THE BRITISH PAIN SOCIETY

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Pain and substance misuse: improving the patient experience

A consensus statement prepared by The British Pain Society in collaboration with The Royal College of Psychiatrists, The Royal College of General Practitioners and The Advisory Council on the Misuse of Drugs

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Introduction

This document aims to identify elements of good practice in the management of pain and in the prescription of opioid drugs. It provides non-specialists with appropriate information to assess the needs of and manage pain in patients who are or have previously been substance misusers. The document also gives guidance on models of collaborative working among relevant healthcare professionals involved in the care of patients with pain who are using, or are at risk of using, drugs inappropriately. It therefore aims to improve practice in managing this group of patients with complex needs.

The document particularly addresses the dual challenges of safe use of opioids for long term pain control and the effective management of persisting pain symptoms in the addicted patient. The group recognizes that substance misusing patients will frequently present to hospital for surgery or following trauma. These individuals will need short term pain management in this acute setting and many hospitals have protocols to guide professionals in these circumstances. Key elements of good practice in acute pain management in this population are outlined in section 5.

A cohesive plan for the management of pain has the patient at its centre. Treatment of pain should not impose additional burdens for the patient. Mutual understanding of the type of problems which may develop, and an agreed plan of how such problems may be managed, improves the patient's experience of treatment. Similarly, if concerns are discussed openly with patients misusing prescribed or illicit substances, it is possible to provide effective management of pain safely.

Persistent pain is common and disabling. Treatment with opioid medication will be appropriate for a significant proportion of patients. Professionals caring for these patients need to be aware that these drugs may be used inappropriately and should be able to identify and manage problems if they arise. Patients with pain and a past or current history of substance misuse pose particular challenges when prescribing analgesics. Lack of understanding of relevant pharmacology and concern regarding potential for misuse of prescribed medication can result in pain being inadequately managed in substance misusers.

This document does not attempt to provide prescriptive guidelines for the management of particular presentations, but accepts that pain needs individualised management. The document considers the epidemiology of pain and of substance misuse, relevant neurobiology and pharmacology as well as definitions, legal requirements and therapeutic interventions to inform clinicians and improve practice. It is not within the scope of this document to discuss all substances of misuse. The focus is on commonly misused substances and those with specific relevance to the management of pain. The document examines the issues as they relate to both acute and chronic pain as well as special populations, as each requires different clinical management.

The document is accompanied by an information leaflet supporting patients at risk of substance misuse in making informed treatment choices about pain management. It helps them and their carers recognise problems that may occur and explains what sort of information needs to be given to professionals from whom they are seeking help, to support a safe and effective management plan.

Methods

These recommendations have been prepared by a consensus group of professionals from the fields of pain management and substance misuse. Additional contributions have been made by experts from other relevant disciplines. Research evidence is referenced, where such evidence is available, however the lack of research evidence available to inform this topic is noteworthy. A provisional version of this publication was launched in April 2006. This was circulated to relevant stakeholder individuals and organisations for consultation. Feedback from this consultation has been incorporated by the consensus group into this final version of the document. In accordance with British Pain Society publications strategy, the document will be revised and updated in 2010.

Competing interests

Members of the group have registered all competing interests. This information is available on request from the Secretariat of The British Pain Society.

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Executive Summary

- Both persistent pain and substance misuse are common in the general population. In addition, substance misusing individuals have additional health and social problems which place them at high risk from conditions that may require management of pain.
- Both pain and addiction are complex neurobiological phenomena with significant affective and cognitive as well as social and environmental influences on the perceived experience and clinical presentation.
- The terms tolerance, dependence and addiction have been variously defined and must be clearly understood not only in the context of substance misuse but also when prescribing controlled drugs for pain management.
- An understanding of the pharmacology of commonly misused substances and treatments for addiction underpins effective management of pain in a substance misusing patient.
- A legal framework exists for the control and regulation of drugs that are considered dangerous or otherwise harmful. Many analgesic medications are controlled within this framework.
- Pain, both acute and chronic, is a complex sensory and emotional experience shaped not only by biological but also psychological social and cultural factors and it should be evaluated in this context. Additionally, persisting pain has a number of predictable psychosocial consequences which will need support and management.
- Opioids have been shown in clinical trials to provide effective analgesia in a number of pain conditions. The primary purpose of prescribing opioids is for pain relief but complete relief of symptoms is rarely achievable: an acceptable balance between useful reduction in pain intensity and side effects is the goal.
- Effective opioid therapy may be complicated by development of a hyperalgesic state.
- The prescription of opioids may result in problem drug use. The likelihood of this occurring may be influenced by a number of social, psychological and health related factors.
- Controlled drugs prescribed for pain may be diverted. Prescribers must be aware of this risk.
- The possibility of substance misuse must be discussed with a patient when prescribing opioids. If concerns arise, they must be explored sensitively and steps taken to minimise the risk of inappropriate medication use.
- Addiction is a complex phenomenon which can be adequately conceptualised only if biological, psychological and social aspects are considered. Labels and preconceptions neither explain behaviour, nor give useful ways to address it, and are therefore unhelpful.
- Patients with a history of substance misuse may have had poor previous experiences of interaction with healthcare professionals. Trust is required from both clinicians and patients.
- Comprehensive assessment of both pain and substance misuse (including alcohol), is mandatory when managing pain in the addicted patient.
- There are a number of reasons why individuals who are drug dependent may have greater than expected needs regarding pain management.
- Management of pain in the patient recovering from addiction presents specific challenges. Management of anxiety is key, as relapse may be precipitated by both anxiety and pain. The management of acute pain in these patients needs to include a clear plan for appropriate cessation of therapy and a plan for appropriate support following discharge from hospital.
- Relationships between primary care, specialist pain management services and addiction medicine services need to be clearly defined to support effective management of patients with a history of substance misuse and safe prescription of controlled drugs for pain.

- Patients with a history of substance misuse who need palliative care services should not be denied opioids, when appropriate, to manage their pain. These will need to be given in addition to any drugs they are receiving as substitution therapy. Withdrawal symptoms need to be recognised and managed, particularly when patients are admitted to an inpatient facility. Collaboration with specialist drug services is important when planning discharge and ongoing treatment.
- Pregnant patients receiving opioid substitution therapy will need appropriate analgesia in labour in addition to their opioid maintenance drugs.
- The prevalence of substance misuse and of painful disorders is high in the prison population. Management of this group must be of comparable standard to that provided in the community. Poor sleep, anxiety and distress can exacerbate the experience of pain. Diversion of prescribed opioids is a significant problem. Supervised medication consumption may be difficult in the absence of 24 hour medical care. The use of modified release oral preparations has advantages in this population.

Section 1: Supporting science

1.1 Epidemiology of pain and of substance misuse

Persistent pain affects around one in seven of the UK population i.e. 13%. This equates to about five million adults in the UK. Generally, pain becomes more prevalent as the population ages, although the prevalence of pain in those under 40 years of age is about 17%. Persistent pain is, by definition, long-standing, with sufferers having had pain on average for six years. The most common causes of persistent pain are back pain, arthritis and headache. Persistent pain is frustrating and distressing and can impair function in a number of domains.

The prevalence of drug misuse in Britain is difficult to assess. A British household survey in 2000 reported that 7% of 16 to 74 year olds were dependent on alcohol. In the same survey, 2% of the population was dependent on cannabis alone and a further 1% on other drugs with or without cannabis. The prevalence of alcohol misuse is high. The British Household survey showed that 19% of the population had used alcohol at hazardous amounts on occasions. The British Crime Survey indicates that in 2000, around one-third of those aged 15 to 59 had taken illegal drugs at some time in their lives, with 11% using in the past year and 6% describing themselves as regular users. The most frequently used drug is cannabis, with only one per cent of the population reporting the use of heroin and crack-cocaine. Only a minority of those who try drugs will develop problems and require drug treatment but it is particularly the opioid misusing population that poses challenges to the adequate and appropriate management of pain.

Deprivation and social exclusion are likely to make a significant contribution to the causes, complications and intractability of drug misuse. Deprivation relates statistically to the types and intensities of drug misuse that are problematic. Similarly, poor housing, or lack of access to affordable housing, is another contributory factor in drug misuse. Other important factors include educational disadvantage, criminal involvement, unemployment and low income.

Drug misuse has been called a chronic relapsing condition. While many drug misusers do successfully recover from drug addiction, most make several attempts to do so, lapsing or relapsing into drug misuse in intervening periods.

Drug misusers present with a myriad of other health and social problems, particularly in relation to physical and psychiatric co-morbidity and social care needs. Drug misusers may present with physical health, mental health, social, and criminal problems all of which must be addressed for effective management. Drug users are more likely to suffer from accidental and non accidental injury, and medical complications related to their drug use. This places them at high risk from physical problems that may require analgesia.

1.2 Neurobiology of pain and addiction

1.2.1 Neurobiology of pain

Pain has been defined as “An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” (International Association for the Study of Pain 1996). It is clear from this definition that pain can be regarded as more than a simple sensory perception and that it has affective and cognitive components. From a neuro-behavioural perspective pain ranks alongside thirst, hunger, fatigue and sexual desire as a motivational driver for a change in behaviour.

Acute pain is an expected consequence of tissue injury, is usually self limiting and is relatively easy to treat. In contrast chronic pain is more complex. There is often a mismatch between the subjective report of symptoms and clear causative pathology. In the case of neuropathic pain (caused by damage to or dysfunction of nervous tissue) the pain signals are generated within the nervous system itself. The neurobiological complexity of the perceived pain experience is being increasingly elucidated by functional imaging studies. The cortical pain matrix describes brain regions that receive inputs from the thalamus and that are involved in the cognitive recognition of pain and the co-ordination of associated behavioural and autonomic responses. These regions include primary and secondary somatosensory, insula and anterior cingulate cortices. In vertebrates this is not a one way sensory recognition system but rather the organism can choose to attend to a noxious input or disregard it if other behavioural drives are conflicting. As a result the perception of pain (and consequent behavioural response) is not directly related to the magnitude of the inciting stimulus. The degree to which the central nervous system itself contributes to the perpetuation of chronic pain is the subject of increasing study. In particular the role of descending influences, both excitatory and inhibitory on injury signals in the spinal cord is being defined. It is by means of these descending pathways that the brain can modulate the pain experience.

1.2.2 Neurobiology of addiction

Misused drugs affect the neurochemistry of reward pathways in the brain. This is axiomatic for if they did not they would not be misused. Social and environmental factors play a large part in the vulnerability to and consequences of drug misuse but the acute and enduring effects of the drugs on neurochemistry are the most important mechanism of action.

One core theory of addiction is that misused drugs are able to ‘hijack’ natural drive and motivational systems. The ascending dopamine pathway from the brainstem ventral tegmental area, projecting up through the nucleus accumbens and thence to the frontal cortex is pivotal in this process. Specifically all “addictive” drugs are able to stimulate dopamine release in the nucleus accumbens in animal models. Demonstrating this in humans has been more problematic. To date, neuroimaging studies have shown this effect for stimulants and alcohol, but not yet for opioids. This dopamine pathway appears to signal the presence of stimuli that predict important events, such as the arrival of drug in the brain. The net result is that drug related stimuli are more attentionally demanding and non-drug related stimuli become less important; abstinence is difficult to achieve and harder to maintain. A general down-regulation of dopamine function is thought to underlie the key features of anhedonia and craving in early abstinence from opioids, stimulants, nicotine and alcohol.

Addiction involves multiple other neurotransmitter systems. The endogenous opioid system is directly affected by opioid drugs, but there is increasing evidence of its involvement in the effects of cannabis, cocaine and alcohol. Many drugs also provoke a surge of noradrenaline in early abstinence. This may be the cause of the insomnia that is such a common feature and frequent cause of relapse. Serotonin systems may play a part in some of the mood consequences of drug misuse. Basal serotonin function is also thought to affect impulsivity and possibly the risk of developing drug misuse problems.

1.3 Substance misuse: terminology

The terms tolerance, dependence and addiction have been variously defined and have been developed in the context of drug use in those without pain. Patients, carers, and health care professionals can confuse these terms and misunderstanding can lead to reluctance both in prescribing analgesia and adhering to treatment with controlled drugs. The following pragmatic definitions aim to distinguish between expected physiological consequences of drug administration and the more complex syndrome of addiction.

Tolerance

Tolerance is a pharmacological phenomenon whereby identical doses of a drug induce decreasing levels of effect. Alternatively, higher doses are required to produce the same level of effect. The time-scale of this process varies considerably. Some drugs are able to induce rapid and transient tolerance over a matter of hours; others require prolonged periods of consistent use. Tolerance may occur to both the desired effect of a drug and to its unwanted effects.

Tolerance can occur as the result of many processes. Pharmacological tolerance can be the result of, for example, a decrease in the number of opioid binding sites, acute depletion of the neurotransmitter released by the drug, or by decreased activity in intra-cellular second messenger systems. Behavioural tolerance is also described, where the drug evokes an equivalent pharmacological response, but the individual learns over time how to compensate for the effects of the drug. Tolerance may vary with time and setting. It has been shown that in habitual users of a drug, the body produces homeostatic mechanisms to partially counteract the effects of drugs. These processes are induced by stimuli that predict drug availability. This means that doses of drug that have previously been safely used can result in lethal overdose if taken in unfamiliar circumstances. This is referred to as “context-dependent tolerance”.

Withdrawal

Withdrawal is a syndrome resulting from cessation of, or reduction in, heavy and prolonged substance use (Diagnostic and Statistical Manual of Mental Disorders - Fourth Edition DSM-IV). It is often divided into psychological phenomena e.g. craving, anhedonia and agitation and physical phenomena such as diarrhoea or tachycardia. The distinction between the two terms is somewhat arbitrary as physical withdrawal always has a psychological component. Physiological withdrawal symptoms are often used to diagnose the presence, or absence, of dependence as distinct to the syndrome of addiction. Withdrawal can also manifest when pharmacological antagonists e.g. naloxone are administered to someone dependent on heroin or other opioids.

Addiction

Addiction is a syndrome and pattern of substance misuse. There is more than one set of diagnostic criteria, but most are based on the six key elements of:

salience	drug and related stimuli become increasingly important
conflict	intra-psychic, loss of control over use of the substance
tolerance	as above
withdrawal	as above
relapse	rapid reinstatement of dependent use after a period of abstinence
mood modification	the substance may induce a pleasant positive effect or remove a negative mood state

Both International Classification of Diseases, Tenth Revision (ICD-10) and DSM-IV definitions have diagnostic criteria based on these elements as well as inclusion of an item on continued substance use in the face of harm caused by its use. Diagnosis requires three symptoms from the list to have occurred at the same time in the past 12 months. Neither set of criteria requires that the substance modify mood, merely that it is psychoactive.

Pseudoaddiction

The term **pseudoaddiction** has been coined to describe behaviours such as drug hoarding, attempts to obtain extra supplies, and requests for early prescription or increased dose, in patients whose pain is undertreated. In such circumstances patients may resort to illicit drug use. These behaviours may be mistaken as signs of addiction, but are an attempt to obtain better pain relief. When pain is relieved these behaviours cease.

Dependence

The confusion in terminology between addiction and dependence has caused misunderstanding in the profession as well as the lay public. Clinicians are often confronted by patients reluctant to take medications that may cause physical dependence because this has been confused with addiction.

Dependence on a substance describes the state of requiring the substance to prevent physiological withdrawal. Addiction describes continued drug use despite harm as described above. Dependence may occur in the context of addiction, but can also occur in the non-addicted patient. Physical dependence may also occur following long-term use of a number of drug classes not associated with misuse and addiction including beta blockers, corticosteroids and alpha-2-adrenoceptor agonists.

Problem analgesic use

Problem analgesic use may be described by reference to the patient's thoughts around, and pattern of use of, analgesic substances rather than the quantity used. Where analgesics are being used to regulate affect, rather than control pain this may indicate a problem or developing potential problem. Evidence of craving, increased salience, or other components of addiction are also likely to be indicative

of problems. The cognitions of the patient regarding their drug use are crucial to an understanding of potential problems and these need to be explored with the patient. For example, the patient may be using the medication to remove fear of pain, or unhappiness caused by pain, rather than for pain reduction.

1.4 Pharmacology of substance misuse

1.4.1 Useful definitions (see figure 1)

Agonist

An agonist drug binds to its receptor and fully stimulates the system in a dose-dependent manner. When all receptors are occupied the system is maximally stimulated.

Partial agonist

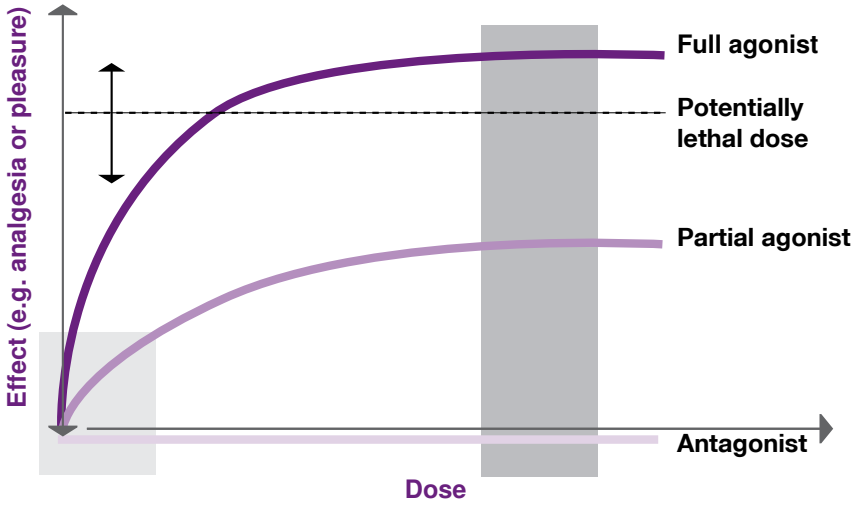
A partial agonist will bind to its site of action and stimulate the system in a dose dependent manner. It will have a lesser effect than a full agonist, so that when all receptors are occupied the system is not maximally stimulated. Partial agonists can act as antagonists in the presence of a competing full agonist (this is the case, for example with the partial agonist, buprenorphine which can precipitate withdrawal in the presence of a full agonist such as diamorphine).

Antagonist

An antagonist binds to its receptor and blocks it from being stimulated. If the system is in an unstimulated state, then this may have no noticeable effect, but if the system is being stimulated by an agonist then this is likely to be displaced and an antagonist effect is produced.

In most cases the level of affinity for a receptor is greatest for an antagonist, followed by a partial agonist, then an agonist. However, this is usually a competitive effect, therefore the blockade produced by an antagonist can sometimes be overcome by large doses of agonist.

Fig 1. A comparison of agonism, antagonism and partial agonism



Small doses
Full and partial agonists behave similarly, with increasing effect as the dose increases.
Antagonists have little effect themselves but block agonist effects

Large doses
Full agonists still have increasing effects which may be over the lethal dose.
Partial agonists have a flat level of effect and block the effect of a full agonist.
Antagonists block the effects of both full and parital agonists.

1.4.2 Pharmacology of specific drugs

A full description of the pharmacology of all drugs with misuse potential is beyond the scope of this document. The drugs described below are selected because they are common, have important implications for persistent pain and its treatment, or both. It is increasingly common to encounter polydrug use and this should be considered when taking a drug history.

Opioids

The term opioid describes all substances active at the opioid receptor: synthetic, endogenous or exogenous. All misused opioids are agonists at the mu opioid receptor. Many are also agonists at the kappa and delta opioid receptors. Exceptions include buprenorphine, nalbuphine and pentazocine. Buprenorphine is a partial

agonist at the mu receptor and antagonist at the kappa receptor. Nalbuphine and pentazocine are both kappa agonists and mu antagonists, although this is only a weak effect of pentazocine. Mu opioid agonists have indirect effects that increase dopamine release in the meso-cortico-limbic system and suppress noradrenaline secretion in the locus coeruleus. The subjective effects of opioids are described as a feeling of calm and relaxation with a sense of being removed from ones environment and free from distress. Care should be taken when prescribing buprenorphine or nalbuphine to patients already opioid dependent as both may provoke acute opioid withdrawal.

All opioid medicines are potentially subject to misuse. In addition to drugs such as pethidine and morphine, misuse may occur with many other preparations including tramadol, buprenorphine, codeine, and dihydrocodeine. Nalbuphine is an injectable opioid that has gained particular popularity amongst bodybuilders who use it to reduce the pain associated with weight training.

The classic symptoms of shivering, goosebumps and runny nose that make up the "cold turkey" of opioid withdrawal are a direct result of the release of chronic opioid suppression of the noradrenaline system. A surge of noradrenaline is released into a supersensitive system causing what is often termed the "noradrenergic storm" of withdrawal.

Cocaine

Cocaine, and crack (the free amide base of the cocaine salt), are inhibitors of the dopamine reuptake pump. They have similar, but lesser, effects on noradrenaline and serotonin reuptake and also block sodium channels. Cocaine and crack differ only in their pharmacokinetics. Subjectively, users describe elation, increased energy and confidence. Withdrawal is characterised by depression, anxiety, malaise, dysphoria, insomnia and craving.

Amfetamine and derivatives

Amfetamine differs from cocaine in that as well as acting as a reuptake inhibitor it directly stimulates the release of dopamine from the presynaptic neurone. The effects of amfetamine are described as similar to cocaine.

The withdrawal syndrome is characterised by depression, anergia, agitation, irritability and craving. There is a small but significant risk of serious depression with suicidality developing some days later.

Amfetamine analogues, like MDMA ('ecstasy'), have very similar patterns of actions with differing relative effects on dopamine, noradrenaline or serotonin neurones. Ecstasy has particularly dominant serotonergic effects. While the effects of amfetamine are described as similar to, but harsher than, cocaine, MDMA evokes feelings of heightened warmth and empathy to others and greater awareness of social surroundings.

Ketamine

Ketamine has enjoyed increasing popularity as a drug of misuse. Its effects as a dissociative anaesthetic are related to its ability to induce altered states of consciousness, often referred to as the "K-hole". Users describe this as an experience of altered reality or deeper understanding. As far as is currently known, the main pharmacological effect is antagonism of glutamate at the NMDA receptor. There is also evidence of some effect in the dopamine, noradrenaline and serotonin

systems. Dependence has been described occasionally and there are reports of compulsive use, tolerance and drug seeking behaviour but no documented withdrawal syndrome. The adverse cardiovascular and psychotomimetic effects of the drug and the propensity to induce psychotic relapse or induce schizophrenia in susceptible individuals has led to the recent control of Ketamine under the Misuse of Drugs Act 1971.

Ketamine is known to have analgesic properties but the evidence for its use in the management of persistent pain remains speculative.

Cannabis

Cannabis is widely used. Most users are "recreational", but surveys also reveal that about 10-20% of patients attending pain clinics self administer illegally obtained cannabis for symptom relief. As a plant compound, cannabis has a rich pharmacology with multiple psychoactive ingredients; the two most important being delta-9-tetrahydrocannabinol (Δ9-THC) and cannabidiol. The exact composition of substances obtained from cannabis plants varies considerably between plants and preparations. The usual mode of administration is by inhalation of combusted materials, a practice which carries well known risks to health.

Two cannabinoid receptors (CB1 & CB2) have been identified to date. CB1 is expressed by neurones of the central and peripheral nervous systems and CB2 is expressed by immune cells. The CB1 receptor is widely distributed in the brain, with particular concentrations in the hippocampus, cerebellum and hypothalamus.

Cannabis is associated with a large number of effects including analgesia, anti-emesis, appetite stimulation, hypothermia and memory and cognitive impairment, in addition to the well described euphoria or "high". There are considerable concerns that even modest use of cannabis is associated with an increased long-term risk of psychosis and other mental disorders. Evidence suggests that there is a small increase in the incidence of psychiatric illness, especially in those who start using at a young age, with a genetic predisposition and other risk factors for psychosis. There is much stronger evidence that cannabis worsens the prognosis in pre-existing psychiatric illness.

The recent advances in the elucidation of cannabinoid pharmacology has provoked interest in the development of cannabinoids as analgesics. Clinical trials of plant derived cannabinoids have shown analgesic efficacy in multiple sclerosis. However, the risk of psychosis is a considerable barrier to the development of such drugs for routine clinical use. Nevertheless, a number of drug-development strategies which could circumvent the psychosis problems are being actively pursued. The immunosupressive effects of CB2 receptor activation should also be borne in mind

Alcohol

Alcohol acts directly to enhance the effects of the inhibitory peptide gamma amino butyric acid (GABA) at the $GABA_A$ benzodiazepine receptor. It also has an inhibitory effect at the excitatory glutamate NMDA receptor. This produces an additive CNS depressant action. There are numerous additional effects, some of which may be secondary to the glutamatergic and GABA effects. It also has direct effects on 5-HT3 receptors. Desentisation of the GABA system is thought to underlie tolerance to alcohol and cross-tolerance with benzodiazepines. Alterations in function are also seen in the dopaminergic and serotonergic systems.

At low doses alcohol induces a sense of disinhibition but at higher doses motor and cognitive function become impaired. It is the complexity of alcohol's action that

confounds the otherwise potential use of alcohol as an analgesic or anaesthetic; for while it undoubtedly has properties which might be expected to modify pain processing, the effects of intoxication are far more prominent.

If alcohol has been consumed heavily and regularly for more than a few weeks, a withdrawal syndrome may be observed on cessation of drinking.

The psychological consequences of alcohol withdrawal include anxiety, panic attacks, depression, insomnia, and in more severe cases hallucinations, and disorientation and clouded consciousness. Physically the symptoms experienced may be restlessness and agitation, tremor and sweating, and raised pulse rate, blood pressure, and temperature. In more severe cases withdrawal fits may occur.

Benzodiazepines

Benzodiazepines augment the actions of the inhibitory CNS neurotransmitter GABA. Many but not all patients taking benzodiazepines chronically for medical reasons become dependent. However benzodiazepines are also misused recreationally. Sometimes their CNS depressant actions are used to counteract the stimulation caused by cocaine and amfetamines, but they are also used to intensify the effects of other CNS depressant drugs such as opioids, or by themselves, to produce relaxant and disinhibitive effects. The available oral dosage forms are commonly injected.

The pattern of benzodiazepine withdrawal is highly variable between individuals. Many of the symptoms resemble those of anxiety disorder. Symptoms may include anxiety, depressed mood, sleep disturbance, tremor and shakiness, headache, and hypersensitivity to touch and pain. The patient may experience perceptual disturbances. Epileptic seizures may develop.

1.4.3 Pharmacological treatment of addicition

Note: For some misused substances such as cannabis and ketamine, there are no specific treatments for addiction. For others such as LSD and anabolic steroids, a addiction syndrome has proved hard to identify and may not exist. For all, the mainstay of treatment is psychological, but may be augmented by the pharmacological treatments outlined below (table 1).

Table 1 Pharmacological treatments for addiction

Misused substance	Pharmacological treatments for addiction
Alcohol	**Acamprosate** Used in the management of alcohol dependence. Its exact pharmacology is unclear. It may antagonise glutamate NMDA receptor function, possibly through an effect on AMPA receptors. **Benzodiazepines** Commonly used to medicate the acute phase of alcohol withdrawal. Needs caution regarding interaction with other CNS depressant drugs such as opioids or continued alcohol consumption. **Disulfiram** Used to deter alcohol use by blocking the inactivation of a major metabolite of alcohol (acetaldehyde). Acetaldehyde thus accumulates following alcohol consumption which provokes an unpleasant reaction. **Naltrexone** A long acting opioid antagonist used to help maintain abstinence by reducing the rewarding effects (this use is unlicensed in the UK). Opioid blockade with naltrexone must be reversed if opioids are needed for pain control. **Anticonvulsants** Carbamazepine is frequently used outside the UK to treat acute alcohol withdrawal. **Thiamine** No alcohol treatment package is complete without vitamin supplementation to reduce the risk of Wernicke's encephalopathy or Korsakoff's psychosis. This may need to be given parenterally.
Benzodiazepines	**Benzodiazepine substitute prescribing** The long acting diazepam is commonly substituted and then slowly withdrawn. Needs caution regarding interaction with other CNS depressant drugs such as opioids and alcohol.

Opioids	**Opioid substitute prescribing** The mainstay of drug therapy for opioid addiction is substitution with either methadone or buprenorphine. The use of diamorphine as a substitute is currently under review, but is not in common use. Initial doses of substitution therapy should be cautious, initiated only with laboratory confirmation of continued use, with upward titration until the patient is stable and not showing signs of withdrawal. This reduces the risk of accidental overdose and allows daily engagement with the patient. The prescribing of CNS depressant analgesics should be undertaken with caution in these patients. The partial agonist action of buprenorphine may effectively antagonise the analgesic effects of full agonist opioid analgesics. **Lofexidine** Used in acute management of opioid withdrawal. As an α2-noradrenergic agonist its actions are to decrease the over-secretion of noradrenaline and so damp down the typical "cold-turkey" withdrawal symptoms described earlier. Clonidine is a similar drug sometimes still used but with more marked hypotensive side effects. **Naltrexone** A long acting antagonist at the mu opioid receptor. If taken orally, blockade will last for around 72 hours. It is usually used as an aid to abstinence from short acting opioids in those who have already passed through the acute phase of withdrawal. Opioid blockade with naltrexone must be reversed if opioids are needed for pain control.
Stimulants	**Stimulant substitute prescribing** Replacement therapy for amfetamine use is not generally available as the risks of abuse, inappropriate routes of consumption and diversion are high. Some treatment programmes offer prescribed dexamfetamine under close supervision. **Antidepressants** Occasionally used to treat depression after acute stimulant withdrawal. Interactions may occur with medicines prescribed for pain management.

1.4.4 Important drug interactions

Table 2 identifies some interactions that have been described between prescribed medicines used in pain control and common misused substances. The list is not exhaustive and omission of a specific combination from this table does not imply safety.

Note that some patients with a history of substance misuse will be taking **HIV medication** or **medicines for TB**. Many of these interact with a wide range of other medicines and prescribers should check safety with a pharmacist or Medicines Information Centre (contact details inside front cover of BNF) if uncertain.

Table 2 Pain control and subtance misuse: important drug interactions

Pain Medication	Substance of misuse	Effects
Carbamazepine	Methadone or buprenorphine	Accelerates methadone or buprenorphine metabolism. May cause withdrawal and require a dose increase.
NSAIDs or aspirin	Alcohol	May increase gastrointestinal bleeding.
Opioids	Alcohol	Additive CNS depressant actions.
	Benzodiazepines	Additive CNS depressant actions.
	Cannabis	Use with care. One study suggests cannabis can potentiate CNS depressant effects of opioids.
	Opioids	Prescribed opioids will have additive CNS depressant actions with street-derived opioids. Avoid buprenorphine or nalbuphine as analgesics in patients dependent on illicit opioids as it might precipitate withdrawal symptoms.
Paracetamol	Alcohol	Possible association with increased hepatotoxicity in alcoholics.
Phenytoin	Alcohol	Chronic heavy intake of alcohol may accelerate phenytoin clearance so that bigger doses are needed.
	Benzodiazepines	Unpredictable. Phenytoin levels may potentially be increased or decreased. Benzodiazepine levels tend to decrease.
	Methadone or buprenorphine	Accelerates methadone or buprenorphine metabolism. May cause withdrawal and require a dose increase.
SSRIs	Ecstasy and amfetamines	Unpredictable. Possibility of additive serotonin effects especially with ecstasy giving "serotonin syndrome". Fluoxetine can also inhibit the metabolism of amfetamines causing toxicity. SSRIs may blunt ecstasy's pleasurable effects. However, SSRIs are often used with MDMA to prolong the effects, reduce the severity of the "mid-week blues" and may also be neuroprotective.
	LSD	May exacerbate "flashbacks" in some individuals. Pleasurable effects of LSD may be reduced.
Tricyclic antidepressants	Alcohol	Additive CNS depressant actions possible.
	Benzodiazepines	Additive CNS depressant actions possible.
	Cannabis	Several case reports of dramatic tachycardia, some requiring emergency intervention.
	LSD	May exacerbate "flashbacks" in some individuals.
	Methadone	Theoretically may have additive effects on the QT interval and cause arrhythmias.
	Opioids	Additive CNS depressant effect possible.
Valproate	Benzodiazepines	Valproate may increase benzodiazepine plasma levels giving rise to CNS depression.
$5HT_1$ agonists ("triptans")	Ecstasy and other amfetamine derivatives	Possibility of additive serotonin effects giving "serotonin syndrome".

For more information see:

Wills S Drugs of Abuse (2nd edition) *Pharmaceutical Press* 2005 ISBN: 0 85369 582 2

Stockley IH Stockley's Drug Interactions (7th edition) *Pharmaceutical Press* 2006 ISBN: 0 85369 624 1

Section 2: Drugs and the Law

2.1 Legal framework

Drugs that are considered "dangerous or otherwise harmful" to individuals or society are controlled and regulated by law. There are three international conventions under which most countries (within their own legislative framework) agree to restrict non-medical use of and trade in certain classes of drugs (United Nations Office on Drugs and Crime):

- Single Convention on Narcotic Drugs, 1961
- Convention on Psychotropic Substances, 1971
- United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances, 1988

In the UK these drugs are controlled by the Misuse of Drugs Act 1971 (the Act) and under the Act drugs are categorized as controlled drugs and their possession, supply and production is prohibited unless a person is specifically authorised to do so. The Regulations made under the Act (the Misuse of Drugs Regulations 2001 - as amended) set out the conditions governing the conduct of those permitted to possess, prescribe, supply or administer controlled drugs.

Many analgesic medications are controlled under the Misuse of Drugs Act 1971 and its Regulations.

2.1.1 Misuse of Drugs Act 1971

The purpose of the Misuse of Drugs Act 1971 is to prevent the misuse (non-medical use) of those drugs controlled by the Act – controlled drugs (CDs) – by establishing a series of criminal offences for their unauthorised, and therefore unlawful, possession, possession with intent to supply, supply, importation and unlawful production.

Drugs controlled under the Act are divided into 3 classes. These classes reflect their relative harm (to individuals and to society) and the maximum penalties which can be imposed in criminal law on persons convicted of any of the offences under the Act, in a descending order of severity, from A-C. The maximum penalties for offences of possession and supply of the main CDs within each class are outlined below in table 3.

Table 3 Penalties for offences of possession and supply of controlled drugs

Drug Class	For Possession	For Supply
Class A – diamorphine (Heroin), Cocaine (Crack), MDMA (Ecstasy), lysergic acid diethylamide (LSD), more potent opioid analgesics e.g. methadone	Up to 7 years imprisonment or an unlimited fine or both	Up to life imprisonment or an unlimited fine or both
Class B – amfetamine, barbiturates, less potent opioid analgesics e.g. codeine,	Up to five years imprisonment or an unlimited fine or both	Up to 14 years imprisonment or an unlimited fine or both
Class C – cannabis, benzodiazepines (and zolpidem) ketamine, anabolic steroids, and gamma-hydroxybutyrate(GHB)	Up to 2 years imprisonment or an unlimited fine or both	Up to 14 years imprisonment or an unlimited fine or both
NB: Any Class B drug in injectable form is treated as Class A. Some Class C drugs are legal to possess – for example, anabolic steroids are Schedule 4 Part II and may be possessed in medicinal form without a prescription		

2.1.2 Misuse of Drugs Regulations 2001 (as amended)

Section 7 of the Act allows for regulations, currently the Misuse of Drugs Regulations 2001 (the Regulations), to be made that authorize and govern activities, including the administration and supply of CDs, otherwise made illegal under the Act. The Regulations identify those who may legitimately handle particular drugs, describe the circumstances in which CDs may be handled and control the purposes for which a particular drug may be supplied. They also regulate where a drug may be produced or supplied. It is a criminal offence to breach any of the Regulations.

The Regulations divide CDs into 5 schedules according to the degree to which their use is regulated. (The schedules are linked to, but are separate from, the 3 classes in which CDs are divided, described above.) Schedule 1 CDs are subject to the greatest restrictions and Schedule 5 the least. Restrictions relate to the manufacture, supply and possession of CDs, as well as safe custody, prescribing (the form and content of prescriptions), dispensing, record keeping, and destruction or disposal.

It is important to remember that, especially in the case of opioid analgesics, the schedule of certain CDs may differ depending on strength, formulation and route of administration of the preparation.

Schedule 1 CDs require a Home Office licence, which is generally only available for carefully controlled scientific purposes.

Sativex is a whole plant medicinal cannabis extract indicated for relief of symptoms of multiple sclerosis (MS). Sativex currently remains a Schedule 1 Controlled Drug. This means that there are no Misuse of Drugs Act or Regulation requirements on the pharmacists to keep records nor on the prescriber to write prescriptions in a form other than that required by the Medicines Act (i.e. a Prescription only Medicine).

The MHRA has issued the manufacturer of Sativex in the UK with a Wholesale Dealers Licence and an Importation Licence, for patients with MS. The Home Office has therefore been able to issue licences for such supplies and has done so by a general licence that covers all doctors who apply on behalf of individual MS patients. Dispensing pharmacists are also covered by this licence, which is triggered by an application by the doctor to the Home Office Inspectorate. Supplies can be made directly from the company's domestic stocks.

Examples of drugs contained in the Regulations are as follows:

- **Schedule 1:** cannabis, ecstasy, LSD
- **Schedule 2:** includes opioids such as diamorphine, morphine and methadone and the major stimulants such as cocaine and amfetamine
- **Schedule 3:** includes buprenorphine, pentazocine and a small number of minor stimulant drugs such as benzphentermine and some benzodiazepines such as temazepam and flunitrazepam
- **Schedule 4:** is subdivided into two parts: Part 1 (CD Benz) contains most of the benzodiazepines, zolpidem and ketamine. Part 2 (CD Anab) contains the anabolic and androgenic steroids together with 5 polypeptide hormones and clenbuterol.
- **Schedule 5:** includes preparations of certain CDs, for example codeine, dihydrocodeine, morphine that are exempt from full control when present in medicinal products of low strength.

Table 4 sets out a summary of legal requirements for drugs in Schedules 2-5.

Table 4 Summary of legal requirements for drugs in Schedules 2-5

	Schedule 2	Schedule 3	Schedule 4(1)	Schedule 4(2)	Schedule 5
Prescription Requirements	Yes	Yes (except Temazepam)	No	No	No
Handwriting Requirements	Repealed except signature				
Record in CD Register if hold/carry stock	Yes	No	No	No	No
Emergency supply allowed	No	No (except phenobarbitone for epilepsy)	Yes	Yes	Yes
Address of prescriber must be in UK	Yes	Yes	No	No	No
Licence required for import/export	Yes	Yes	Yes	Yes unless the substance is in form of medicine and for administration by person to himself	No
Period on prescription	Up to 30 days Good practice guidance	Up to 30 days Good practice guidance	Up to 30 days Good practice guidance	Up to 30 days Good practice guidance	Not specified
Validity of prescriptions	28 days	28 days	28 days	28 days	6 months if POM
Repeat prescriptions allowed	No	No	Yes	Yes	Yes
Private prescriber identification number required on Private prescription	Yes	Yes	No	No	No
Private CD Prescription to be written only on standardized form	Yes	Yes	No	No	No
Private CD prescriptions forms to be sent to relevant agency	Yes	Yes	No	No	No
Pharmacist must ascertain identity of person collecting CD	Yes	No	No	No	No
N.B. Some products contained in Schedule 5, such as codeine and dihydrocodeine, are available "over-the-counter" as Pharmacy Only [P] medicines.					

Adapted by kind permission of the Royal Pharmaceutical Society of Great Britain from *Medicines, Ethics and Practice: A Guide for Pharmacists and Pharmacy Technicians.* Number 30, July 2006

2.1.3 How to write a Schedule 2 or 3 CD prescription

Following a change in the Misuse of Drugs Regulations in November 2005, it is no longer a requirement for a Schedule 2 or 3 CD prescriptions to be handwritten – for example, they can now be computer generated or typed - ***provided*** that the prescriber signs the prescription and the prescription meets the following requirements: Please note that the requirements listed below apply to all prescriptions, whether or they are written by hand or are computer/machine generated.

The prescription must:

- be in ink or otherwise indelible and be signed by the prescriber;
- be dated (since November 2005 a computer generated date has become acceptable);
- except in the case of an NHS or local authority prescription, it must specify the address of the person issuing it. NB The Medicines Act requires that all prescriptions for prescription only medicines (POMs) contain the prescribers' address;
- specify the name and address of the person for whose treatment it is issued;
- specify the dose to be taken;
- specify, in the case of preparations, the form and where appropriate, the strength of the preparation and either the total quantity (in both words and figures) of the preparation or the number (in both words and figures) of dosage units, as appropriate, to be prescribed must be specified;
- specify the total quantity (in both words and figures) of the CD to be supplied. NB The Home Office has expressed the view that a dose of 'as directed' or 'when required' is not acceptable, but 'one to be taken as directed/or when required' is acceptable;
- in the case of a prescription for a total quantity intended to be dispensed by instalments, contain a direction specifying the amount of the instalments which may be dispensed and the intervals to be observed when dispensing.

A Controlled Drug prescription must not be supplied by any person:

- unless the prescription complies with the provisions set out above;
- unless the prescriber's address on the prescription is within the United Kingdom;
- unless the supplier is either acquainted with the prescriber's signature and has no reason to suppose that it is not genuine, or has taken reasonably sufficient steps to satisfy his/herself that it is genuine;
- before the date specified on the prescription (It is good practice for the prescriber to specify a start date for the prescription – this may not be the same as the date of the prescription);
- later than 28 days after the date specified.

The two CDs that are licensed for the treatment of opioid dependence are methadone and buprenorphine. The dosage and frequency of dosage used are not the same as those used in the treatment of pain. The aim of treatment of addiction is the reduction of the opioid withdrawal syndrome and for the majority of patients a once a day dosage regimen is adequate to suppress this. However, it needs to

be recognised that such a regimen is not adequate for the treatment of pain. A few drug misuse patients may be receiving prescriptions for diamorphine, but this is still rare. The prescribing of diamorphine for the treatment of addiction is only permissible if the prescribing doctor has been issued with a license from the Home Office. This differs from the regulations governing the prescribing of diamorphine for pain.

In England the NHS prescription form FP10 (MDA) is used for instalment prescribing of CDs by treatment centres and General Practitioners (GPs). A maximum of 14 days supply of any Schedule 2 CD, buprenorphine, and diazepam can be prescribed for the treatment of addiction using this form. In Wales two types of NHS prescription form are used for the treatment of substance misuse by instalment: WP10 (MDA), issued by GPs and WP10 (HP) Ad, used principally by drug treatment centres. Up to 14 days supply of drugs listed in Schedules 2 to 5 of the MDRs will be reimbursed. In Scotland, NHS prescription forms HBPB (A) and HBP are issued by drug misuse centres and hospitals and can be used to prescribe, in instalments, any drug used in the treatment of addiction. GPs may prescribe by instalment on forms GP10.

The maximum period of treatment allowed on the NHS installment prescription form FP10MDA is 14 days

2.2 Emergency prescribing/out of hours supply/prescribing

Emergency prescribing/supply of CDs in the general hospital in the acute medical situation is covered by the regulations and protocols relating to CDs.

A more contentious issue is the prescribing/supply out of hours in Accident and Emergency Departments (AEDs). It is recommended that patients known by their treating drug service/ prescriber to be likely to present to AEDs have a joint care plan drawn up with the AED. It is further recommended that patients presenting with a request for drugs without an identified physical need are not prescribed in AED but advised to attend GP or drug services during working hours. A protocol regarding the prescribing/supply of controlled drugs in such circumstances should be in place and jointly owned by the AED and the Specialist Drug Service and known to the staff on the unit.

The addicted patient in pain should not be denied pain control and should be managed as the non-addicted patient in assessment of analgesic need. Advice and information should be sought from the local Specialist Drug Service or prescribing GP if in Shared Care. Corroboration of history can be obtained via urinalysis.

It should be remembered that the addicted patient will have an expectation of immediacy of effect of analgesia and therefore will require information and reassurance.

2.3 Non-Medical Prescribing – Current Position on Controlled Drugs

***Nurse Independent Prescribers*:** are currently able to prescribe twelve Controlled Drugs independently, including diamorphine, morphine, buprenorphine and fentanyl solely for certain specified medical conditions. The specified conditions include transdermal use of buprenorphine or fentanyl in palliative care; use of diamorphine or morphine in palliative care, for pain relief in respect of suspected myocardial infarction, or for relief of acute or severe pain after trauma, including in either case post-operative pain relief.

Pharmacist Independent prescribers are currently unable to prescribe any Controlled Drugs independently (though community pharmacists can sell some Schedule 5 CDs from a registered pharmacy)

Both ***Nurse and Pharmacist Supplementary prescribers*** can prescribe Controlled Drugs under an agreed Clinical Management Plan for a patient in partnership with a doctor.

Patient Group Directions: a number of specified Controlled Drugs can be supplied and/or administered under a Patient Group Direction in certain specified circumstances. The drugs and circumstances are listed in the 2001 Misuse of Drugs Regulations.

Future:

Joint Medicines Healthcare products Regulatory Agency/Home Office Consultations

MLX 336 – Patient Group Directions: This proposes changes to the legislation governing the supply of controlled drugs by nurses and pharmacists working under Patient Group Directions (PGDs) to allow an expansion of the range of CDs that can be supplied and/or administered by nurses and pharmacists. One proposed change is the addition of morphine for palliative care pain relief in respect of suspected myocardial infarct. The consultation period for MLX 336 ends on 20 April 2007 with implementation of agreed changes anticipated late summer 2007.

Public Consultation – Independent Prescribing of Controlled Drugs by Nurse and Pharmacist Independent Prescribers: This consultation seeks views on the proposal to expand the range of CDs that can be prescribed by Nurse and Pharmacist Independent Prescribers to independently prescribed CDs and, in particular, whether nurse and pharmacist independent prescriber should be allowed to prescribe specific Schedule 2 CDs to addicts for the management of their addiction. The consultation period for these proposals finishes on 15 June 2007.

2.4 The Shipman Inquiry - Implications for controlled drug prescribing

The Shipman Inquiry was set up in January 2001, following the conviction of a GP, Harold Shipman for the murder of 15 of his patients. The inquiry focused on the methods used by Harold Shipman to divert, undetected, large quantities of potentially lethal controlled drugs and the reasons it was possible for him to do so for so long without detection. Six Inquiry reports were published. The fourth of these, *The Regulation of Controlled Drugs in the Community*, was published on 14 July 2004. The 4th Report addressed the systems for ensuring the safe and appropriate use of controlled drugs. The Government's response to the 4th Report, *Safer Management of Controlled Drugs* was published in December 2004. The document endorses the recommendations of the Inquiry that the existing systems for management of controlled drugs need to be strengthened to minimize the risks of diversion and inappropriate use whilst acknowledging the need to avoid barriers to effective and timely care of patients requiring controlled drugs to manage their symptoms. In particular, aspects of audit and record keeping, storage and disposal of CDs, prescription writing, and patient information have been reviewed and have been or are in the process of being updated.

Section 3: Clinical Issues

3.1 Current good practice in pain management

3.1.1 Key principles

It is important to recognize that pain, both acute and chronic, is a complex sensory and emotional experience shaped not only by biological but also psychological, social and cultural factors and it should be evaluated in this context. Additionally, persistent pain has a number of predictable psychosocial consequences which will need support and management.

Diagnosis

Acute pain is usually easy to diagnose and the relationship to tissue damage reasonably clear. In the case of persistent pain conditions diagnosis is not always possible. A careful assessment is important to evaluate the biomedical, social, and psychological contributors to the patient's presenting complaint.

Factitious disorders are rarely seen amongst those presenting for management of persistent pain. However, the likelihood of such disorders being diagnosed in error may be more prominent in this group of patients as their complaint is subjective and pain is frequently poorly understood by the non-specialist assessor. It is common for the significance of investigations (which rarely elucidate the mechanisms of persistent pain) to be over-emphasised in comparison to the patient's account. Further, the context of medical encounters, where the patient fears being disbelieved, dismissed, and undertreated, affects both patient presentation and clinician judgement, mitigating against satisfactory understanding of pain.

Progressive conditions

In a proportion of patients the underlying disease will be expected to deteriorate, in both cancer and non-cancer related conditions.

Non-drug interventions should be considered for all patients. Advice on activity and lifestyle should underpin other interventions and the importance of self management emphasised. Physical interventions such as Transcutaneous-Electrical Nerve Stimulation (TENS) or acupuncture may benefit some patients and have some support in the scientific literature.

Pharmacological interventions should be increased to full therapeutic and tolerated doses before switching to a different agent. Pain is a biologically complex phenomenon and there is a rationale for combining drugs with different mechanisms of action. All treatments need to be individualised to specific patient requirements.

Psychological dimension

Pain always has a psychological impact, from anxiety about the cause or implications to frustration and depression at the limitations on the individual's usual roles and satisfactions. Assessment, formulation and intervention using cognitive and behavioural principles can bring about improvements in pain experience, mood, activity level and range (including social involvement and work), and reduced use of health care resources. Cognitive behavioural skills and an understanding of pain are required to be effective, and this work is usually undertaken by a clinical psychologist within a multidisciplinary team, involving particularly medical and nursing personnel and physiotherapists.

3.1.2 Opioids in the management of persistent pain: general considerations

Opioids have been shown in clinical trials to be effective analgesics in a number of pain conditions. They should be prescribed as part of a rehabilitation plan which may include other medical, physical, psychological, social and vocational interventions.

The pain management plan, with goals, aims, and time scales, should be discussed and agreed with the patient (and, where appropriate, his or her carer/s).

The primary purpose of prescribing opioids is for pain relief but complete relief of symptoms is rarely achievable: an acceptable balance between useful reduction in pain intensity and side effects is the goal. This balance must be assessed regularly. Improvement in physical, psychological and social function are secondary outcomes. Good pain relief is marked by improved function in all these domains, and in reduced requests for health and social care interventions. Progress towards each of these should be monitored.

For pain associated with cancer, use of modified release analgesic preparations to provide background analgesia with rapidly acting formulations for breakthrough pain is recommended. In the case of persistent non-cancer pain it is usual to use sustained release preparations only. Pain intensity fluctuates so an opioid dose which provides relief of the most severe symptoms could result in considerable, and potentially dangerous overmedication during periods when the pain is less severe. Patients with non-cancer pain are encouraged to accept that they will have periods of increased symptoms when sustained release opioid preparations are used. Opioids are often prescribed in conjunction with other pain relieving drugs and with non-pharmacological therapies.There are few data in the literature to support the use of particular opioid drugs or preparations for specific pain conditions. The response of patients to different drugs remains largely a matter of trial and error. Drugs should be tried in a sequential manner, with monitoring of therapeutic effect and adverse effects over a period sufficient to allow conclusive comment regarding the efficacy of a given preparation for the individual patient.

There should always be discussion of adverse effects of opioids to be balanced against benefits. Common adverse effects in particular, sedation, sweating, nausea, mood change and constipation should be highlighted. Patients should be made aware of potential long term problems including hormonal dysfunction and immunosuppression. Symptoms and signs of intoxication and withdrawal from opioids should also be discussed. Adverse effects require regular monitoring, and where appropriate, the report of a third party (such as a carer) may be sought. When a prescription for an opioid is first written, patients may be worried about becoming "addicted". It is good practice to address these concerns and to discuss their relevance with the patient, depending upon individual circumstances (see below).

The plan for opioid use also should include a plan for action in the event of possible deviations from the agreed treatment schedule and failure to meet appropriate outcomes.

It is helpful to augment the information given to the patient during the consultation with written or taped material to refer to outside consultations.

The plan for opioid use must include brief screening for past or present history of substance misuse. This may include urinalysis (with appropriate consent) if there is reasonable doubt. The accurate assessment of contemporaneous treatment for addiction is mandatory as many of these treatments have important implications for the management of pain with opioids (see Table 1).

When a patient is started on opioids, it is usual for prescriptions to be issued by a single practitioner who monitors benefits and adverse effects and adjusts the dose accordingly. Close liaison should be maintained with other professionals involved in the patient's care.

3.1.3 Opioid therapy: potential problems

Pain caused by analgesic therapy

- Opioid induced hyperalgesia

  There is a potential for development of a hyperalgesic syndrome following effective opioid administration. The emergence of increasing pain following opioid therapy has usually been assumed to be a phenomenon of pharmacological tolerance. However, there are both preclinical and clinical data to support the development of a state of abnormal pain sensitivity following opioid administration. This may be mediated by:

  - central glutamatergic mechanisms
  - increase in the synthesis of excitatory neuropeptides such as dynorphin
  - descending facilitatory mechanisms arising in the medulla

  The relative contributions of these mechanisms may vary between drugs and routes of administration. It is not clear to what extent these phenomena are important in routine clinical practice but there are important therapeutic implications. An opioid-induced pronociceptive state will be worsened by increasing opioid dose, whereas a patient who has increased pain as a result of tolerance would be expected to improve with further opioid administration.

  This pronociceptive state is difficult to diagnose in practice as, unlike hyperalgesic syndromes associated with neuropathic pain, it is not associated with allodynia. Therefore, someone exposed to opioids long-term either through analgesic treatment or use of illicit opioids is likely to be particularly sensitive to at least some types of pain.

- Medication overuse headache

  Recurring headaches may encourage the frequent use of simple analgesia which can develop into a chronic daily habit. Additionally a state of neuronal hypersensitivity occurs which is exacerbated by further consuming analgesic drugs. The analgesics involved include normal doses of paracetamol, aspirin and ibuprofen as well as over-the-counter multi-ingredient preparations. Daily administration of triptans and the now rarely used ergotamine can also cause this phenomenon. Female migraine sufferers seem to be at particular risk.

The headache caused by analgesia overuse occurs frequently – at least every other day – and can be almost constant in some patients, becoming apparent immediately on waking. The pain may be a dull, generalised headache, or a more intense pain that occurs between doses as the effects of analgesia wane.

This problem is eventually rectified if all analgesia is stopped, but this is not easy to accomplish since intense 'rebound' headaches occur during withdrawal, together with sleep and mood disturbances. The most intense phase of withdrawal can last ten days or more, but useful symptomatic improvement may take several weeks. Patients need support during the process of withdrawal. It has been advocated that antidepressants or anticonvulsants, and a short initial course of steroids may be helpful, but the published evidence to support these interventions is weak.

To minimize the risks of developing analgesia related problems: patients self-medicating with simple analgesics for recurrent headaches or migraine should be advised not to take painkillers every day.

3.1.4 Problem drug use when prescribing controlled drugs for pain

Risk of addiction to prescribed opioids

Although the definition of addiction is well developed, the risk for iatrogenic addiction during opioid treatment for pain in patients without a known history of substance misuse is variably reported. Retrospective and prospective data are available from the literature but the criteria for defining addiction vary considerably between reports. If patients require opioids in the long term, dependency may have no adverse implications for the individual as long as medication supply and compliance continues. The literature suggests that the risk of developing problem drug use is somewhat lower when treating cancer pain than when managing pain of non-cancer origin. However, cancer patients may be reluctant to admit to substance misuse therefore the incidence may be significantly underreported in this population.

The probability of addiction is likely to be influenced by a number of factors. These predictors have not yet been empirically established; however, based on clinical experience, they may include the following:

- Social factors
  - Family history of substance misuse
  - Substance misusers in social network
  - Current victim of abuse
  - Occupational risk
- Psychological factors
  - Major unresolved emotional issues
    - Abuse
    - Trauma
  - Anxiety problems
    - Generalised anxiety
    - Sleep problems
    - Panic
    - Social phobia

- Personality disorders
  - Dissocial
  - Impulsive
  - Borderline
- Extreme low self-esteem

- Other current or previous substance use/misuse including:
  - Benzodiazepines
  - Alcohol

Suspecting misuse or addiction to medication

A number of behaviours may be indicative of problem drug use. Most published accounts of such behaviours are based on clinical observation but the predictive value of these observations in identifying drug misuse has not been validated. Behaviours which may cause concern are summarized in table 5.

Table 5 Some examples of worrisome behaviour in patients addicted to prescribed drugs

- Unsubstantiated report of withdrawal symptoms when further supplies of the drug are refused or the dose reduced
- Simulating an exacerbation of the underlying medical condition if a prescription is refused or dose reduced
- Giving a history of inefficacy or poor tolerance of alternative medicines without misuse potential, or non-pharmacological treatment options
- Asking for prescriptions to be re-issued because of repeated unsubstantiated episodes of prescription loss; claiming that supplies have run out early; altering the quantity or identity of drugs to be supplied on a prescription; approaching a second doctor in order to obtain supplies if the first one refuses
- Stealing medication or prescriptions; buying supplies of medication from illicit domestic sources, from abroad, or via the Internet
- Making threats, or offering bribes, to prescribers or those supplying medication

Diversion

Healthcare professionals have a legal and ethical responsibility to uphold the law and to help protect society from drug misuse. They have a responsibility to prescribe controlled substances appropriately, guarding against abuse while ensuring that patients have required medication available when they need it.

They have a personal responsibility to protect their practice/service from becoming a target for drug diversion.

Diversion can include:

- transfer of prescription drugs from intended recipient to others in pain;
- unlawful transfer of prescription drugs from legitimate to illegal channels of distribution;
- theft from manufacturers or wholesalers;
- theft from pharmacies, hospitals, surgeries, veterinary practices, care homes, hospices;
- "prescription fraud";
- use of over-the-counter or prescription medicines to synthesise more potent drugs with a higher street value;
- use of over-the-counter medicines to augment the effect of prescribed or 'street' drugs i.e. the sedating anti-histamines such as cyclizine, promethazine or dyphenhydramine to produce a 'buzz' with methadone.

There are currently no UK data that describe the extent of prescription drug misuse in the UK.

Avoiding opioid medication misuse

Opioid use may escalate gradually. Patients may not see that this may be problematic. The patient may be aware that their use of opioid is increasing but be afraid to discuss this with their pain team for fear of the prescription being reduced or curtailed. A clear explanation to the patient at the outset of the need to be aware of an emerging problem will reduce this risk. A relationship of trust between prescriber and patient will reassure the patient that developing problems can be discussed safely.

If aberrant drug-related behaviour is suspected, the prescriber will need to discuss concerns sensitively with the patient. Increasing frequency of clinic visits and prescription of small quantities of drug may improve adherence to the agreed treatment plan. Clinicians may be asked to provide replacement prescriptions for drugs or prescriptions that have been lost or stolen. If there are concerns at the start of the treatment plan patients should be advised that lost or stolen drugs or prescriptions should be reported to the police and that documentary evidence of this should be given to the prescriber. If such loss is recurrent it is reasonable to terminate the prescription of opioids.

Aberrant behaviours that appear during therapy must be comprehensively assessed and documented. This alerts future prescribers to the potential for problems. If the differential diagnosis of addiction is made, the patient can be appropriately referred to an addiction specialist for treatment.

3.2 Current good practice in addiction medicine

Like pain, addiction is a complex phenomenon which can be adequately conceptualised only if biological, psychological and social aspects are considered. Labels and preconceptions neither explain behaviour nor give useful ways to address it, and are therefore unhelpful.

Biological aspects of addiction include tolerance, and withdrawal, as previously outlined. These are experienced equally in the context of opioid prescribing for pain and in patients with addiction problems.

Psychological features of addiction include learnt aspects of behaviour, pleasure seeking, and distress avoidance (which can be conceptualised by learning theory). Equally drug use can be seen as an attempt to manage aversive emotions, that can stem from a wide variety of conditions.

Social concerns are a vital component when defining substance misuse or addiction. In the social context where a drug which induces dependence is available in a secure supply, is affordable, and is not sanctioned socially, much of the problematic behaviour associated with substance misuse is not observed. Social aspects influencing substance misuse include economic factors, deprivation, the social milieu, social exclusion, and the experience of reduced opportunities. These problems are usually addressed through social interventions.

Diagnosis

The biological aspects of addiction are also seen in chronic prescribing of opioids for pain. The syndrome of pseudoaddiction mimics that of drug seeking behaviour in addiction. The management of addiction is in principle very similar to the management of chronic pain, and therefore the fine points of diagnosis should take second place to adequate assessment of the biological, psychological, and social factors involved, and the management of these.

Non-drug interventions

Adequate social support is important, the interventions should be tailored according to the particular needs of the patient, whether the support be referral for financial advice, housing advice, or helping with an abusive relationship for example.

Pharmacological interventions

Adequate dosing of replacement opioids is required. With the use of supervised consumption large enough doses of Methadone can usually be prescribed to achieve stability, without concerns about diversion. When abstinence from illegally obtained opioids is achieved, with stabilisation of lifestyle, a planned reduction of the prescribed opioid can be instituted.

Relationships with heathcare professionals

The immediacy of distress reduction experienced by the drug misuser by using their drugs of choice, leads them to an expectation that the correct drug will provide rapid relief, for example from pain. In addiction they may be experiencing high levels of arousal from a number of possible causes which respond quickly to pharmacological interventions, but rapidly require escalating doses for the patient with an addiction problem to experience the same effect. In this context the expectations of patient and pain therapist can be radically different, and the interaction frustrating for both. This can lead to the clinician feeling bombarded by the frustrations of the patient, and the patient being inadequately treated by the clinician, who has anxieties about compounding the addiction problems of his/her patient.

It is most helpful for the prescriber to lay out openly the boundaries of the encounter with the patient. Thus the prescriber can offer clear advice on what are realistic expectations, and what cannot be achieved. Frankness is generally accepted well in this patient group, who often perceive professionals as indirect and consequently insincere.

Patients may well have had poor previous experience of interaction with healthcare professionals, perhaps related to their own pressing needs for distress relief. Tolerance is required from both parties. The clinician may be aware of being beyond their knowledge base in dealing with a substance misusing patient and close liaison with addiction services is helpful. Appropriate training in addiction management for non-specialist clinicians would improve their confidence in supporting and understanding of these clinical challenges.

3.2.1 Assessment

Comprehensive assessment of the patient is important and should include specific consideration of the following points:

- Does the patient have physical dependence or addiction (see above)? Note: Physical dependence is the *expected* outcome of regular administration of certain drugs, in sufficient dosage, over a period of time. It most commonly occurs with opioids and benzodiazepines.
- Does a request for increased dose of drug reflect changes in tolerance or addiction? Tolerance develops with regular consumption. On withdrawal of the drug tolerance is lost rapidly, both to the analgesic and toxic effect.
- If the patient has pain, is the level of analgesia appropriate? Many addicted patients receive inadequate levels of analgesia.
- Sensitive assessment of current drug and alcohol consumption and past history should be obtained irrespective of site of presentation and treatment. **There are no characteristics of the patient with a past or current substance misuse problem that are pathognomonic**. Some features of presentation however, when evaluated within the wider clinical picture may alert the prescriber to potential problems. These are summarized in table 6. Urine analysis should be routine to corroborate any history of drug misuse/addiction or to identify such if suspected but not declared by the patient. If possible this should be carried out before starting treatment.
- The clinician should be aware of barriers to effective assessment. These include reluctance or inability of the patient to declare drug use and reluctance or inability of the clinician to assess drug misuse/addiction.
- It is important to determine whether other treating agencies are involved, including the patient's general practitioner.

Table 6 Features of presentation that may alert practitioner to the possibility of substance misuse

- Cutaneous signs of drug abuse - skin tracks and related scars on the neck, axilla, groin, neck, forearm, wrist, foot and ankle. Such marks are usually multiple, hyper-pigmented and linear. New lesions may be inflamed. Shows signs of "pop" scars from subcutaneous injections.
- Being assertive, aggressive or emotionally labile
- Current intoxication/withdrawal
- May show unusual knowledge of controlled substances.
- Gives medical history with textbook symptoms or gives evasive or vague answers to questions regarding medical history.
- Reluctant or unwilling to provide reference information. May have no General Practitioner.
- Will often request a specific controlled drug and is reluctant to try a different drug.
- Generally has no interest in diagnosis - fails to keep appointments for further diagnostic tests or refuses to see another practitioner for consultation;

3.2.2 National Guidelines

A number of national guidelines is available outlining best practice in the management of the addicted patient. These include;

Drug Misuse and Dependence - Guidelines on Clinical Management. London Department of Health 1999

Evidence-based guidelines for the pharmacological management of substance misuse, addiction and comorbidity: recommendations from the British Association for Psychopharmacology. J Psychopharmacol. 2004 ;18(3):293-335.

Models of care for treatment of adult drug misusers. National Treatment Agency for Substance Misuse 2002

The NHS Improvement Plan: Putting people at the heart of public services. London Department of Health 2004

Methadone and Buprenorphine for the Management of Opioid Dependence – NICE Technology Appraisal Guidance 114 National Institute for Health and Clinical Excellence 2007 http://guidance.nice.org.uk/TA114

None of the above addresses the issue of pain management in the addicted patient (with the exception of the management during labour in the pregnant addict.) All support full assessment for drug misuse across settings and *Drug Misuse and Dependence* (DH) contains advice on AED management, including the

recommendation that ‘doctors should ensure there are clear guidelines available to staff to respond to requests for medication (opioid and non-opioid) and injecting equipment’. The treatment recommendations in the same document are restricted to the management of overdose.

The document *Models of care for treatment of adult drug misusers (2002)* recognises that this population has multiple problems that require effective co-ordination of treatment, that several specialist and generic providers may be simultaneously involved in the care and treatment, that consistency and parity of approach should be ensured nationally and that access to care should be based on individual need not historical arrangements. However the physical treatments of this population are not addressed.

Section 4: Practical solutions

4. 1 Pain control in the addicted patient

4.1.1 Patient needs

There are a number of reasons why individuals who are drug dependent may have greater than expected needs regarding pain relief:

- Compared to those who are not dependent, the presence of a drug misuse syndrome seems to worsen the experience of pain and individuals may have previous experiences of self medication to remove pain and psychological distress
- Drug misusers have a low tolerance of non-pharmacological interventions to achieve pain control
- By nature of their chronically relapsing condition, drug misusers have frequent episodes of intoxication, and withdrawal, which may alter the intensity of the pain experience
- Virtually all forms of addiction are associated with sleep disturbance and this is a well established exacerbating factor in chronic pain
- Depression and anxiety are common features in addiction and these have an important influence on the pain experience
- Drug users are more likely to suffer from accidental and non accidental injury, and medical complications related to their drug use. This places them at high risk from physical problems that may require analgesia.

4.1.2 General guidance

When a known substance misuser presents with a need for analgesia:

- A full substance misuse and medication history should be taken. This can be used to check for drug interactions (see Table 2 and BNF) and to assist with choice of an appropriate analgesic. When assessing the impact of interactions it is also important to ask about medicines which the patient may obtain over the counter, and from complementary medical practitioners or suppliers. It is important to discuss the patient's use of alcohol as this also has specific relevance to the experience of and management of pain (see table 7).

  The accurate assessment of contemporaneous treatment for addiction is also mandatory as many of these treatments have important implications for the use of opioid medication (see table 1).

Table 7 Alcohol and pain: important considerations

- Use of alcohol can increase in response to distress related to chronic pain
- Problems with alcohol intoxication including carelessness with other medication and accidents
- Alcohol related physical comorbidity
- Interactions between alcohol and other drugs
- Risk of respiratory depression (high risk when alcohol, opioids and benzodiazepines used chaotically)
- Use of alcohol correlates with depression and anxiety compounding distress from pain
- Alcohol reduces quality of sleep compounding distress from pain

- Pain symptoms must be properly evaluated including relevant investigations and taking note of potential contributors to the patient's current experience of pain.
- If non-pharmacological interventions are known to have utility for the pain condition described they should be offered to the patient, with a clear explanation of why such interventions are likely to help. Similarly non-opioid medications should be used where supported by evidence, again with clear discussion of the rationale for any drug used.
- Patients already tolerant to a long-term illicit or prescription opioid taken for addiction will derive little analgesic effect from their regular dose. If the patient needs opioid analgesia these drugs will have to be prescribed in addition to any existing prescribed regimen. For those using illicit opioids, prescribed doses must include replacement of the patient's usual opioid consumption.
- There is little published guidance for management of patients who have chronic pain requiring opioid therapy, and who currently exhibit aberrant behaviour which may indicate misuse or addiction, or have a history of substance misuse. Nevertheless, some general principles may be applied:
  - The therapeutic regimen should be selected with the risk of aberrant drug-related behaviours in mind. For example, short-acting opioids (e.g. pethidine) are widely acknowledged to have greater abuse potential than long-acting or sustained release preparations. Also, non sustained release tablets can be more easily crushed and injected. A patient may refuse to consider a transition to a sustained–release preparation. Although addiction may be a possibility, consider also fear, lack of additional coping strategies and true physiologic effect of the drug on the pain, remembering that individual patients may respond differently to different opioids.
  - The prescriber must communicate clearly with the patient about setting reasonable expectations or goals for therapy and about the necessity to frequently assess the progress toward these goals. This must include a regular review of the prescription.
  - The process of building trust between clinician and the patient should include a candid discussion of acceptable and unacceptable behaviour. The results of such a discussion should be written down and given to the patient. This may take the form of a treatment contract although this is not required by law.

- Be aware of the various potential presentations of drug seeking behaviour (see tables 5 & 6). Refer patient to, or seek advice from, a pain specialist or substance misuse specialist at an early stage where appropriate.
- Treatment decisions need to be made in compliance with pertaining laws and regulations.
- Response to treatment including degree of pain control and progress towards agreed goals needs to be assessed frequently.

- There are specific considerations for patients receiving methadone, buprenorphine or naltrexone.

  Methadone

  If an opioid analgesic is appropriate, a non-methadone opioid may be co-prescribed. It is not necessary to "rationalise" the patient's entire opioid requirements to one drug.

  Buprenorphine

  The partial agonist action of this drug (when used as opioid substitution therapy) means that it should not be prescribed as an analgesic to patients receiving full agonists (e.g. methadone, heroin) as withdrawal may be precipitated. Similarly, patients taking high dose buprenorphine as substitution therapy may be relatively refractory to opioids prescribed for analgesia.

  Naltrexone

  This drug is a long-acting opioid antagonist and patients receiving it as therapy for addiction are likely to be refractory to opioid analgesia. In addition, administration of opioid antagonists leads to upregulation of opioid receptors with a consequent period of opioid sensitivity. When opioid therapy is introduced after cessation of naltrexone, careful monitoring will be required. In order to maintain an appropriate level of support for the patient, discontinuation of Naltrexone should be discussed with their drug worker. In cases where there is an urgent need for opioid analgesia this will require continuous infusion to displace naltrexone from the opioid receptors. However the patient will require close continuous monitoring as, once the naltrexone has been displaced, there is a risk of opioid toxicity from the agonist agent.

- Consultation with others involved in the patient's care should underpin management. It is particularly important that the substance misuse team and the patient's primary care team are kept informed of progress with pain management. This is normal good clinical practice, but also supports safe pain management by generating accurate information regarding a patient's current prescribed treatment and minimises the risk of a patient seeking medications from more than one source.

4.2 Patients recovering from addiction

Prolonged substance misuse leads to permanent change in the neural reward circuitry. This gives rise to the potential for reactivation of a substance misuse problem if drugs of misuse need to be prescribed for pain control. This results in considerable anxiety for the patient,

who may underreport his/her symptoms, and concerns for healthcare professionals who may undermedicate pain for fear of inducing relapse. Both anxiety and pain can precipitate relapse in this population so it is important to reassure the patient that their pain will be adequately treated. It may be necessary to manage anxiety pharmacologically. Patients and clinicians need to understand that drug exposure is only one component of relapse and that a careful plan for pain management with involvement of appropriate expertise can facilitate optimal treatment. The management of acute pain in these patients needs to include a clear plan for cessation of therapy and a plan for appropriate support following discharge from hospital.

4.3 Common clinical scenarios

The scenarios presented below are quite commonly encountered. There are no right answers which apply in all similar situations, but the notes below are offered to guide thinking.

I have a patient who I suspect is addicted to her pethidine, which I don't think that she needs. How do I tell? What do I do?

An initial candid, but sensitive, discussion with the patient, airing the prescriber's concerns honestly and allowing the patient to describe hers, may open the door to an attempt at gradual withdrawal. Drug withdrawal symptoms should be described and the need for a gradual dose reduction emphasized. It is helpful if the patient helps to determine the rate of planned withdrawal as this will impart a feeling of control. Alternatively a trial conversion to a different opioid might be a basis on which to attempt withdrawal. It is important to ensure adequate analgesia or the patient will lose confidence in the process. If the patient indicates a willingness to change but is having difficulties adjusting, it may be appropriate to admit the patient to hospital.

Some patients will refuse to take an alternative drug and will not accept even a trial withdrawal. Ultimately it is usually impossible for prescribers to refuse to continue to prescribe analgesia if the patient says it is necessary to control pain. In these situations prescribers should be strict about quantities supplied and avoid dose escalation.

Pethidine is a poor choice of analgesic for long term pain control. Its high lipid solubility and rapid onset of effect predispose to tolerance and problem drug use. The active metabolite of pethidine, norpethidine is neurotoxic and can induce seizures. Pethidine does not produce less muscle spasm than equipotent doses of other opioid preparations and confers no advantage for the management of visceral pain. This is particularly important in the management of conditions such as pancreatitis.

My patient is dependent on oxycodone. How do I wean him off? Should I put him on methadone?

If the patient has continuing pain which responds to the drug, the patient and prescriber should be reassured that dependence is to be expected and can be managed by maintaining supplies and monitoring dose. Dependence becomes problematic if the dose needs to be reduced or the drug stopped, in which case withdrawal symptoms may occur. These should be discussed with the patient and if they occur despite caution in dose tapering, should be actively managed. Towards the end of the dose reduction it may be helpful to introduce a weak opioid drug.

I have a known heroin user needing surgery. He'll be nil by mouth for three days. What analgesia do I use and how do I decide the dose? Should I use IV methadone?

It is not appropriate to use IV methadone as dose equivalence can be difficult to determine. There are means of estimating possible oral methadone equivalence to street heroin, but these are not always reliable. However, the equivalence of oral to IV methadone is unclear because of the variable bioavailability of oral methadone.

For patients taking street heroin, or on maintenance methadone, it is more appropriate to manage both potential opioid withdrawal and pain with a conventional opioid such as morphine via infusion. Use of a patient controlled device with a constant rate background infusion can be helpful. Patients will need to be monitored carefully for pain, opioid withdrawal, and overmedication. It is important to involve the hospital acute pain team to monitor opioid prescribing and response and to advise on alternative modes of analgesia such as local anaesthetic techniques.

I have a patient who I think is shamming pain in order to get analgesia from me. Where do I stand ethically if I refuse to supply?

It is important to obtain a substance misuse history for both patient and family and to review medical notes available to see if other prescribers have expressed concerns. It is helpful to discuss the presentation with other professionals involved in the patient's care. A full pain history including relevant up to date investigations should be documented. In accordance with good practice it is reasonable to try non-pharmacological and non-opioid therapies initially.
If there are reasonable grounds for suspicion, discuss problems of long term indiscriminate use of opioids with the patient and refer for specialist pain assessment. Drug screening may be considered and should also be discussed.

I have a patient who has previously had an opioid addiction, but is now abstinent and in recovery. They have chronic non-cancer pain that is proving difficult to manage with NSAIDs. Where do I go from here?

It is important to involve both specialist pain and addiction medicine services for this type of problem. Non-pharmacological and non-opioid pain management strategies should be explored. If opioids are going to be used, psychological support needs to be offered to avoid relapse of addictive behaviour. This is more important than the dose of opioids used. Modified release preparations with lower abuse potential should be used. Prescribing should be monitored carefully and open discussion with the patient maintained.

4.4 Model for relationships between primary care, pain management services, and addiction medicine services

4.4.1 General Practice and Pain Management Services

Good liaison is important when opioids are prescribed for non-cancer pain generally and particularly when there may be a possibility of addiction. Initial telephone contact between specialist and GP is ideal. Such contact:

- allows frank discussion of any concerns, and more rapid exchange of information
- allows exploration of patient history that may increase suspicion of a tendency to addiction problems
- confirms what the GP is prepared to prescribe
- Allows clear agreement regarding which team member should be the lead prescriber
- Facilitates development of an agreed care plan

Ongoing rapid communication is useful. There are a number of advantages to this:

- the patient with an addiction problem may obtain multiple prescriptions from different medical sources and prompt information regarding prescribing information helps to reduce this risk
- recent changes in medication regimen can be made known to others in the healthcare team
- recent life events which may have a bearing on coping strategies can be discussed and managed

Methadone in primary care

Methadone has been used to good effect as an analgesic, and can safely be prescribed by GPs. It is particularly beneficial for patients with an addiction problem because of its long half-life. Liaison with specialist pain or addiction medicine services may be necessary before starting this prescription regimen. It is important to remember that methadone is prescribed to be taken only once a day when used in the treatment of opioid dependence compared to twice or three times daily when used for pain control.

4.4.2 Liaison with Specialist Addiction Services

There are a significant number of addicts who suffer from chronic pain, and addiction develops in a number of chronic pain patients. Particular problems of access to services can occur for both these patient groups. Joint working in the form of a combined pain and addiction clinic (with medical specialists in pain medicine and addiction medicine and support from clinical nurse specialists and CPNs working with addiction services) can address the following issues:

- Patients who have developed an iatrogenic addiction to opioids may, understandably, not perceive their problem is one of addiction, and refuse to attend for specialist addiction advice. A joint clinic allows these issues to be addressed in the first instance.
- Drug users who experience chronic pain often describe unhelpful experiences of hospital medicine. They drop out of treatment, leaving their chronic pain unevaluated and untreated. Joint working in the form of a shared clinic can improve their uptake of pain services, with a consequent lower reliance on opioids.

- Switching from short-acting to long-acting opioids can result in increased patient anxiety because of the expectation of immediacy of effect in this client group. Specialist guidance and monitoring from addiction services, seen to be closely connected with the pain clinic, can allow these drug substitutions to be performed more easily.
- Where patients require reduction of their opioids, advice to the patient and prescriber from addiction medicine specialists can facilitate this process.

Within these assessment clinics it is important to have access to immediate drug screening to aid with decision making in further prescribing. Access to both pain clinic and drug workers' notes is also important, as is close liaison with GPs and other people involved in day to day management of the patient.

The needs of these patients often mean that relatively frequent follow up is required with ongoing support in the community. By using existing addiction service infrastructure in primary care and linking with pain management expertise it should be possible to optimise management of the complex problems with which this population present.

Section 5: Special circumstances and populations

5.1 Acute pain management

Patients with a history of substance misuse may need acute pain management in hospital following surgery, trauma or other illness. Fear is common amongst these patients who expect their pain to be badly managed, anticipate that analgesic medication will be withheld and have considerable anxiety related to the possibility of drug withdrawal. It is not appropriate to use an acute hospital admission as an opportunity to address the underlying substance misuse problem. Any attempt to do so will lead to mistrust, drug seeking behaviour and confrontation that quickly becomes difficult to resolve. Careful planning of the analgesia provided during this period is essential to avoid this conflict. Early involvement of the in-patient pain team is recommended. In the case of patients needing surgery, preoperative anaesthetic evaluation and assessment by the acute pain team is mandatory.

The primary objectives during this period are to manage the patient's pain and avoid the consequences of withdrawal. These aims need to be discussed clearly with the patient and healthcare staff in order to foster an environment of trust enabling the patient to discuss drug use openly in order to inform an effective pain management plan. Reassurances regarding confidentiality will assist in developing patient trust. In some hospitals the planned analgesic strategy is structured into a more formal contract that the patient agrees to and may be asked to sign. Discussion with local specialist drug services is important at this stage. The patient may be known to the addiction medicine team who will be able to inform the treatment plan, assist in a reliable conversion from street drugs to prescribed analgesics and help plan a smooth transition from acute pain intervention to ongoing management of the patient's substance misuse.

It is important to maintain sufficient background medication to avoid withdrawal in addition to that needed to provide analgesia. Background opioid requirements can be maintained with oral methadone or by opioid infusion with additional analgesia provided by epidural, or other appropriate regional technique, or by using intravenous patient controlled opioid analgesia (PCA). The PCA will usually need to be at a higher dose than usual, including increased size of bolus dose and addition of a background infusion. Careful observation and dose titration when setting up the PCA is mandatory to ensure both safety and adequacy of pain relief. Epidural analgesia alone, even if containing an opioid in the infusion solution will not prevent withdrawal symptoms. The co-administration of paracetamol and NSAIDs in a multi modal regimen will improve analgesia and may reduce the amount of opioid needed for effective analgesia. It is important to remember that continuing management of the patient's medication on discharge will need support from the local drug dependency team and advice from the team needs to be sought when weaning to oral analgesia so that this can be planned in parallel with establishing an appropriate opioid maintenance regimen.

5.2 Palliative care

The principles of analgesic practice in substance misusers are fundamentally no different from those for other adult patients needing palliative care. Substance misuse is a risk factor

for other medical conditions and is also a cause and an effect of psychological difficulties or psychiatric illness. Substance misusers may present with lung, hepatic or head and neck malignancy, vascular disease, neuropathy, ostemyeltis or pancreatitis. They may lack organisational skills to follow complex dosing regimes and vary in their ability to attend clinic for regular follow-up. Staff concerns about their personal safety are a serious consideration when behaviour becomes abusive, and clear boundaries for behaviour require unequivocal explanation whilst maintaining a focus on rational therapeutic plans for care.

Addicted patients may receive maintenance therapy from a substance misuse service and this should be regarded as a separate prescription from that for analgesia when attending as an outpatient. Drug misusers will commonly receive all their medication from inpatient units during an admission, but a clear plan for separate follow-ups for substance misuse and symptom palliation should be in place on discharge except during the terminal phase of an illness. Titration of non-opioid, opioid and adjuvant analgesics should be regulated against analgesic response in the usual way; distinctions between symptoms of poor analgesic response and withdrawal should be recognised. Symptoms of drug withdrawal on inpatient admission are common, and usually occur as a result of cessation of recreational drugs.

There are likely to be psychological, social and existential issues influencing pain perception and behaviour. When engaging with the patient and carers it is helpful for the multidisciplinary team to look beyond the misuse to its causes and implications. It is common for there to be resonance between the generations in families and siblings often share misusing behaviour; this has implications for bereavement care.

The multidisciplinary team approach to the delivery of palliative care offers realistic hope for substance misusers facing the end of life. The context of severe illness and impending death provides the opportunity to make meaningful contact with family and carers. Focus on important issues in a supportive environment may facilitate acknowledgement and sufficient resolution of some of the concerns of this group of patients.

5.3 Pain relief in labour

In practice, intrapartum analgesia for women with a past or current history of substance misuse rarely poses problems. As for all women, non-pharmacological options such as immersion in water, TENS, mobilisation and relaxation techniques should be encouraged. The use of Entonox is also acceptable. Pain relief options should be discussed in the antenatal period with a specialist midwife or anaesthetist.

Pregnant women maintained on opioid substitute medications, (methadone or buprenorphine) will still require an assessment of their analgesia needs. These women will be tolerant to their maintenance dose of methadone or buprenorphine and therefore, should still have the option of further analgesia as required. The maintenance (daily) dose of methadone or buprenorphine should still be given at a regular time throughout the labour period.

When women request opioid analgesia during labour or following operative or instrumental delivery, the standard dose range of opioids (diamorphine, morphine, pethidine and fentanyl) should be tried initially. If this provides inadequate, additional doses can be carefully administered.

Following Caesarean or instrumental delivery, usual doses of post-operative opioids (intrathecal, epidural or intravenous) can be used although careful additional

supplementation may be required. Analgesia should be balanced with paracetamol and a non-steroidal anti-inflammatory drug (if not contraindicated).

Women receiving maintenance dosages of the partial agonist buprenorphine will have a reduced analgesic benefit from additional opioids. This is a dose-related effect and becomes a significant problem at levels above 8mgs of buprenorphine daily. It is advisable to avoid supplementing with long acting opioids as further dosages of buprenorphine may precipitate opioid withdrawal.

Epidural/intrathecal analgesia with local anaesthetic (or with local anaesthetic in combination with an opioid) can provide effective pain relief (during labour, Caesarian Section or instrumental delivery) for women receiving opioid substitution therapy. If analgesia is initially ineffective, it is usual to first increase the concentration/dose of local anaesthetic rather than the epidural opioid dose. If further analgesia (in addition to spinally administered drugs) is needed following operative delivery, sublingual doses of buprenorphine can be given until analgesia is satisfactory **if local policy allows for this**. This can also be supplemented with paracetamol and a non-steroidal anti-inflammatory drug.

Practitioners sometimes worry that systemic opioids in labour may trigger relapse. There is no evidence to support this. Appropriate discussion of all options and their relative advantages and disadvantages is recommended in the antenatal period. Additional psychological support may be helpful during labour and delivery.

5.4 Pain management and substance misuse in the prison setting

Background

The prevalence of substance misuse is high amongst offenders entering prison. The 1997 Prison Psychiatric Morbidity study showed that 40% of men and 47% of women on remand were severely drug dependant. Current clinical observation suggests that these rates are even higher in 2006. Prisoners have a significant physical and psychiatric co morbidly. In a study in 1994 of the physical health of male prisoners, 46% of prisoners reported a long-standing disability or condition, the commonest being musculoskeletal problems.

Those with severe drug dependency suffer from poor health either, directly related to their drug habit and also resulting from the low priority that they give to their overall health. Teeth and dental hygiene are often affected. Toothache can often be a severe problem when substance misuse management is reassessed.

Prisoners with chronic pain are entitled to the same expert assessment of their needs and the same pain management as they would expect to receive in the community.

Assessment

At the time of reception into prison, all prisoners undergo a health screening process. This assesses significant health problems, such as drug dependency, physical and mental health problems and immediate vulnerability for suicide. At this time all existing treatment regimes, including opioid maintenance prescriptions and analgesics, should be confirmed with the community prescriber. Those who are drug dependant will be assessed further for appropriate needs based treatment, either detoxification or maintenance prescribing,

if remanded or on a short sentence, accompanied by a psychosocial interventions. At the same time all other co-morbidities will require reassessment.

Pain management

Acute or chronic pain may occur in patients with a concurrent substance misuse problem and may be exacerbated when their substance misuse problems are reassessed in prison. Pain can occur when opioid drugs are reduced or as a result of stopping cocaine, crack and or alcohol. Such patients may need frequent re-assessment of their pain during this period. Reduction in drugs and alcohol, compounded by poor sleep and anxiety can exacerbate the pain of a chronic condition. Toothache is a common problem requiring urgent referral to the dentist. Advice should be sought on the management of more complex cases from a specialist substance misuse doctor and a pain management specialist.

Opioid-based analgesics may be subject to misuse in a prison setting. Illicit trading of these medications may occur due to the presence of large substance misusing population. Bullying may also occur. Prisoners may be coerced into obtaining prescriptions for analgesia or if legitimately treated with these drugs, can be bullied into passing them on to others. The latter results in the patient receiving inadequate treatment for their pain. Inadequate pain management can then lead to increased anxiety and distress and an increased risk of self harm.

A prisoner with chronic pain should have a full assessment and be managed in the same way as a patient in the community. This may present problems to the clinician and the patient. The responsibility for commissioning health services for prisoners now lies with the NHS. If a specialist recommends treatment, or a change of management these needs should be discussed with the prison health team so that prison staff , supported by others involved in the patient's care, can try to meet them, This might include attention to the patient's mattress, regular medication, complimentary therapies, antidepressants, aids and adaptations. If a prisoner is in high risk category, consideration may have to be given to assessing them "in-situ" in the prison. The experience of pain may be exacerbated in prison. This may be related to the stress of arrest and imprisonment, and alterations in lifestyle including decreased activity and fewer attentionally diverting activities. Simple measures invoked at home such as lying in a warm bath, may be restricted in prison and other strategies will need to be explored.

It is not uncommon for prisoners to seek opioid-based analgesia for mild or moderately painful conditions. Doctors and dentists can by put under considerable pressure by their patients to prescribe these types of drugs.

All prisons should have a prescribing formulary to take account of medication likely to be misused, including the possibility of accidental overdose or addiction. Such formularies, drawn up in conjunction with local specialists, should include a range of non-opioid based medications, with consideration given to the effects when taken in overdose.

Prisoners may also request opioid analgesics when attending hospital. Prison healthcare teams should work together with their local hospitals, in particular the Accident and Emergency Departments to avoid inappropriate prescribing of these drugs.

Prison Service Order 3550 (Clinical Services for Substance Misusers) requires that "administration and consumption of controlled drugs and other drugs subject to misuse within a prison setting must be directly observed". This clearly includes all opioid analgesics, and can therefore pose practical problems for those who need their medication at frequent intervals, or specific times which are not in keeping with the medication

dispensing times of the prison. It may be more appropriate for longer acting preparations or transdermal preparations to be prescribed although the use of patches as route of administering analgesia is not without risk of diversion in a prison setting. In view of the difficulty in ensuring compliance, slow-release oral formulations of opioid analgesics should be considered as a viable alternative to transdermal administration.

Before arrest, a prisoner's pain may have been managed locally by his/her G.P. and possibly a local specialist service. Prisoners when sentenced are frequently moved away from the local prison and the prisoner will need to be referred to another specialist team if pain continues to be a problem.

The management of pain in the prison setting where substance misuse is a common problem is complex. Patients should however be able to achieve a similar degree of symptom relief to that which they achieved in the community, although their treatment may need some adjustment. Pain management regimens need to be delivered to the individual for whom they are intended, in a safe manner, which does not expose the patient, or others with whom he/she associates, to unnecessary risk.

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Further Information

Websites

National Institute on Drug Abuse http://www.nida.nih.gov
US site. The most comprehensive website on substance misuse research, harmful effects and patient information.

DrugScope http://www.drugscope.org.uk
UK site. Similar scope to the above but less comprehensive. Has some good basic introductory materials for non-specialists.

Virtual Clearinghouse on Alcohol, Tobacco and Other Drugs
http://www.atod.org/
International site devoted to sharing policies and guidelines on substance misuse from around the world.

Daily Dose http://www.dailydose.net
UK news sevice for substance misuse.

National Treatment Agency UK http://www.nta.nhs.uk/
A special health authority, created to improve the availability, capacity and effectiveness of treatment for drug misuse in England.

National Institute on Alcohol Abuse and Alcoholism
http://www.niaaa.nih.gov
Comprehensive US site dealing with all aspects of the misuse of alcohol.

Drug Misuse Information Scotland
http://www.drugmisuse.isdscotland.org/
Information, statistics and research on drugs misuse in Scotland.

American Pain Society and American Academy of Pain Medicine. Consensus statement: The use of opioids for the treatment of chronic pain.
American Pain Society Website:
http://www.ampainsoc.org/advocacy/opioids.htm

American Academy of Pain Medicine, the American Pain Society and the American Academy of Pain Medicine. Consensus statement: Definitions related to the use of opioids for the treatment of pain.
American Pain Society Website:
http://www.ampainsoc.org/advocacy/opioid2.htm

The British Pain Society. A consensus statement: Recommended guidelines for pain management programmes for adults.
The British Pain Society website:
http://www.britishpainsociety.org/pmp_0306_v9.pdf

The British Pain Society. Consensus statement: Recommendations for the appropriate use of opioids for persistent non-cancer pain.
The British Pain Society website:
http://www.britishpainsociety.org/opioids_doc_2004.pdf

Books

Wills S Drugs of Abuse (2nd edition) *Pharmaceutical Press* 2005 ISBN: 0 85369 582 2

Schuckit MA Drug & Alcohol Misuse: A Clinical Guide to Diagnosis and Treatment (5th edition) *Kluwer Academic/ Plenum Publishers* 2000 ISBN: 0 306 46230 3.

Departments of Health (England, Scotland and Northern Ireland) Drug Misuse and Dependence – Guidelines on Clinical Management, 1999 ("orange guide").

Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine: Acute Pain Management: Scientific Evidence 2nd edition 2005 ISBN: 0-9585208-6-0

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