Pain can have various origins, ranging from physical damage related to trauma to musculoskeletal changes associated with normal aging. Physicians can offer therapies including rehabilitative exercise and palliative medication. However, in spite of medical intervention, many patients continue to experience pain, and some may disregard recommended dosages for pain medication. The extent of risk that patients take to obtain pain relief might be reflected in the number of fatal overdoses associated with prescription medications: recent research revealed that nearly 75 percent of prescription deaths are accidental [1]. The research identified the most common medications involved in accidental deaths as opioids, benzodiazepines, and antidepressants—medications often used by sufferers of chronic pain. Patients living with chronic pain may feel that their physicians do not fully comprehend their experience of pain and may be at greatest risk for overdose.

In appropriately evaluating and treating pain, physicians engage in a dialogue with their patients to identify characteristics of pain and its time course. During a typical exam, patients communicate their subjective experience of pain, and physicians seek objective signs of tissue disease or damage. But the subjective experience of pain and its toll on the patient's life can be impossible to convey. As a consequence, many patients with pain do not gain satisfaction from the interaction with their clinicians. On the other hand, when patients believe that their physicians acknowledge and understand their pain, the perceived pain can be reduced by as much as 30 percent [2]. Physicians must approach the clinical encounter as an opportunity for their patients to share if not *paint* the picture of their health. In fact, one historical figure—Frida Kahlo—chose to paint about her health and experience with pain.

The Mexican artist Frida Kahlo (1907-1954) is known around the world for her numerous self-portraits and volatile marriage to Diego Rivera. In her self-portraits, Kahlo wears beautiful clothing and jewelry from her native Mexico and accents her hair with colorful ribbons and flowers. To the surprise of many observers, Kahlo prominently features her unibrow and facial hair and a stoic and distant facial expression that avoids any semblance of a smile. The expression is observed not only in her self-portraits but also in photographs. As acknowledged by several art historians, Kahlo's expressions reflect the many physical and emotional challenges that she faced in her life [3-5].

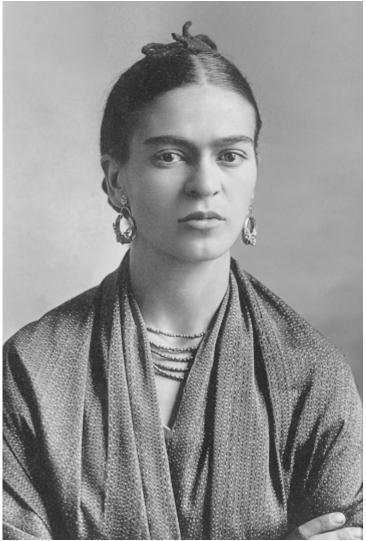


Figure 1. Portrait of Frida Kahlo, by Guillermo Kahlo. Copyright © Sotheby's.

At the age of 6, Kahlo's body was weakened and deformed when she contracted the poliomyelitis virus. During her formative years, she witnessed the uncertainties and destruction of the decade-long Mexican Revolution. As a teenager, she narrowly escaped death in a streetcar accident when a metal handrail pierced and disfigured her body, causing significant damage to her spinal column and pelvic organs [6]. Her challenges with physical and emotional well-being would continue into adulthood as she struggled with chronic pain, infertility, and depression. Kahlo's poor health and chronic pain inevitably became prominent themes in her artwork.

By distilling and depicting the emotions surrounding her traumatic accident and subsequent medical complications, Kahlo painted experiences that people could recognize and relate to—feeling pain, being hospitalized, and fearing isolation. In the iconic painting *Broken Column* (1944), Kahlo portrays the effect on her body of the injuries sustained in the streetcar accident. She offers her body for study by exposing her bare breasts and uncovering her spinal column. With metal construction nails

sticking into her body, moreover, she conveys the sharp and diffuse nature of her pain.

Kahlo provides another example of the perception of her body image in the painting *Landscape* (1946). Lying contorted in the middle of a desolate landscape, her body is an ill-defined form without clear features to identify it as being female or even alive. Kahlo, who as an adult underwent numerous spine operations and extended periods of convalescence, portrays her body as disfigured and scarred. While the observer can perceive structural forms that represent her extremities and bones, little else is recognizable. Kahlo may have hidden the face in this work to express the shame and embarrassment she felt about her damaged body. Later in life, Kahlo developed gangrene of the right leg that eventually required an amputation. Though she had experienced terrible pain in her right leg, the amputation devastated Kahlo. In her personal diary, she illustrated herself as a one-legged figure and wrote, "I am DISINTEGRATION" [3]. Overcome by depression and the disfigurement of her body, Kahlo attempted to commit suicide on several occasions [5, 7].

As Kahlo lived and struggled with chronic pain, painting offered her an opportunity for escape and emotional catharsis [8]. However, as she grew older and weaker, her pain and depression worsened [9]. She became desperate for relief and consumed increasing amounts of alcohol [5, 9]. Her physicians managed her pain with meperidine and morphine, though eventually this therapy became an addiction [3, 5, 9]. As the substance abuse and pain increased, her artistic skill declined [3, 9, 10]. Obsessed with obtaining medical treatment, Kahlo actively sought out physicians who offered surgical intervention for her back pain [3, 7]. During her lifetime, she underwent more than 30 surgeries on her spinal column in both the United States of America and Mexico [3, 8]. Tragically, her physical pain could not be alleviated and instead served as a trigger to the painful memories of a volatile marriage and failed pregnancies [3, 11].

In her lifetime, Kahlo experienced numerous miscarriages and at least three therapeutic abortions. Out of love for her husband Diego Rivera, Kahlo tried repeatedly to conceive a male child. Unfortunately, the streetcar accident had rendered her body unable to support a pregnancy. Unable to carry a child to term, Kahlo created works exploring themes of infertility in a manner that shocked many of her contemporaries. In the painting *Henry Ford Hospital* (1932), for example, Kahlo shows her body lying on a hospital bed—naked and hemorrhaging after a miscarriage and tethered to a stillborn fetus and objects symbolizing the anatomic structures of reproduction. Her emotional pain is evident from the tear falling down her face and the amount of blood. Her isolation is conveyed by the barren landscape surrounding her hospital bed. Though numerous industrial buildings are observed in the distant landscape, Kahlo utilizes their remoteness to represent the literal and figurative distance between Rivera and herself—he was working on a mural in Detroit while she suffered the miscarriage alone at the hospital.

Another evocative painting is *My Birth* (1932), which draws on painful memories of a miscarriage and the death of her mother. Kahlo structures the painting with elements from the *ex voto* tradition, in which a near-tragedy event is illustrated along with the religious figure intervening protectively. In this painting, however, Kahlo recounts her birth not as near-tragic event but simply as a tragic event. No family members or friends are present to support her mother, suggesting her birth is unwelcome. She paints herself emerging from her mother's body as a stillborn child, suggesting to the observer that her failing health began on the day she was born. Having lived a life of pain and disillusionment in health and marriage, Kahlo may have retrospectively deemed her entire life as worthless.

Kahlo perceived her infertility as a failure in her role as a woman and a wife in Mexican society. Unfortunately, her marriage suffered for reasons beyond her infertility. Kahlo experienced severe mental anguish during her marriage due to Rivera's numerous extramarital affairs with artists, models, actresses, and photographers. Early in her marriage, Kahlo tried to ignore the affairs; she believed Rivera would only seek short-lived, casual liaisons. But Rivera's paramours would include Kahlo's own sister Cristina. The discovery of Rivera's and Cristina's betrayal devastated Kahlo and she ceased to paint for several months. When she did begin to paint again, her anguish is clearly evident. In the painting Memory (1937), Kahlo communicates emotional pain by portraying her body with a gaping wound in the chest and her eviscerated heart lying on the ground, hemorrhaging blood. As Kahlo biographer Hayden Herrera notes, "the greater the pain she wished to convey-especially pain caused by rejection from Diego-the bloodier Frida's selfportraits became" [7]. In the painting Self-portrait with Cropped Hair (1940), Kahlo reflects on her marriage and divorce from Rivera and the emotions fueling her pain: desolation, devastation, and defeat. Unlike previous works in which Kahlo adorns herself with colorful clothing and beautiful jewelry, she now wears an ill-fitting dark suit, implying a renunciation of femininity. With a pair of scissors in her right hand, Kahlo completes the transformation by cutting off her beautiful long black hair.

In Kahlo's works, we observe the dehumanizing effects of her physical and emotional pain. She exposes her physical injuries and emotional suffering so that we may understand her life and challenges. Yet, among the many dozens of paintings in her body of artwork, Kahlo never painted the streetcar accident that wounded her teenage body. According to Herrera, "[t]he accident was too 'complicated' and 'important' to reduce to a simple comprehensible image" [3]. While memories of the accident were too traumatizing for Kahlo to revisit, she found strength and catharsis in painting the other painful memories of her life. The depiction of physical and emotional pain in the artworks by Kahlo has not gone unnoticed in the health care community. For example, a New York psychologist uses Kahlo's artwork in therapy sessions to help women talk about their experiences of emotional and physical trauma such as infidelity, violence, and infertility [12]. The experience of pain and the damage done by it can be palpable in Kahlo's work. The hope of the author is that Kahlo's work will empower more patients to talk about their own pain. Frida Kahlo's life and artwork can serve as a resource for physicians who want to better comprehend the experience and dehumanizing consequences of pain. Her paintings are a medium to visualize pain and the effect of pain on the human condition. We witness the suffering, grief, and doubt in Kahlo's paintings; through them, we can contemplate the experience of pain from the perspective of the patient. Patients living with pain are acutely aware of their bodies in ways that healthy people may not be. Pain can be discernible and persistent as well as dynamic and indefinable. Pain, moreover, can bring about a transformation in a person that manifests both physically and mentally. Living with pain can have a paralytic effect on a person's goals and dreams, in addition to family, marriage, and career. Though the practice of medicine often focuses on diagnosis, treatment, and education, the role of the physician demands much more. By understanding pain as a complex phenomenon that affects many aspects of life, we as physicians can fulfill our role to comfort and heal.

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entitled "Frida Kahlo—The Forgotten Medical Student." Readers can follow him on Twitter at @AnteloMD.

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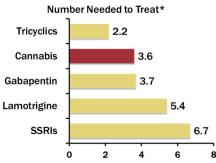
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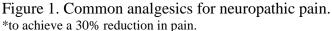
OP-ED

Medicinal Cannabis and Painful Sensory Neuropathy Igor Grant, MD

Painful peripheral neuropathy comprises multiple symptoms that can severely erode quality of life. These include allodynia (pain evoked by light stimuli that are not normally pain-evoking) and various abnormal sensations termed dysesthesias (e.g., electric shock sensations, "pins and needles," sensations of coldness or heat, numbness, and other types of uncomfortable and painful sensations). Common causes of peripheral neuropathy include diabetes, HIV/AIDS, spinal cord injuries, multiple sclerosis, and certain drugs and toxins. Commonly prescribed treatments come from drugs of the tricyclic and selective serotonin reuptake inhibitor (SSRI) antidepressant classes, anticonvulsants, opioids, and certain topical agents. Many patients receive only partial benefit from such treatments, and some either do not benefit or cannot tolerate these medications. The need for additional treatment modalities is evident.

Animal studies and anecdotal human evidence have for some time pointed to the possibility that cannabis may be effective in the treatment of painful peripheral neuropathy [1]. Recently, the Center for Medicinal Cannabis Research (CMCR) at the University of California [2] completed five placebo-controlled phase II clinical trials with smoked or inhaled cannabis [3-7]. Another study reported from Canada [8]. Patients included people with HIV neuropathy and other neuropathic conditions, and one study focused on a human model of neuropathic pain. Overall, the efficacy of cannabis was comparable to that of traditional agents, somewhat less than that of the tricyclics, but better than SSRIs and anticonvulsants, and comparable to gabapentin (see figure 1).





Number needed to treat (NNT) = 1/(E-P), where E is the proportion improved in experimental condition and P is the proportion improved on placebo. Example: If 60% "improve" (according to a given definition) in the experimental condition, while 30% "improve" in the placebo condition, then NNT = 1/(.6-.3) = 3.3. Data adapted from Abrams et al. [3] and Ellis et al. [4].

The concentrations of tetrahydrocannabinol (THC) in these studies ranged from 2 to 9 percent, with a typical concentration of 4 percent resulting in good efficacy. Side effects were modest and included light-headedness, mild difficulties in concentration and memory, tachycardia, and fatigue. Serious side effects (e.g., severe anxiety, paranoia, psychotic symptoms) were not observed. Mild cognitive changes resolved within several hours of drug administration.

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While these were short-term trials with limited numbers of cases, the data suggest, on balance, that cannabis may represent a reasonable alternative or adjunct to treatment of patients with serious painful peripheral neuropathy for whom other remedies have not provided fully satisfactory results. Because oral administration of cannabinoids (e.g., as dronabinol, marketed as Marinol) can result in inconsistent blood levels due to variations in absorption and first-pass metabolism effects, inhalational (or potentially sublingual spray, e.g., nabiximols, marketed as Sativex) administration remains preferred to oral administration.

Cannabis as a smoked cigarette, while demonstrating efficacy, poses a number of challenges, inasmuch as it remains illegal under federal law, even though it is permitted in an increasing number of jurisdictions on physician recommendation. Figure 2 (see next page) provides a schematic approach for physician decision making in jurisdictions where medicinal cannabis is permitted [9].

This decision tree suggests key points that a physician should consider in making a determination. In the case of a patient assumed to have persistent neuropathic pain, the first determination to be made is that the patient's signs and symptoms are indeed consistent with a diagnosis of neuropathy. Assuming a patient does not respond favorably to or cannot tolerate more standard treatments (e.g., antidepressants, anticonvulsants) and is willing to consider medicinal cannabis, the physician proceeds to compare risk and benefit. Among these considerations is whether the patient has a history of substance abuse or a serious psychiatric disorder that might be exacerbated by medicinal cannabis. Even the presence of such a risk does not necessarily preclude the use of medicinal cannabis; rather, coordination with appropriate substance abuse and psychiatric resources is necessary, and, based on that consultation, a risk-benefit ratio can be formulated. In patients for whom the ratio appears favorable, the physician should discuss modes of cannabis administration including oral, smoked, or vaporized. Once risks and benefits are evaluated and discussed with the patient, cannabis treatment may commence as with other psychotropic medications, with attention being paid to side effects as well as

efficacy. Attention must also be paid to possible misuse and diversion, which can then trigger a decision to discontinue the treatment.

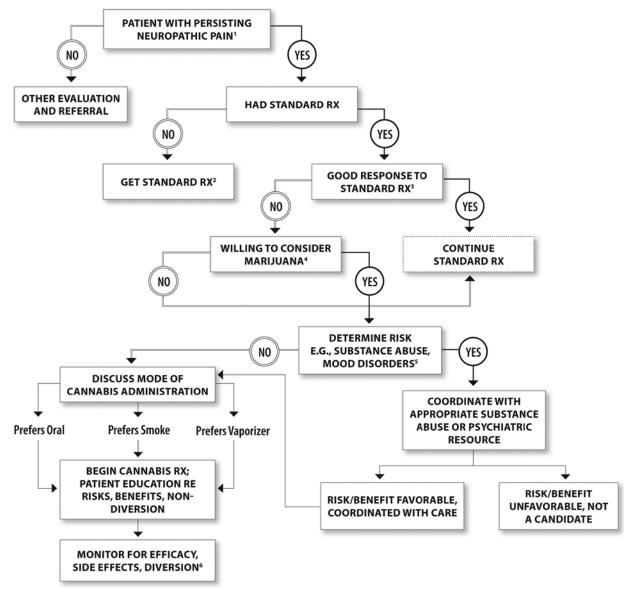


Figure 2. A decision tree approach for physicians who may be considering recommending medicinal cannabis to a patient (from Grant et al. [9]). Key

- 1. Daily or almost daily pain with typical neuropathic characteristics for at least 3 months; affects life quality.
- 2. Standard Rx = e.g., antidepressants, anticonvulsants; opioids; nonsteroidal anti-inflammatory drugs.
- 3. For example, at least 30% reduction in pain intensity.
- 4. Consider past experience, possible past history of side effects; willingness to smoke.
- 5. Determine history of substance abuse. If yes, or at "high risk" of aberrant drug behavior; proceed with close observation; possibly coordinate with substance abuse treatment program.
- 6. Efficacy = at least 30% reduction in pain intensity.

In summary, there is increasing evidence that cannabis may represent a useful alternative or adjunct in the management of painful peripheral neuropathy, a condition that can markedly affect life quality. Our society should be able to find ways to separate the medical benefits of making a treatment available to improve lives when indicated from broader social policy on recreational use, marijuana legalization, and unsubstantiated fears that medicinal cannabis will lead to widespread cannabis addiction [10-12].

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Suggested Readings and Resources

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Virtual Mentor

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