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## Review

# Pain management in heroin and cocaine users

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## ABSTRACT

Drug addicts often seek medical help for pain. Numerous fears and beliefs may hinder the recognition, evaluation, and management of pain in addicts. Nevertheless, the same fundamental principles apply to these patients as to other patients in terms of pain evaluation, analgesic selection, and dosage adjustment. Clarity of the medical prescription is crucial. Specific points that require attention in addicts include the effects of the abused drugs on the nociceptive system, the nature and amount of abused drugs, concomitant nondrug addictions, co-morbidities, and the nature of the pain symptoms. Also crucial is differentiating current abusers from former abusers and from abusers taking replacement therapy, as different management strategies are required in these three situations. Detailed information on the history of drug abuse is necessary to avoid unwanted events (e.g., overdosing or withdrawal syndrome) or an exacerbation of the addictive behaviors. In practice, hospital admission should be avoided to the extent possible. The use of strong opioids should be kept to a minimum (although this important rule may be difficult to follow, for instance in surgical emergencies). The best route of administration and galenic formulation vary with each individual situation but, in general, intravenous administration of strong opioids is highly undesirable. A treatment contract established with the patient is crucial and must indicate the nature of the drug or replacement agent used and the treatments given for pain control.

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## 1. Introduction

Pain is a common reason for physician visits and even hospital admission in drug addicts. Pain modulation differs markedly between opioid addicts and opioid-naïve individuals. A painstaking analysis of the pain must be conducted, and drug prescriptions must be appropriate and monitored closely. The drugs used, as well as any co-morbidities, may lead to serious complications (e.g., cardiac events) with which the physician must be familiar, most notably when anesthesia is required. The challenges raised by the recognition, evaluation, and management of pain in drug addicts require the involvement of multiple professionals in a variety of medical fields. The clinical situations vary, and an important distinction is that of acute pain (e.g., due to trauma or surgery) versus chronic pain.

Here, we will discuss the various situations (illicit drug use, pain patterns) and specific features seen in drug addicts. We will seek

to determine whether prescribing strong opioids to current drug addicts is legitimate and, if it is, under what circumstances. Another important question is whether specific prescription rules exist for former addicts or addicts on replacement therapy. We will confine our discussion to users of heroin and/or cocaine.

## 2. Definition and epidemiology of drug abuse

Drug abuse is an addictive behavior that produces numerous neurophysiological effects. Three phenomena may develop in patients who repeatedly use opioids: tolerance, characterized by a gradual decrease in effectiveness with an increase in the dose needed to obtain a given analgesic or psychodysleptic effect [1–4]; physical dependency (with a transient withdrawal syndrome if the drug use is stopped abruptly); and psychological dependency (with compulsive drug-seeking behaviors that persist after drug discontinuation).

Heroin is by far the leading illicit drug associated with specific medical needs (e.g., for infection or overdosing) [5]. The prevalence of some of the heroin-related complications has been decreased in France by risk-reduction policies such as over-the-counter syringe sales since 1989 and availability of replacement therapy since 1996 [5]. However, the drug-addiction scene changes continuously

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(introduction of new drugs, new combinations, and new methods of procurement). Heroin addicts often abuse several drugs [5]: most of them use stimulants (amphetamines), other strong opioids (cocaine), and drugs that potentiate the heroin high or alleviate the drug craving (benzodiazepines and barbiturates). Many prescription drugs are abused by heroin addicts, such as antiparkinson drugs, antidepressants, glucocorticoids, anabolic agents, and anesthetics.

### 3. Neurophysiology and opioid system in regular users of strong opioids

Addiction and hyperalgesia develop rapidly in users of strong opioids. These clinical manifestations may be related to central-nervous-system sensitization with changes in excitatory neuromediators (glutamate), inhibitory neuromediators (gamma-aminobutyric acid, GABA), and cyclic adenosine monophosphate (cAMP) [6]. When taken repeatedly, opioid agonists bind to the opioid receptors, which are cAMP-dependent [7]. Chronic morphine exposure in rats results in neuronal plasticity events involving an effect of glutaminergic systems on the N-methyl-D-aspartic acid (NMDA) receptors [8]. Major changes in the central nervous system may explain the differences in pain sensitivity between opioid addicts and opioid-naïve individuals [1,9], with the former experiencing opioid-induced hyperalgesia [6,9]. The pain relief provided by opioid use in the short term may be followed later on by a rebound effect. These events are dose-dependent and related to the excitatory neuromediator NMDA [10,11]. During anesthesia, strong opioids are used in combination with the powerful NMDA agonist ketamine to prevent postoperative hyperalgesia. After some time, opioid-exposed individuals become more sensitive to pain. Similar observations have been made in heroin users.

Replacement therapy with methadone or buprenorphine is used to treat opioid dependence. These opioid receptor agonists decrease the use of illicit drugs and diminish mortality and morbidity rates [7]. However, a decrease in the pain sensitivity threshold has been documented in methadone-treated patients [12].

In conclusion, the repeated use of strong opioids results in increased sensitivity to pain with a diminished analgesic response.

### 4. Epidemiology of pain in drug addicts

#### 4.1. Prevalence

The prevalence of pain in drug addicts is difficult to evaluate. Pain due to emergencies (e.g., infection and trauma) is very common. In a study done between 2000 and 2001 in New York State, the prevalence of chronic (> 6 months) moderate-to-severe pain was 37% among 390 patients receiving maintenance methadone therapy and 24% among 531 inpatients in short-term residential treatment facilities [13]. Among these patients with chronic pain, 65% in the methadone group and 48% in the residential-treatment groups reported severe adverse effects on physical and psychosocial functioning. The patients were often also addicted to other substances; for instance, alcohol was used for pain control by 34% of the methadone patients and 51% of the residential-treatment patients. Among patients with chronic pain, those taking methadone were significantly more likely to have been prescribed pain medications than those in residential treatment (67% vs. 52%,  $P=0.01$ ). The prevalence of chronic pain in both groups was considerably higher than reported in the general population (20% of individuals had chronic neuropathic pain in the STOPNAP survey in France [14]). The results also highlight the high prevalence of multiple substance abuse [13].

#### 4.2. Types of pain

The vast spectrum of clinical situations includes trauma-related pain in emergency-room patients; pain due to an injection-site infection or bloodstream infection; pain related to childbirth; pain before and after an emergent or scheduled surgical procedure; and chronic pain related to an active disease or persisting after resolution of a disease. The quality of the initial interaction with the patient is crucial, as it has a lasting effect on the therapeutic relationship. Explanations and reassurance must be given to the patient and a treatment contract should be established immediately. A careful history and physical examination is needed to determine whether treatment with an opioid is appropriate (medical history, use of illicitly obtained and prescribed drugs, body weight, nutritional status, hydration, condition of the peripheral veins).

### 5. Beliefs and behaviors of healthcare providers regarding drug addicts with pain

Physicians and other healthcare providers have their own representations and prejudices regarding pain and behavioral patterns in drug addicts [15]. They may feel the pain is being simulated or exaggerated as a means to obtain drugs or that a regular drug habit or replacement treatment eliminates pain. Another prevalent belief is that opioid therapy is useless because it is not effective in drug addicts. A common concern is that prescribing strong opioids may exacerbate drug craving and dependency, thus increasing the relapse risk in former addicts and creating a risk of overdosing with respiratory and/or central-nervous-system depression. Finally, physicians who specialize in pain control are sometimes viewed as no different from drug dealers.

Healthcare providers involved with treating drug addicts often report considerable concern about possible aggressive or manipulative behaviors. Drug addicts have complex personality disorders characterized by impulsiveness and a risk of physical violence. In addition, pain or any other health-related event may cause psychological decompensation.

Developing a sound patient-physician relationship is therefore crucial. A therapeutic partnership must be established during the first few conversations. The drug addict must be viewed as a genuine patient. Listening is vital, and the physician should build trust by acknowledging the reality of the pain. During each visit, the addictive and psychiatric facets of the patient's situation must receive attention, in addition to the somatic facets. Consequently, drug addicts with pain are best managed by a multidisciplinary team that includes a psychiatrist and any healthcare providers involved with the patient at addiction-treatment facilities.

### 6. Pain in drug addicts: three clinical situations

Situations in which drug addicts seek medical help for pain fall into three main categories [4].

#### 6.1. Current drug addiction

These patients are often addicted to multiple drugs (heroin, cocaine, amphetamines, crack, cannabis, alcohol, benzodiazepines, codeine, and others). Only heroin, cocaine, and crack users are at risk for withdrawal syndromes.

#### 6.2. Drug addict on replacement therapy

Two drugs are used by physicians to treat drug addiction, methadone and buprenorphine.

### 6.2.1. Methadone

Methadone replacement therapy is authorized in France in accredited centers. Methadone is a pure opioid agonist with a slow onset of action (no sudden high) and a long half-life allowing once-daily administration. In methadone-treatment centers, the patients are evaluated and monitored in terms of drug use and psychological status. Methadone also has analgesic effects. It not only activates the opioid receptors, but also antagonizes the NMDA receptors involved in some forms of pain such as neuropathic pain. Very rarely, methadone is used to control refractory pain, in multiple daily doses. In this situation, methadone is helpful for opioid rotation, particularly in patients who are inadequately relieved by high doses of other opioids.

### 6.2.2. Buprenorphine

Buprenorphine replacement therapy can be prescribed in France by any board-certified physician. Buprenorphine is an agonist-antagonist of the opioid receptors. However, a ceiling effect occurs (as seen with the previously used drug Temgesic®) and is consequently difficult to use in some cases when anesthesia must be performed.

### 6.3. Former heroin-cocaine addict

The risk is a relapse into drug abuse, which is higher in patients who still use other substances (e.g., alcohol, tobacco, and/or psychotropic agents) and in those with a poor social support network. Information on the treatment goals and type of analgesic therapy must be given to help support the patient and family.

## 7. The fundamental principles of pain management in drug addicts

Several fundamental principles must be followed when managing pain in a patient currently abusing drugs or taking replacement therapy. Close follow-up is mandatory to detect early symptoms of withdrawal syndrome or overdosing. Treatment with strong opioids may be unavoidable in patients with severe acute pain or during the postoperative period. In patients with chronic pain, however, strong opioids should not be prescribed, given the risk of inducing an addiction. Co-morbidities should be evaluated and the least invasive administration route should be preferred. The dosage should be chosen to produce the best possible risk/benefit ratio. Strong opioids are best avoided, particularly via the intravenous route (which produces a sudden high), and local or regional anesthesia methods should be preferred over general anesthesia [9,16–19].

In current drug addicts who require anesthesia and/or pain control, the dose of analgesic needed is the dose that, when added to the amount of illicit drug used, will produce the required analgesic effect. A clear contract must be established between the patient and healthcare staff [15,19,20]. Hospital admission should be avoided to the extent possible. When admission is required, steps must be taken to prevent a withdrawal syndrome, relieve the pain and anxiety, and inform the patient. Efforts must be made to help the patient understand the need for telling the truth, refraining from using non-prescribed drugs, accepting discomfort when necessary, and refraining from manipulative behavior. When patients receiving treatment for pain obtain illicit drugs and change from one drug or combination to another without informing the healthcare team, complications may develop. Finally, an emergency or nonscheduled admission should not be used as a pretext for drug withdrawal. Drug withdrawal should be prepared and undertaken only with the consent of the patient.

Withdrawal syndrome and overdosing are the two main risks in admitted patients. Withdrawal syndrome may result from the

sudden discontinuation of the substance of abuse or replacement drug, due to a medical event (e.g., injury with immobilization) or to underestimation of the patient's needs. Symptoms of overdosing may occur if the patient uses drugs in secret, the usual consumption of illicit drugs is overestimated, or the amount of replacement drug used is not taken into account when determining the dosage of the analgesics. Staff meetings are crucial to ensure that all staff members follow the same strategy toward the patient when difficulties arise. Good coordination is needed between all the healthcare providers involved (referring physician, hospital ward staff, anesthesia-intensive care unit, addiction unit, and mobile pain-control team if it is involved).

### 7.1. Acute painful condition requiring surgery

#### 7.1.1. Current drug addiction

Patients should be evaluated for hydration, nutritional status, co-morbidities, peripheral venous access sites, and current heroin use (as accurately as possible) [19–23]. The dosage of strong opioid should be equal to the amount needed to avoid a withdrawal syndrome (replacement dose), to which the amount needed to control the pain is added if needed. Among strong opioids, morphine is the easiest to use in anesthesia. Morphine is only half as potent as heroin, but heroin preparations contain only 10 to 50% of pure heroin. To avoid giving an excessive dose of morphine, titration is helpful: the dose needed to avoid withdrawal symptoms and to control the pain is determined by adding 2 to 5 mg of morphine intravenously every 5 min. Once the morphine requirements have been determined, a subcutaneous or intramuscular injection can be given once every 4 h under close monitoring. Peripheral analgesics are added routinely, as well as a long-half-life benzodiazepine to avoid seizures due to benzodiazepine withdrawal, as most heroin users also use benzodiazepines. This combination also potentiates the opioids and prevents anxiety and agitation. In the event of a heroin overdose, there is no time for preoperative preparation, and endotracheal ventilation must be started. Naloxone injection is not used given the risk of sudden withdrawal syndrome.

**7.1.1.1. Preoperatively.** Preoperatively, if no drugs have been taken in the past 3 h, replacement therapy is started (if available) or an equianalgesic dose of morphine hydrochloride (dose equivalent to the amount of illicit drug used) is given, to avoid withdrawal symptoms [21,24–27]. However, as a precaution, the lowest dosage indicated in equivalence tables is used and the patient is monitored very closely (Table 1).

**7.1.1.2. Intraoperatively.** Intraoperatively, local or regional anesthesia should be preferred whenever general anesthesia is not mandatory. Concomitant sedation can be used. Intravenous local anesthetics (lidocaine) can trigger seizures in cocaine users [21,24–26]. During general anesthesia, attention should be given to the risk of cardiac arrhythmia in users of heroin, cocaine, and/or amphetamines. There is an absolute contraindication to use mu-receptor agonist-antagonists and antagonists in heroin users.

**7.1.1.3. Intraoperatively.** Postoperatively, tramadol is easy to use as a continuous intravenous infusion or via the oral route, particularly as it exerts both opioid and adrenergic effects. Strong opioids are best avoided and when indispensable should be given subcutaneously whenever possible [20,21,24–27]. Patient-controlled analgesia is not recommended. Instead, a multimodal analgesic regimen is preferred in order to minimize the dosage of strong opioids (concomitant use of other analgesics, addition of ketamine for 48 h as an opioid-sparing and anti-hyperalgesia agent). Local and regional routes of administration are always preferable. When strong opioids are given intravenously, the preferred method is a

**Table 1**  
Opioid dose equivalencies.

|                      | Ratio                 | Equivalency with oral morphine         |
|----------------------|-----------------------|--|
| <i>INN</i>           |                       |  |
| Dextropropoxyphene   | 1/6                   | 60 mg = 10 mg of oral morphine         |
| Codeine              | 1/6                   | 60 mg = 10 mg of oral morphine         |
| Dihydrocodeine       | 1/3                   | 60 mg = 20 mg of oral morphine         |
| Tramadol             | 1/5 to 1/6            | 50–60 mg = 10 mg of oral morphine      |
| Pethidine            | 1/5                   | 50 mg = 10 mg of oral morphine         |
| <i>Oral morphine</i> |                       |  |
| IV morphine          | 3                     | 1 mg = 3 mg of oral morphine           |
| SC or IM morphine    | 2                     | 1 mg = 2 mg of oral morphine           |
| Oral oxycodone       | 2                     | 5 mg = 10 mg of oral morphine          |
| Hydromorphone        | 7.5                   | 4 mg = 30 mg of oral morphine          |
| SL Buprenorphine     | 30                    | 0.2 mg = 6 mg of oral morphine         |
| SC nalbuphine        | 2                     | 5 mg = 10 mg of oral morphine          |
| Transdermal fentanyl | Variable              | 25 µg/h = about 60 mg of oral morphine |
| <hr/>                |                       |  |
| Agents               | Intravenous dose (mg) | Oral dose (mg)                         |
| Morphine             | 10                    | 30                                     |
| Hydromorphone        | 1.5                   | 7.5                                    |
| Methadone            | 2 (precautions)       | 2–3 (precautions)                      |
| Oxycodone            | 10                    | 20                                     |

Reference data committee of the French Society for Anesthesia and Critical Care (SFAR), Formal expert recommendations, Perioperative management of chronic treatments and medical devices, June 2009 (p. 37.) Some variability exists across published data.

10 mg of IV morphine = 1 mg of epidural morphine = 0.1 mg of intrathecal morphine. INN: International non-proprietary name.

continuous infusion with added boluses if needed. The boluses can be delivered via patient-controlled analgesia if, and only if, a clear contract has been established with the patient and the pump is set to limit the deliverable dose [20,21,24–27]. The oral route should be used as soon as the patient can eat. A withdrawal syndrome may develop within 6 h after the last heroin dose, and the heroin replacement substance should therefore be given every 4 to 6 h.

### 7.1.2. Patients on replacement therapy

In patients on maintenance methadone therapy, the methadone should be continued, even on the morning of the surgical procedure (if surgery is elective). When the oral route cannot be used, an equianalgesic dose of morphine should be given. Patients on buprenorphine replacement therapy should be given strong opioid agonists that displace the buprenorphine from the opioid receptors (remifentanyl, alfentanil, or sufentanil) [20,21,24–27].

Preoperatively, when a strong opioid analgesic is added in a patient on maintenance methadone therapy, the methadone should be continued to prevent withdrawal symptoms. This rule avoids confusion between replacement drugs and analgesics. Methadone-treated patients may develop tolerance to opioid analgesics, and their pain may therefore prove difficult to control, requiring dosage escalation via careful titration. Patients should always be asked about the use of other illicit or prescribed drugs. On the morning of the surgical procedure, the daily dose of the replacement agent should be given, irrespective of the anesthesia technique used. In patients with nothing-per-os orders, morphine should be given subcutaneously or intravenously.

Intraoperatively and postoperatively, the management is the same as in current drug addicts.

Postoperatively, the replacement drug should be continued throughout the hospital stay to prevent a withdrawal syndrome by meeting the basal opioid requirements of the patient.

### 7.1.3. Former drug users

Patients who have stopped using heroin may be abusing other substances such as alcohol or psychotropic drugs. The relapse risk is estimated at 20% and varies with a variety of factors such as the duration of drug use. There is a lifelong risk of dependency. The

same principles apply during the pre-, intra-, and postoperative periods. As a general rule, opioids should be avoided and regional anesthesia methods used whenever possible. There is a preference for using non-opioid analgesics such as clonidine, neuroleptics, and short-half-life benzodiazepines. If morphine is used, evaluation by a multidisciplinary team is in order.

## 7.2. Chronic pain

### 7.2.1. Main principles of chronic non-cancer pain management in rheumatology—role for strong opioids

Strong opioids are not appropriate for the treatment of chronic pain in known substance abusers.

In patients with no history of substance abuse, the use of strong opioids to treat chronic pain should follow a number of rules. Recommendations are available [28–33]. In 1999, a task force of the Pain Section of the French Society for Rheumatology (CEDR) issued recommendations on the use of strong opioids to manage chronic noncancer pain due to rheumatic conditions [28]. A 2009 update of these recommendations has been presented at several conventions and is in the process of being published.

Short courses of opioid therapy can be considered in patients with chronic inflammatory joint disease, osteoporotic vertebral fractures, or inadequately controlled acute pain. There is a recommendation to avoid strong opioids for the treatment of chronic pain. Osteoarthritis is an exception, however, given the good level of evidence: in nine studies (Jadad score  $\geq 4$ ), opioids were found useful in some forms of osteoarthritis pain [30–33]. Thus, opioid therapy may be advisable in selected patients, but only when standard treatments fail to provide adequate relief or are contraindicated, when surgery is contraindicated, or while waiting for joint replacement surgery [34–38].

### 7.2.2. Practical considerations about strong opioid treatment of chronic noncancer pain in rheumatology

In general, and particularly in doubtful cases, advice from a pain clinic should be sought before introducing a strong opioid. The objective of strong opioid therapy should be clarified with the patient: to improve the pain and above all the functional impairments in order to allow the resumption of physical activity [34,38]. Failing this precaution, the treatment will be of limited effectiveness. It is important to evaluate the modalities and criteria for treatment discontinuation [28,35], pain intensity, impact of the pain, relevant patient-related factors, and co-morbidities ([30], [www.npecweb.org](http://www.npecweb.org)). In 2007, a 10-point assessment protocol for opioid use to treat chronic pain was published [39]. The points include a definite diagnosis; a prior evaluation of pain and function; a psychological evaluation (with an assessment of the risk of addiction, which is higher in younger individuals and in patients who take psychotropic drugs, alcohol, cannabis, or other substances); acceptance of the treatment; informed consent; adjustment of the opioid regimen according to the other treatments; regular reevaluations (of pain, function, adverse effects, abuse, and co-morbidities); and management by a physician who keeps abreast of new data on opioid therapy.

### 7.2.3. Warning signs of addiction in chronic pain patients

**7.2.3.1. High-risk populations.** Several risk factors for pain medication abuse have been identified [32,36,40,41]. They include a history of self-medication; eating disorders; abuse of, or psychological dependency, on substances such as alcohol, tobacco, medications, or marijuana; psychopathology; unstable social and economic living conditions; and young age.

**7.2.3.2. Warning signs.** During the treatment, patients should be monitored for signs of psychological dependency such as an

unusual dosage increase in the absence of an exacerbation of the underlying disease; reports of increasing pain severity; prescription of opioids by multiple physicians; failure to show previous prescriptions or reports by the patient that prescriptions or drugs were lost; an unwillingness to switch to another drug or to use generics; a deterioration in social, family, and occupational activities; irritability or anxiety; and sleep disorders [18,35]. The risk of dependency may be greater with injectable or immediate-release forms (sudden high).

## 8. Conclusion

A dependency on illicit opioids raises major challenges regarding the evaluation and treatment of pain, particularly in rheumatology. Drug abusers have complex personality disorders and require specific precautions and safeguards. Measured decisions are particularly difficult to take in emergency situations. However, a number of simple principles are useful for guiding the management of acute situations: unnecessary pain must be avoided, physicians must be familiar with the specific modalities of analgesia and with the symptoms of withdrawal and overdosing, and combinations of nonopioid analgesics should be given preference. We must combat our own reluctance to take substance abusers under our care. A multidisciplinary approach is crucial, if only to share the treatment decision and choices.

For some causes of chronic pain (e.g., chronic low back pain, reflex sympathetic dystrophy syndrome, and fibromyalgia), there are no studies or recommendations to support the use of strong opioids. Patients with these conditions should be educated and offered alternative strategies (including nonpharmacological methods) associated with a lower risk of iatrogenic events.

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FL: conflict of interest with Bristol Myers Squibb (BMS).

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FA declares that he has no conflicts of interest concerning this article.

SP: conflict of interest with BMS, Janssen, and Mundipharma.

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