

# Opioid Dependence vs Addiction

## A Distinction Without a Difference?

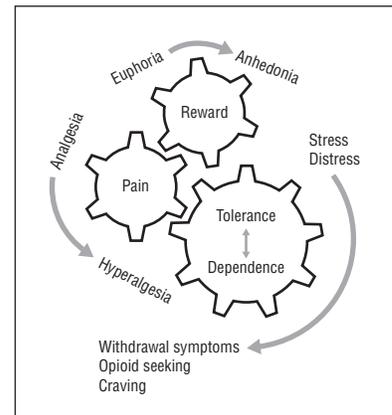
**B**Iologically, opioid addiction can be understood in terms of neuroadaptations that arise when exogenous opioids are taken continuously and long-term.<sup>1</sup> Tolerance and dependence are 2 such central adaptations. Tolerance is the need to increase dose to achieve the same effect, and dependence is the physiologic response either to an uncompensated increase in tolerance or to the withdrawal of a drug.<sup>2</sup> Tolerance may develop for both the euphoric and the analgesic effects of opioids and can be produced by psychological as well as pharmacological factors. Dependence is manifest as withdrawal symptoms (eg, sweating, anxiety, insomnia) that are caused by rebound at central noradrenergic nuclei, and the less well-understood effects of hyperalgesia (increased pain sensation) and anhedonia (inability to feel pleasure).<sup>3,4</sup> Withdrawal hyperalgesia and anhedonia may explain the worsening of pain and mood that is seen during an opioid taper or after detoxification. Withdrawal symptoms are powerful drivers of opioid seeking, which in turn can be induced by factors that change tolerance (**Figure**). Addiction is further defined by aberrant opioid-seeking behaviors that, when persistent, result in irreversible changes in the brain.<sup>1</sup>

Standard drug addiction criteria have long been unsatisfactory when attempting to characterize iatrogenic addiction.<sup>5</sup> For the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders*, tolerance and withdrawal (physical dependence) will be specifically excluded from the diagnostic criteria for substance use disorder that arises during medical drug treatment, so that the diagnosis will be based solely

on aberrant behaviors.<sup>6</sup> For pain patients, drug-seeking behaviors are different from behaviors that are listed by standard criteria and are focused on obtaining opioids from prescribers. Aberrancy in pain patients may include doctor shopping, frequent lost prescriptions, and repeated requests for early prescriptions, while the behaviors listed in the fourth or fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders*, eg, “failure to fulfill major role obligations at work, school or home,” tend to be attributed to pain rather than to addiction. In fact, pain patients who are treated continuously with opioids may not manifest any aberrant behaviors because they are effectively receiving maintenance therapy, which suppresses craving. However, when opioids are suddenly not available, tolerance occurs, or attempts are made to taper, craving and addiction behaviors emerge. Recent teaching has been that this should be thought of as *pseudoaddiction*, a misleading term that suggests that aberrant opioid seeking is predominantly a consequence of inadequate pain relief and should be addressed by increasing opioid dose. The concept of pseudoaddiction implies that opioid seeking ends when an adequate dose is reached, but this is not apparent in the long-term treatment of chronic pain. It is noteworthy that patients are often more willing to diagnose their own addiction than are their providers, who have been taught that addiction to prescribed drugs is rare.

### THE WASHINGTON STATE EXPERIENCE

Washington is the first state in the United States to attempt to limit the opioid doses that are prescribed for



**Figure.** Interdependence of mood, tolerance/dependence, and pain. Even in normal individuals, pain and mood are interdependent, in part through endogenous opioid mechanisms. Individuals who are taking exogenous opioids continuously over the long-term adapt by developing tolerance and dependence. Psychological factors can alter tolerance and thereby induce withdrawal symptoms. For the dependent individuals, the need for more opioids becomes the predominant reaction to stress. Although pain is seen as the primary reason to dose escalate, this pain is augmented by psychosocial stressors.

chronic pain. Rule 2876 was passed by the legislature in 2010 and came into effect in stages between July 2011 and January 2012. Broadly, the rule sets a ceiling (in terms of daily morphine equivalent dose) on the amount of opioid that can be prescribed for chronic (not acute or cancer) pain without consultation with a pain specialist, unless the individual is functioning well on a stable or tapering dose. The legislation is a response to Washington State's high death rates from prescription opioid overdose<sup>7</sup> and aims to offer expert help and education to community clinicians who frequently resort to opioid dose escalation without achieving lasting improvement in pain or function.

As the rule comes into effect, clinicians are beginning to taper high-dose opioid therapy in their patients. In some cases, this tapering

has occurred because the rule has been misunderstood, leading prescribers to taper doses in patients who have been stable for years, resulting in the reemergence of severe pain and extreme anhedonia, both of which are likely to be withdrawal effects. What we have learned from these attempts at tapering doses in patients who have been receiving established therapy for many years is that tapering may destabilize the patients, leaving persistent craving and aberrant behavior in its wake. The opioid dependence that we once believed to be short-lived or easily reversed is sometimes seen to persist as complex persistent dependence for months after a taper. The question is whether to maintain these patients on a regimen of opioids with the usual precautions or to try to taper their doses at least to a safer level.

## CONCLUSIONS

The Washington State experience attests that there are many patients who are currently being treated with high-dose opioids and who are unwilling to taper their opioids despite persisting pain and known risk. These patients are highly demanding to their providers. There are also patients, usually with shorter-term or more intermittent use, who are motivated to taper, and their doses can be tapered relatively easily either in an outpatient or an inpatient setting.<sup>8</sup> For the recalcitrant cases, understanding dependence and accepting that this dependence demands therapy similar to addiction maintenance treatment, in-

cluding regular and continued counseling and monitoring, will go a long way toward being able to treat the patients without removing a class of medications on which they have become dependent. In light of new evidence that is revealing the limitations and dangers of high-dose long-term opioid therapy, we can and must question the wisdom of providing such therapy in the first place. However, for the patients who are already affected, the solution cannot lie in abandoning them as they struggle with established dependence.

Dependence on opioid pain treatment is not, as we once believed, easily reversible; it is a complex physical and psychological state that may require therapy similar to addiction treatment, consisting of structure, monitoring, and counseling, and possibly continued prescription of opioid agonists. Whether or not it is called addiction, complex persistent opioid dependence is a serious consequence of long-term pain treatment that requires consideration when deciding whether to embark on long-term opioid pain therapy as well as during the course of such therapy.

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