The term “chronic benign pain” contains a contradiction in terms. If chronic pain is debilitating enough to compel patients to seek medical relief, then it is hardly benign. Chronic “idiopathic” pain is an equally problematic term. It implicates what medicine cannot explain, not that the pain is not there. Explanation or not, chronic pain patients besiege American medicine, with a recent study estimating that 31% of the adult US population suffer from chronic pain, most commonly lower back or osteoarthritic pain [1].

Humans hurt in so many ways, and chronic pain is a nasty business, both for the sufferer and the prescriber. It takes empathy, acumen and judgment to diagnose properly the source of a patient’s pain. When a source cannot be found, it takes a leap of faith on the physician’s part to grant that the patient complaining of pain in the absence of demonstrable objective findings — or pain out of proportion to the clinical findings — has “real pain” worthy of the doctor’s attention and care. Yet, clinical populations are replete with sufferers of headache, back pain, arthritis, gastrointestinal distress, muscle soreness and other forms of pain — afflictions as diverse as the sufferers and their abilities to describe the ways they hurt. Lucas cautions of a multitude of chronic pain types, “many of which are not clearly understood” [2].

Many somatic therapies — specifically medications — bear the Federal Drug Administration’s (FDA) imprimatur permitting their legal prescription. Sometimes they work; sometimes they do not. Nonsteroidal antiinflammatory agents, opiates, anticonvulsants, tri-cyclic antidepressants and corticosteroids are some of the classes from which analgesics are chosen [2]. With sedation, weight gain, cardiac toxicity and gastrointestinal bleeding among the many potential complications associated with these drug classes, their side effect profiles are potentially noxious.

With a five-millennium history of use throughout the world, including a century when it was part of the official American pharmacopeia, cannabis — or medical marijuana (MM) — has a pedigree longer and more distinguished than such herbal-derived pharmaceutical staples as digitalis, colchicine and quinine [3]. Why cannabis among the several classes of drugs that contain both legitimate and illegitimate members has been singled out in the US for special vilification seems to have to do with hysteria whipped up by the popular and the movie industry in films like “Reefer Madness” (1936) that asserted “marihuana” (sic) — caused depraved behavior and insanity [3,4]. In addition, western and southwestern legislators, associating the drug with migrant workers and immigrant Mexicans who purportedly committed criminal acts under its influence, pushed for taxes mid-20th century on its use. It was removed from the US Dispensatory in 1942, and in 1970, even as casual recreational use was exploding in the general population, the federal government branded cannabis with Schedule I status, a designation that declared it to have no medical value whatsoever [3]. This signification has made it astronomically harder for drug companies to develop cannabis-based medications and seek authorization of them through the customary FDA protocol process used to legitimate all American prescription pharmaceuticals. Multiple investigators cite a growing body of literature attesting to MM’s benefit against refractory neuropathic pain in conditions like multiple sclerosis and rheumatoid arthritis, peripheral neuropathy in HIV/AIDS and cancer-related pain [2,5,6]. Some even assert that it is immoral for physicians to deprive their patients of a potentially helpful treatment like MM. “Patients have a right to all beneficial treatments,” state Clark et al., “and to deny them this right violates their basic human rights” [7].

Ironically, if mainstay opiates are compared to fringe cannabis for lethality risk and addiction potential, cannabis is far safer. Lethal respiratory suppression by cannabis has never been reported, and there is no phenomenon like the current epidemic of prescription opioid-related deaths attributable to cannabis. Moreover, the endocannabinoid system, not yet discovered in 1970 when cannabis was officially demonized, has become a new frontier for novel analgesic development. Declaring the system “a unique opportunity to develop multitarget analgesics,” Maione et al. describe what they call the “endocannabinoidome,” a “whole system of endogenous chemical signals potentially involved in pain and inflammation” that includes a host of endocannabinoids and endocannabinoid-like mediators with both direct and indirect effects on pain modulation and homeostasis [8]. Botanically derived 9-delta-tetrahydrocannabinol (THC) acts upon this system. Next to THC, cannabidiol (CBD) is the most well known of the botanical cannabinoids. It does not have psychoactivity itself but modulates the psychotropic effects of THC.

Starowicz and Di Marzo underscore the challenge of distinguishing the analgesic effects of THC from its unwanted psychotropic effects, noting that the “magic bullet” approach of single-cannabinoid agents like dronabinol and nabilone may not be as effective as “multiple-target strategies” [9]. Currently, among commercial pharmaceuticals, only Sativex (nabiximols), with its precise ratio of THC and CBD, uses a multitarget strategy. smoked marijuana, intriguingly, is in a class by itself, delivering dozens of poorly characterized but unique cannabinoids to the brain and body. The synergistic interactions of these many cannabinoids are believed to be more effective for both pain relief and side effect reduction than THC.

Given the “rapid and efficient delivery of THC to brain” via inhalation, smoking cannabis has its advantages compared to parenteral forms of ingestion, with their unpredictable onset of effect and uncertain bioavailability [10]. In contradistinction to usual practice in which doctors select the strength of a medication for a patient, smokers titrate the MM dose to effect, with the twin goals of personally maximizing analgesia and minimizing undesired
psychotropic effects. Vaporized cannabis and sublingual preparations like Sativex avoid the hazards of combustion while enhancing bioavailability and rapidity of onset [3].

Zvolensky branded marijuana use as a “maladaptive coping strategy,” specifically when smokers are using it to “help manage aversive emotional states” associated with their pain experiences [11]. Though unable to predict directionality, his team found in a population study that a history of lifetime chronic pain is associated with an increased risk of current marijuana use. They wrote disapprovingly of patients using it for emotional palliation, even as contemporary models describe pain as much more than a specifically somatosensory phenomenon. While cannabis can be addictive — about 10% of those who initiate use before age 25 become dependent on the drug [3] — the fact of use does not indicate dependence or even abuse in the absence of evidence that it is interfering with social and work goals. By comparison, opiates have a much higher dependence rate and the risk for dependence is omnipresent, no matter what the age of the user. Recent reports suggest that cannabis can work synergistically with opiates to reduce the amount of opiate needed to achieve a given level of pain control [12].

Cannabis can — and should — be prescribed responsibly, which assumes an ongoing therapeutic relationship between doctor and patient. Grant et al. list suggested guidelines from the state of California for MM prescription that include (a) taking a comprehensive pain history and conducting a proper physical examination; (b) promulgating a treatment plan with specific objectives; (c) gaining informed consent and discussing risks and benefits of treatment; (d) periodically reviewing the treatment’s efficacy; (e) seeking consultation from colleagues as appropriate; and (f) documenting the rationale behind the MM recommendation [10].

I do not mean to minimize the dangers associated with cannabis. I do not endorse cannabis mills such as those described in Colorado in which physicians may see patients only once, briefly, and send them out their office doors with prescriptions for the MM dispensary next door [13]. I do mean to point out that the consideration of cannabis’ appropriate use for chronic pain cannot — and should not — be contemplated in fastidious isolation from the reality that no perfect, universally legal alternative solutions for dispelling chronic pain exist. Moreover, in increasing numbers of states in which MM has been legalized, physicians who do not come to terms with the reality that their patients are using it are like ostriches with their heads firmly planted in the loam of the hemp patch. Purists can wring their hands while dithering about a broad range of problems associated with cannabis use — early onset and intensified psychotic illness in the susceptible; addiction in 10% of users who start smoking before age 25; inanition syndromes that are not nearly as funny as a Cheech and Chong movie; potential pulmonary pathology. While cannabis can be addictive — about 10% of those who initiate use before age 25 become dependent on the drug [3] — the fact of use does not indicate dependence or even abuse in the absence of evidence that it is interfering with social and work goals. By comparison, opiates have a much higher dependence rate and the risk for dependence is omnipresent, no matter what the age of the user. Recent reports suggest that cannabis can work synergistically with opiates to reduce the amount of opiate needed to achieve a given level of pain control [12].

What should guide the prescriber of anodynes for chronic pain, I believe, is not the specific agent he or she prescribes per se but rather the functional status of the patient while using that agent. Key to evaluating chronic pain is taking the measure of its deleterious effects it on work and relationships. Based on our own research with a series of adolescents whose function failed to improve in an intensive, psychologically based pain rehabilitation program, we have hypothesized that their self-admitted marijuana use has hindered their improvement. With its known potential for dulling motivation and initiating, it could have been the wild card that interfered with these teenagers’ capacity for accepting their chronic pain and working to transcend the limitations pain was imposing upon them. We have become concerned enough about the deleterious effects of any covert substance use that we have instituted routine toxic screens in all entrants to the program so that we can gauge its contribution to our patients’ progress — or lack thereof [14].

In sum, it would be so much easier if there were simple and definitive answers to complex questions about whether physicians should prescribe cannabis for chronic pain. Both proponents and critics call for more randomized controlled studies of cannabis as well as pharmaceutical research and development based upon new understandings of the modulatory role of the endocannabinoid system in pain perception. (Lucas: many chronic pain types, some poorly understood) While advocating for “adequate clinical trials,” the eminently reasonable Grant et al. endorsed MM being “prescribed, dispensed, and regulated in a manner similar to other medications that have psychotropic effects and some abuse potential” [10]. In the absence of simple answers, MM should be available as one more tool at physicians’ disposal for carefully and deliberately building effective analgesic programs for their patients.

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References