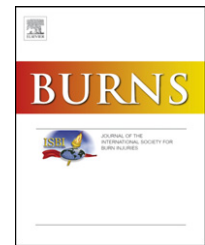


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## Review

# The management of pain in the burns unit

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### ABSTRACT

The adverse sequelae of inadequate pain control in the burn population have been long recognised, yet control of pain remains inadequate globally. The dynamic evolution of burn pain both centrally and peripherally, and the many factors which influence pain perception illustrate the need for a therapeutic plan which is similarly dynamic and flexible enough to cope with the facets of background, breakthrough, procedural and post-operative pain. Regular, ongoing and documented pain assessment is key in directing this process.

The family of opioid analgesics provide the backbone of analgesia to burn patients. Together, they provide an excellent range of potencies, duration of actions and routes of administration. However, they must be used judiciously as side-effects may be clinically relevant and furthermore, recent data has implicated them as being capable of inducing pain. NMDA receptor antagonist such as ketamine and gabapentin are increasingly recognised as useful adjuncts, capable of marked opiate sparing effects in this population. The simple analgesic paracetamol (acetaminophen) has both anti-pyretic and opioid-sparing properties and justly deserves its place in the pharmacological treatment of every burn patient.

Non-pharmacological methods of pain control can play an important role in suitable patients but resources vary widely between units.

With this review article, we have set out to give practical guidance to all healthcare professionals with examples from our practice. We have found the addition of pain specialists as an integral part of the burns multi-disciplinary team, and an environment where pain is given a high clinical priority to be invaluable in our approach to pain control.

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Burn pain is severe and good pain control is necessary for more than simply humane reasons. The negative consequences of poor pain control are wide ranging. Fear and anxiety induced by a bad acute pain experience risk poor compliance with rehabilitation therapies, increased pain perception and loss of faith in the burn team [1]. Uncontrolled acute burn pain increases the incidence of chronic pain and associated depression [2], and correlates with suicidal ideation at time of discharge from hospital [3]. Post-traumatic stress disorder is a notable sequelae of major burn and is linked both as a cause and effect with poorly controlled burn pain [4,5]. Failure to implement effective acute pain control increases the stress response [6,7].

Despite major advances in burn wound management and survival, burn pain is inadequately treated globally [8]. This is attributed to its complexity and to lack of specific education in health care professionals [9–11]. Burn pain evolves and changes over time; drug handling is altered and the patients' psychological needs evolve. Staff caring for burn patients face unique challenges including the repeated infliction of pain on already traumatised patients, with therapeutic procedures, physiotherapy and provision of hygiene needs all having the potential to cause pain and distress. Personal coping strategies used by burns staff to distance themselves from a patient's pain have been identified as a barrier to effective pain management [12]. A multi-disciplinary approach and a culture where pain is given a high clinical priority increase the chance of getting it right.

This review seeks to identify currently available methods of achieving effective pain management and to provide practical guidance in the adult burn population. Specialist groups, such as children and the cognitively impaired are mentioned but not addressed in full.

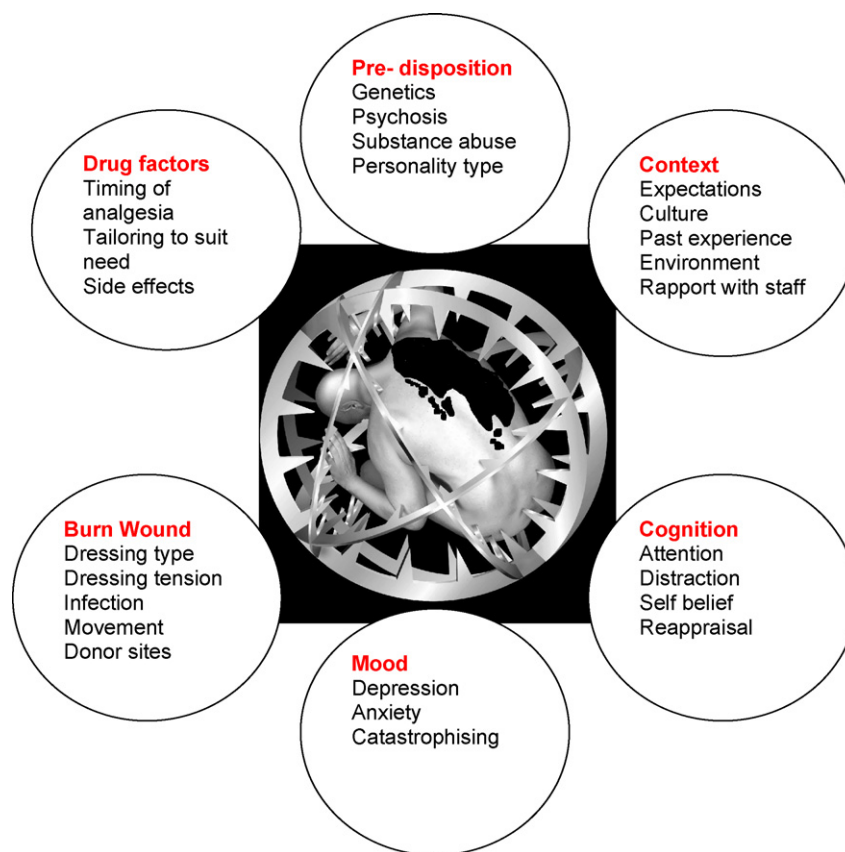
An understanding of the mechanisms of burn pain is a necessary starting point.

## 1. Pain mechanisms after burn

Burns are classified by thickness and area affected, yet pain does not always correlate accordingly. Afferent nerve destruction associated with deeper burns theoretically reduces the amount of pain experienced, but in clinical practice this is not a reliable predictor [9,13]. Different individuals do not feel the same pain from the same wound or injury. In addition, the pain experienced will change with tissue regeneration and evolving physiological, psychological and environmental influences.

Pain is perceived at the time and site of burn, due to stimulation of local nociceptors and transmission of the nerve impulse in A $\delta$  and C fibres thereby relaying the pain message to the dorsal horn of the spinal cord. The magnitude of impulse is modulated here by both concurrent peripheral sensory inputs and descending influences from higher cortical areas. Each of these has the potential to exert powerful effects and may have the capability to override the unpleasant sensation of pain entirely in extreme situations. Conscious perception of pain occurs as the resultant impulse is transmitted onwards to the brain and into areas collectively known as the pain matrix. These remain to be fully defined anatomically, but activity appears centred on cortical areas and the thalamus [14]. Many factors influence the conscious perception of pain (Fig. 1). Those that are subject to external influence are targets for therapeutic manipulation. These varied contributory factors are what make the pain experience unique to each sufferer. Successful pain management plans are consequently highly individual.

The inflammatory response is initiated within minutes of injury and persists for days. The 'inflammatory soup' of irritant chemicals continues to sensitise and stimulate pain fibres throughout this time. The site of burn injury remains painful, and markedly sensitive to mechanical (touch and



**Fig. 1 – Factors influencing the patient’s perception of pain from a burn wound.**

movement) and thermal stimuli. This is known as primary hyperalgesia. Secondary hyperalgesia, increased sensitivity and pain perception to mechanical stimuli (yet not thermal) is observed within minutes in the adjacent undamaged skin as C fibres facilitate A $\delta$  input from neighbouring neurons [15].

Continued or repeated pain stimuli, which occur when inadequate background or procedural analgesia is provided, will give rise to adaptations throughout the central nervous system whereby pain signals, and hence perception, become facilitated and amplified to a given stimulus: hyperalgesia. With time, these changes may become irreversible and chronic pain is risked as a result. This ‘wind-up’ mechanism involves sensitisation of peripheral receptors, increased excitability at the dorsal horn centred on NMDA receptor systems and activation of facilitating pathways descending from higher centres [16]. The NMDA receptor modulating drugs ketamine [17,18] and gabapentin [19,20] are of benefit in the multi-modal pharmacological management of pain.

Opioids, while mainstay analgesics, are recognised as having the potential to induce hyperalgesia through central sensitisation [16] and this is discussed more fully later.

As the acute inflammatory response abates, the pain may change in quality. Reported pain intensity may vary but is typically maximal at sites of upper/mid-dermal skin loss, such as areas of skin donation, and decreases with wound closure. Infection of a burn at any stage of the healing process will be accompanied by a resurgence of the inflammatory response and augmentation of pain. Rebirth of new tissue is associated with paresthesia and local discomfort [21] and healed burn

areas remain primed to show enhanced mechanical hyperalgesia following subsequent injury [22]. Anxiety and poor pain experience will increase the perception of pain [13].

The pain experienced will alter with treatment of the burn. Surgery to debride or excise the burn will adjust the depth of the tissue injury. Covering the burn area with autograft or allograft skin, or a synthetic dressing typically reduces the pain. Skin harvest donor sites are usually associated with more pain than the injured area itself.

Severely damaged nerves in deep dermal or full thickness burns may lead to a relatively insensate area initially, but regeneration will occur within 5–6 weeks of wound closure [23]. Neuropathic pain can result from disordered regrowth with sprouting to neighbouring nerves, spontaneous firing or neuroma formation. The nature of this pain is described as tingling, lancing, shooting and like electric shocks. Neuropathic pain often responds poorly to traditional analgesics such as opioids, and therapeutic strategies for managing this particular type of pain need to be employed.

Long-term or chronic pain remains a problem for a significant number of burn survivors and this has been estimated at 52% [24]. Phantom limb pain has a higher incidence in amputations following electric shock injury [25].

## 2. Pain assessment

Regular, ongoing pain assessment is essential to guide the dynamic analgesic regime necessary to cope with the evolving

**Table 1 – Burn pain assessment.**

How to assess burn pain	Pitfalls in pain assessment
Ensure the patient understands the pain score.	Do NOT alter a pain score from a self-reporting scale, to what you think it should be!
Question the patient about background, breakthrough and procedural pain.	Some well intentioned questions are misleading e.g. 'Would you like any pain killers?'. They may be making the patient feel sick and the answer will be 'No' despite pain.
Ask 'Do you have any pain?' and listen.	If you are reviewing pain control – ask the patient yourself about their pain, not your colleague.
Stick to the present tense.	
Ask where and when the pain is felt, and what makes it better or worse.	
Record the answer the patient gives.	
Any patient in pain should have pain scores recorded hourly. All patients should be assessed a minimum of twice a day.	

nature of burn pain and its response to medication. Background pain (at rest and during movement), breakthrough (unpredictable pain surges through the day), and procedural pain all warrant individual assessment and recording throughout the phases of burn recovery [4]. Site of pain, aggravating and alleviating factors are important to define, in particular the response to analgesics. A thorough pain assessment may require examination of the patient in order to guide the clinician towards the cause of the pain and therefore effective management of it. For example pain may result from a tight dressing needing release, tissue oedema in a dependant limb requiring elevation, wound infection or muscle necrosis in compartment syndrome. The words used to describe the pain may guide the clinician to suspect a particular pain mechanism, for example the 'electric shock' quality of neuropathic pain.

Accurate recording of a subjective experience, by another individual, can be skewed by a number of things, including bias and assumption. Several papers reported discrepancies between patient and nurse pain scoring [26–29] and education is undoubtedly the key to improving practice. Table 1 illustrates points that we have found to be useful when teaching staff. Some patients are concerned to be on as few drugs as possible and may deny pain to themselves and to staff. Stressing the importance of good analgesia to allow maximum gain from therapies, and potentially faster rehabilitation, is important.

Scoring pain conveys a sense of staff empathy and makes the patients' 'complaint' valid. Simple, patient-friendly scales yield useful practical data and show trends and 'hot-spots' in the patient's day. Assessment scales are of many types. Adjective scales require a word to be selected to equate with the pain intensity (e.g. none, mild moderate severe) and numeric require selection of a number (e.g. 0–3, 0–5, 0–10). The visual analogue thermometer has been validated as a sensitive and useful tool in the burned population [30]. Use of this device requires the assessor to slowly move a strip from a position of 'No Pain' to 'Unbearable Pain' with the patient indicating when to stop. Other more complex tools, such as the McGill Pain Questionnaire [31] are useful for research or audit purposes. The abbreviated burn specific pain anxiety scale will identify and quantify anxiety [32].

Pictorial representation of the scale may be more suitable to guide self-report in young children [33]. Tools based on

behavioural observations have been validated for use in those who may not be able to reliably self-report pain; amongst these are the Abbey pain scale [34] for use in the elderly and cognitively impaired, and the FLACC score [35] in young children and infants.

Staff scoring pain will need to be aware of target pain scores and this will depend on the system used. Fig. 2 is an example of a pain score record chart used in our institution and this guides and documents a cycle of evaluation and appropriate drug adjustments. We advocate assessment occurring 2–4 hourly in the early phase and at a minimum of 12 hourly in the pain controlled patient to ensure that optimal management efficacy is maintained. It is our experience that the simplicity of a 0–3 scale is adequately sensitive for the purposes of identifying trends in pain severity, and effectiveness of analgesic regimes.

### 3. Pharmacological methods of burn pain control

Before prescribing any drug to a burn patient, the clinician must have an understanding of the altered pharmacokinetic state resulting from well-described pathophysiological changes that follow burn injury. During the first 48 h, decreased organ blood supply will reduce clearance of drugs, but the subsequent hypermetabolic phase (48 h after injury) is associated with increased clearance. Variations in levels of acute phase plasma proteins lead to changes in drug binding and free fractions available for end action. The volume of distribution of a drug may be further affected by alterations in total body water. Using regular and repeated pain assessment to quantify the effect of analgesic agents reduces the impact of these changes. Doses vary widely between individuals and over time with the same individual. This review therefore will not comment on doses other than in specific cases.

#### 3.1. Opioid analgesics

Opioids are the cornerstone of burn pain control. They are effective and the variety of drugs available provides a range of potencies, methods of administration and duration of actions. The positive effects extend beyond the subjective feeling of pain-free comfort. Morphine has been shown to correlate with

### St Andrew's Burns Centre Pain and Itch Score Chart

**Background/Breakthrough pain** should be assessed at least 4 hrly until stable then at least twice a day.

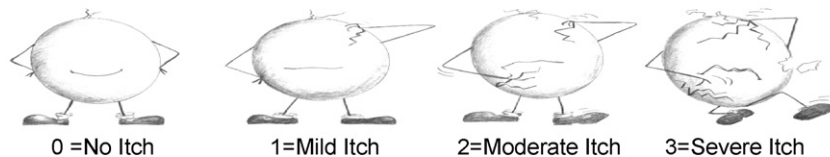
**Pain scores should be 0-1.** Take action if >1. Document action and evaluate effect of analgesia at 30mins. **Procedural pain** to be documented and action recorded.

**Itch** should be reviewed daily and treated as per the St. Andrew's Itch ladder

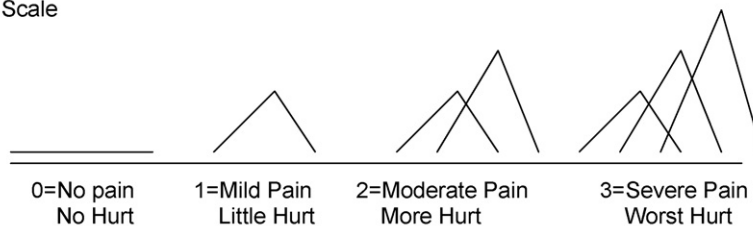
Date	13/9																			
Time	14.00																			
3																				
2	✓																			
1																				
0																				
Procedure*	DC																			
Analgesia given/time	Yes 14.15																			
Itch score	0																			

Comments

#### Itch Scale



#### Pain Scale



\*Procedure key:

DC=dressing change, B=Bath, P=physiotherapy O= Other. Define in comments

**Fig. 2 – St. Andrew's Burns Centre Pain Score and Itch Chart.**

reduced post-traumatic stress syndrome symptoms [36]. The effects of opioids are wide ranging and include clinically relevant side effects such as respiratory depression, itch, nausea and vomiting.

Doses can vary widely and escalate rapidly during burn treatment. This relates not only to wound healing and pain modulation, but may also occur with the development of opioid tolerance or the more recently defined state of opiate-induced hyperalgesia (OIH). Tolerance is defined as increasing doses of a particular opioid being required to achieve the same analgesic effect and applies equally to side effects. It is more common following the use of short acting opioids, particularly when administered as an infusion [37] but is otherwise unpredictable. It is no more common in the burn patient than any other [38]. The precise mechanism of tolerance is unclear but its link to OIH is increasingly recognised [39]. OIH is demonstrated clinically by increased pain sensitivity, diffu-

sely and throughout the body following opiate exposure. Although opiates provide excellent analgesia they are poor at preventing central sensitisation to pain [40]: pain scores and opiate requirements have been shown to be higher in post-operative surgical patients following the use of intra-operative remifentanyl infusions [41]. Mu-agonist opioids induce this hyperalgesic state through effecting neuroplastic pro-nociceptive changes in afferent neurons and the spinal cord, which may persist long-term [16]. NMDA/glutamate receptor systems play a critical role supported by the fact that both gabapentin [42] and ketamine [43] have been demonstrated as reducing these changes. Ketamine is effective in reversing opiate tolerance [44,45]. Although the relationship between opiate tolerance and hyperalgesia is complex and poorly understood, it has been suggested that mechanisms of hyperalgesia may be responsible for inducing the state of tolerance [46].

It would be imprudent to extrapolate these findings and suggest that opioids should be avoided for the control of acute or burn pain. Their role remains valuable, but there is a rationale for using them in reduced doses and in combination with other non-opioid analgesics [47]. Non-steroidal anti-inflammatory drugs and paracetamol reduce central hyperalgesia [48] and are opiate sparing [49,50] – effects also demonstrated by ketamine [44,17,18] and gabapentin [19].

Changing to a different opioid, ‘an opioid switch’, can help to restore analgesia in a tolerant patient [51] and switching to methadone has been reported as successful in burn patients [52,53]. Methadone has weak NMDA receptor properties [54] which may provide an explanation for this.

Physical dependence commonly occurs in patients on long-term opioids and they should not be stopped abruptly, to avoid precipitating withdrawal symptoms. Physical dependence is not to be confused with addiction or psychological dependency, which is characterised by an alteration in behaviour with cravings and compulsive opiate use despite evidence of harm. The development of this latter state is extremely rare in patients taking medically indicated opioid drugs, yet unfortunately patients continue to have these drugs withheld for fear of addiction [55].

Burns patients potentially require long-term opioids, and the aim is to establish an effective background regime based upon oral slow-release preparations, with short acting elixirs for breakthrough pain. Procedural pain is managed separately, using well-timed and effective doses of opioids adjusted according to patient response.

Any opioid drug may be used for burn pain management, but the following offer particular benefits in the burns unit setting.

### 3.2. Morphine

Morphine is the gold standard opioid drug against which all others are measured. The oral preparation undergoes extensive first pass metabolism meaning that to achieve an equianalgesic dose, the intravenous dose to be increased two- to threefold for oral administration. Accumulation of the active metabolite morphine-6-glucuronide can occur in renal impairment when a dose reduction or change of opioid may be needed.

Intravenous morphine will provide more rapid control of pain than an oral preparation with peak effect occurring at 10 min compared to 30–90 min and may be useful for initial pain control upon presentation. Oral (elixir and sustained release) use is preferred in the burns patient, although intravenous medication is more appropriate during the resuscitation phase when delayed gastric emptying may occur. The peak effect of intravenous dosing is at 10 min, compared to 30–90 min following an oral dose. Absorption from subcutaneous and intramuscular injections may be unreliable and these are best avoided. The efficacy of morphine as a topical agent in burns has been studied with no convincing evidence of benefit [56,57].

### 3.3. Oxycodone

Oxycodone is an effective alternative to morphine, some patients tolerating one more than the other. There is no evidence that oxycodone is more effective than morphine. Both can cause opiate side effects, but there are reports that

hallucinations and histamine-induced itching are less with oxycodone [58].

Oxycodone has superior bioavailability than morphine, and only half the oral morphine dose is administered as oral oxycodone. They are equipotent when administered intravenously.

### 3.4. Fentanyl

Fentanyl is a rapid onset, potent, short acting synthetic opiate. It is consequently well placed to provide good procedural analgesia. It can be administered by a variety of routes, and recent developments have led to novel techniques, most notably transmucosal administration. Intravenously it is a potent respiratory depressant and continuous infusions induce both rapid tolerance and drug accumulation. Short-term fentanyl infusions as sole agent for burns dressing change [59] or as patient controlled analgesia (PCA) can be safe and effective [60].

Fentanyl administered intranasally (IN) reaches therapeutic levels within 2 min [61] and this may offer a practical advantage over bitter tasting oral morphine preparations. In adults using patient-controlled IN a mean total dose of 1.48 mcg/kg PCIN equates to 0.35 mg/kg of oral morphine [62]. There is evidence of safe use in paediatric patients [63].

Fentanyl lozenges (for absorption via the buccal mucosa) were originally developed for the management of breakthrough cancer pain, usually at a starting dose of 200 mcg. There are now reports of its use for control of procedural burn pain, for which higher doses are required; 10 mcg/kg as a starting dose and subsequently titrated according to response [64]. The lozenge is rubbed over the oral mucosa rather than swallowed and onset of analgesia is at 3–5 min, with peak effect at 20–40 min. In paediatric patients 10 mcg/kg is equianalgesic to oxycodone 0.2 mg/kg [65]. The fast clearance time of the drug makes this particularly attractive in patients with renal impairment.

### 3.5. Remifentanyl

Remifentanyl is an ultra-short acting opiate, useful only as an infusion. Peak effect is reached within 1–3 min and it has a very short half-life (3.5 min) as a result of its organ-independent yet predictable metabolism. The high incidence of respiratory depression, especially in the opiate naïve patient requires that it is given only by trained anaesthetic personnel and in a suitable environment. It has gained an established place in the Intensive Care Unit for the management of short bursts of pain, and to assist with weaning from mechanical ventilation.

Experience of its use as a sole agent for undertaking dressing changes in spontaneously breathing, non-intubated burn patients shows it to provide good analgesia and high levels of patient satisfaction [66]. The clinician must be prepared for the abrupt offset of analgesia and appropriate background pain relief should be administered in a timely fashion.

### 3.6. Alfentanil

Alfentanil is a short acting opiate with peak effect reached within 1 min of injection. Its half-life is 90 min and, unlike remifentanyl, can provide some post-procedural analgesia.

It is shorter acting than fentanyl and for this reason it is favoured by some as the opiate of choice for control of procedural burn pain both as a sole agent [67] and in combination with propofol [68].

Alfentanil undergoes hepatic metabolism to inactive, non-toxic metabolites which are renally cleared [69]. Of all the strong opioids, it has the most evidence to support its safety in severe renal impairment.

### 3.7. Methadone

Methadone is a synthetic opioid drug with excellent bioavailability and long duration of action. Once daily dosing gives predictable action and avoids the 'highs and lows' of shorter acting opiates. This is why it is widely used for the control of opiate cravings in addicts. The steady state blood levels of methadone vary between individuals due to genetic influences in hepatic metabolism and this raises safety concerns particularly with regard to respiratory depression [54].

Methadone exerts its analgesic effect not only through opiate receptor binding, but also through a weaker action influencing pain modulation at spinal NMDA receptors. For this reason, it is a useful drug to consider when undertaking an opiate switch described in burns patients in both in the acute and chronic settings [52,53].

## 4. Simple analgesics

### 4.1. Paracetamol

Paracetamol (acetaminophen) acts both centrally and peripherally to inhibit pain. A weak analgesic as a single-agent, when used in combination with opioids it has a synergistic effect producing an analgesic effect comparable to a higher opioid dose. It has an excellent risk profile and few contraindications. Paracetamol should be used, regularly, in all (non-contraindicated) burn patients at its maximal dose of 90 mg/(kg day) with 4 or 6 hourly dosing. A review of paediatric burn patients showed that 7.3% of children require paracetamol alone for pain relief, although interestingly this was judged higher at 50.6% a decade earlier [70].

Paracetamol is established as an effective anti-pyretic, probably through reduction in thermoregulatory set point, an effect seen in both adults and children [71].

### 4.2. Non-steroidal anti-inflammatory drugs (NSAIDs)

NSAIDs offer effective analgesia, anti-inflammatory properties and anti-pyretic effects. Like paracetamol, they are also synergistic with opioids and can reduce doses and hence side effects [49].

Although highly effective against inflammatory pain, NSAIDs unfortunately cannot be recommended for routinely use in patients with significant burn injuries due to the already increased risk of renal failure [72] (particularly in the elderly), and peptic ulceration. In our institution they are restricted to cautious use in fit, younger patients with smaller burns (<10%). Renal function and fluid balance are carefully monitored and prophylaxis for gastric ulceration co-adminis-

tered. The anti-platelet effects potentially increase bleeding following the necessary large surface area surgery in burn patients. The potential for skin graft failure is of some concern, but there is no published evidence to support this.

The cyclo-oxygenase 2 (COX-2) inhibitors were launched with hopes of an improved side-effect profile, in particular in relation to reduced risks of gastro-intestinal complications. These drugs have fallen from favour following studies identifying an increased risk of thrombotic cardio-vascular events. However, they may be useful in carefully selected patients.

## 5. Other drugs useful in burn pain management

### 5.1. Gabapentin

Gabapentin, initially developed as an anti-convulsant, is now also licensed for management of neuropathic pain. The mechanism of action is probably not fully defined, but involves inhibition of central sensitisation to pain. It is known to bind to presynaptic calcium channels involved in pain hypersensitivity, and it will indirectly inhibit NMDA receptor over activation [47] thereby explaining the drug's ability to limit long-term pain sensitisation [42].

A small, retrospectively matched, case controlled study showed a reduction in morphine requirements in acute burn patients following addition of gabapentin for a 3-week period, commencing on day 3 after burn. A reduced morphine requirement continued for 3 weeks after the gabapentin was stopped [19]. A small case series of 6 patients with neuropathic pain, poorly responsive to opiates, achieved effective analgesia when gabapentin was added [20].

The recommended dose for the management of neuropathic pain is 300 mg tds with titration if necessary up to 3600 mg/day. Children start at 10 mg/kg with titration 40–50 mg/kg. Pregabalin is a similar compound and given twice daily.

Gabapentin has also been shown to reduce burn itch [73].

### 5.2. Ketamine

Ketamine, used at anaesthetic doses (over 1 mg/kg iv) induces a state of dissociative anaesthesia; the patient may appear awake but is detached from their surroundings. Its advantages over other sedative analgesics are that airway reflexes are maintained and heart rate and blood pressure are preserved, due to an elevation in circulating catecholamine levels. Hyper-salivation through sympathetic stimulation increases the risk of laryngospasm, estimated as occurring in 0.4% of patients [74]. Psychomimetic side effects of ketamine (hallucinations, emergence delirium) can be troublesome although the occurrence is reduced in children. Attenuation may be achieved by pre-medication with benzodiazepines [75] or the co-administration of propofol/ketamine infusions [76].

Ketamine has a powerful analgesic action through its action as a non-competitive NMDA receptor antagonist at the NMDA receptor and has been the subject of recent interest in the acute pain setting. Meta-analysis has shown that low dose

(0.1 mg/kg) ketamine can reduce opiate consumption by approximately 30% in the post-operative surgical setting and that it can act as a effective rescue medication of pain poorly responsive to opioids [44]. A Cochrane review similarly reported sub anaesthetic dose ketamine as reducing morphine requirements in the 24 h after-surgery, thus reducing adverse effects such as nausea and vomiting [17].

Experimentally, ketamine has been shown in healthy volunteers almost to abolish sensitisation to pain when given in combination with morphine in both adults [17] and children [18].

Safe and effective protocols have been developed to allow ketamine to be given both intravenously [77] and orally [78] by appropriately trained non-anaesthetists. Escalating doses of ketamine may be required for repeated procedures.

### 5.3. Clonidine

Clonidine is an alpha-2 agonist with analgesic, sedative and anxiolytic properties, acting by augmenting descending inhibitory spinal cord pathways. It is effective in the management of alcohol, opiate and nicotine withdrawal [79–81] and this is useful in the burns unit setting. It can safely be used and effective in the management of burn pain in children [82,83].

In the authors' institution, clonidine is frequently added to the analgesic regime of adults and children at a dose of 1–3 mcg/kg tds orally or intravenously. When no longer required the dose must be reduced gradually to avoid withdrawal and rebound hypertension.

Dexmedetomidine is has a similar mechanism of action, but is not available on the UK market at present.

### 5.4. Benzodiazepines

Non-pharmacological techniques of reducing fear and stress are best considered as the first line treatment, but anxiolytic drugs have their place in the treatment of burn patients as adjunct analgesics [84].

Increasing fear and tension decrease pain tolerance [2], see Fig. 1. Benzodiazepines have no analgesic properties and should not be used as such, but they are useful and effective in reducing the perception of pain in the anxious patient. Lorazepam 1 mg with opioid has been shown to produce better pain relief in burns patients with high baseline pain scores, than opioid with placebo, and this was most evident in patients with high state anxiety. Patients with low baseline pain scores did not demonstrate a beneficial effect [85].

Lorazepam is favoured over diazepam in the burn patient. Diazepam shows a prolonged half-life, relying on hepatic enzyme metabolism, which may be severely reduced in this population [86]. Midazolam is an appropriate choice where a rapid onset shorter acting drug is required.

### 5.5. Amitriptyline

This tricyclic anti-depressant drug, used in low doses, has an established role in the management of neuropathic pain. Mood altering effects occur at higher doses. It acts by augmenting descending inhibitory pain pathways in the spinal cord. Sedation is a side effect, which can be useful to

help induce sleep when used at night time. Dosing at this time reduces the subjective unpleasantness of the anti-cholinergic effects of dry mouth and blurred vision. Doses should start low at 10 mg nocte and increase every few days if required and as tolerated. Optimal effect is achieved at variable doses, and it is unusual to need more than 75 mg in the responsive patient. Up to one-third of patients fail to achieve this due to intolerable adverse effects [87]. Paediatric burn survivors with phantom limb pain following traumatic amputations showed a good response to amitriptyline [25].

### 5.6. Lignocaine by intravenous infusion

Lignocaine infusions have been shown to be effective in alleviating neuropathic pain, an effect most notable where there is nerve damage [88]. A case report describes successful management of acute burn pain in a patient unresponsive to opiates [89]. However, a Cochrane Review was unable to identify any published randomised controlled trials to support or refute the use of lignocaine intravenous infusions in the management of burn pain [90].

### 5.7. Entonox

Nitrous oxide (N<sub>2</sub>O) is a weak anaesthetic agent with potent analgesic properties. It is supplied as a 50:50 mix with oxygen as entonox or equinox. It provides rapid (within seconds) onset and offset of analgesia with minimal serious side effects. It is well placed to relieve short-term pain such as may be experienced during dressing changes. Its use can be limited by the occurrence of nausea and vomiting.

N<sub>2</sub>O interferes with B<sub>12</sub> metabolism and prolonged and excessive use can cause sub-acute combined degeneration of the cord [91]. This is a rare complication, but patients with poor nutrition are at increased risk.

Entonox is self-administered, and as such, depends on the burn patient's ability to hold the mask or mouthpiece for inhalation.

## 6. Non-pharmacological methods of pain control

The issues presented by the burn patient combine to present a much greater challenge than the provision of pharmacological pain relief alone. Multidisciplinary work with psychologists, psychotherapists, physiotherapists and pain specialists should be started early in the burn patient's recovery, to ensure a comprehensive plan is initiated.

The correlation between the patients' perception of burn pain intensity and baseline anxiety is strong and well established [1]. Psychological techniques are beneficial in alleviating anxiety and equip the patient with coping strategies for the variable levels and duration of pain involved in burn rehabilitation. These include relaxation, distraction and cognitive behavioural therapy (CBT). CBT been shown to be effective in a range of people with complex and difficult pain problems, and levels of fear, anxiety and distress associated with an activity or environment are moderated using this range of techniques [92–94].

Disrupted sleep occurs in more than 50% of burn patients [95,96], and often continues after discharge from hospital [97]. Poor sleep patterns and tiredness may hinder an individual's recovery, exerting a detrimental effect on mood and energy. Pain appears to exacerbate and prolong sleep disturbances, just as quality of sleep affects severity of pain experienced [98]. Sleep patterns are disturbed by pain, anxiety, itch, discomfort, stress, and flashbacks. Difficult though it is in the Burns ICU setting, a bedtime regime and normalisation of the 24-h day should be the aim. Noise levels, lighting and physical and psychological comfort should all be considered at night time, as well as the individual's usual bedtime routine. Anxiolytics, analgesia and night sedation play their parts in providing restful sleep for the burn patient.

Hypnosis is described as a state characterised by increased suggestibility, attention and relaxation [99] and has been used in pain and stress management for several decades. Its use in burn pain management has concentrated on procedural pain and anxiety and there is growing evidence for its clinical usefulness [100], supported by neurophysiological studies [101]. Success depends on the individual's hypnotic susceptibility [102], a high enough level of baseline pain [103] and the skills of the practitioner [104].

The use of virtual reality systems that immerse the patient in a virtual world has shown promise in procedural pain control [105,106] and superiority over commercial handheld video games [107]. Costly, bulky equipment limits the practicality of using such systems and the headsets are not suitable for young children. A hand-held sound and video device, providing augmented reality, has been specifically designed and developed for use in children undergoing repeated procedures, such as dressing changes. Trialled on 3–14-year olds undergoing burns dressing changes, patient and parent reported pain scores were significantly lower than in a group receiving standard distraction and relaxation alone [108].

## 7. Practical considerations

### 7.1. Background pain

While the choices may seem overwhelming, the rationale behind good pain management is to use a multi-modal approach and to keep it simple. If morphine is unproblematic and effective, there is no need to change or choose other opioids. Modified release oral opiates, administered twice daily, provide constant background analgesia, and dose-adjustments can be made in response to patient assessment so that the patient suffers no, or only mild pain, both on movement and at rest.

Adverse effects should be pre-empted and treatments (e.g. laxatives, anti-emetics and opiate antagonists) co-prescribed. Paracetamol should be administered regularly to every patient and has few contra-indications. NSAID use should be cautious, but they are of benefit in carefully selected patients.

Intravenous preparations of morphine are more appropriate in patients suffering larger resuscitative burns or requiring artificial ventilation, where delayed gastric emptying will reduce enteric absorption. Intravenous morphine will provide more rapid control on initial presentation. Oral dosing is preferred in the longer term for safety reasons and to limit the development of tolerance. 1 mg intravenous morphine is equivalent to 2–3 mg oral morphine. Suggested starting doses are given in Table 2.

Patient-controlled analgesia has been described as safe and effective in the management of pain on admission and is used successfully in some burn units in both adults and children [109–111]. In our experience, lack of manual dexterity in burns patients limits the success of this technique and we have found modified release preparations to be superior in providing reliable background analgesia.

Additional analgesics and the neuropathic drugs useful in the management of more complex pain are not usually routinely prescribed. Poly-pharmacy can make it difficult to evaluate what works and what may be causing problems, both for the patient and staff. Additions or changes are best made one at a time in order to evaluate effect.

Patients with burn pain and pre-existing opioid dependence from drug abuse present a challenge, and it is important that opiates are not withheld if indicated for analgesia. Excellent communication between hospital and community staff will be required. The principal of management is that a substitute opiate, usually methadone is administered both regularly and as required to control symptoms of dependence, and an analgesic dose of an opioid (such as morphine) is administered for pain management as in the non-dependant patient. Patients often know the dose of methadone required to maintain their well being, and the aim is to achieve a once daily dose as quickly as possible to avoid a cumulative effect due to the long half-life of the drug. This population commonly takes a variety of substances, and may require other supportive symptomatic control. Obtaining a candid history is paramount, and admitting staff must have the necessary skills to elicit this information without prejudice.

### 7.2. Breakthrough pain

Every prescription chart must carry a script for 'as required' medications, such as morphine elixir, with frequent, usually

**Table 2 – Suggested doses of opiates for the initial management of burn pain.**

Child over 1 year	Adult
Oral morphine: 200–400 mcg/kg repeated 2 h	Oral morphine: 10–15 mg repeated 1–2 h
Intravenous morphine: 20 mcg/kg iv repeated every 3–5 min. Monitor reusability, respiratory rate ± oxygen saturation	Intravenous morphine: 1–2 mg repeated every 3–5 min
Titrate until pain controlled and aim to commence on regular oral opiates when possible. Naloxone 200–400 mcg/kg as prn to be prescribed with regular opiates; every patient and every injury is unique and effective doses will vary between individuals.	

hourly, dosing. The daily pain review should include evaluation of frequency and dosage of 'as required' pain medication so that modifications to long acting, background drugs may be made. The effective dose of analgesics will vary through the analgesic treatment period, but a sudden increase in pain levels should alert staff to the possibility of complications such as wound infection.

The pattern of breakthrough pain is important in guiding its control. For example, the timing of drug administration may require rationalisation to better anticipate pain.

### 7.3. Procedural pain

Burn pain is recognised as being maximal during therapeutic procedures [13] and wound debridement can be more painful than the burn injury itself [112]. Under treated pain risks poor compliance with treatment, post-traumatic stress, further 'wind-up' of pain and increased anxiety, all of which serve to worsen the pain experience during subsequent treatments. The management continues to challenge burn specialists and this is highlighted by the lack of consensus on strategy.

The ideal method would provide analgesia potent enough to cope with short, intense burst of pain, whilst not rendering the patient unconscious when unstimulated. Loss of consciousness, as with general anaesthesia, requires the patient to undergo a period of starvation thereby significantly compromising the necessary increased calorie intake following burn injury. Repeated general anaesthesia is not without risk in this population but may be a necessary course to take if other methods fail.

The most suitable analgesic plan for a procedure requires knowledge of what is likely to occur and must take into account local resources and staff skills. A wound inspection may be best undertaken in an operating theatre under general anaesthesia if debridement is thought likely. A dressing change in a low dependency area will require the patient to remain conscious throughout and we use a technique of oral ketamine and midazolam [78]. Infusions of the opiates fentanyl, alfentanil and remifentanyl, with or without sedative

agents such as propofol have been described earlier in this review as providing effective control. The use of patient-controlled sedation with propofol/alfentanil has been shown to be safe and give higher satisfaction and patient preference than anaesthetist-controlled infusions, despite no improvement in pain score [68]. The sense of control appears to be reassuring and beneficial to the patient. Ketamine/midazolam pain-controlled analgesia is similarly successful [113].

Less stimulating procedures may be undertaken with oral, intranasal or transmucosal opiates. Entonox is a useful adjunct in all cases.

Feedback is essential to guide management of subsequent therapeutic events. Appropriate pain relief can be standardised locally by the use of a step-ladder such as shown in Fig. 3. As the nociceptive input for the procedure reduces or increases or the patient report more or less pain, the analgesic plan may be selected from up and down the ladder.

This is the area of burn pain management where non-pharmacological methods have the most to offer. Resources available will vary between departments and suitability differs between patients, but their role should always be considered.

The paediatric population have unique psychological needs during burns procedures. Parental presence [114], play therapy and other distraction techniques [108] have a role to play in alleviating unnecessary suffering. The drugs used successfully are similar to the selection in adults and this specialist area is comprehensively discussed by others [115].

### 7.4. Post-operative pain control

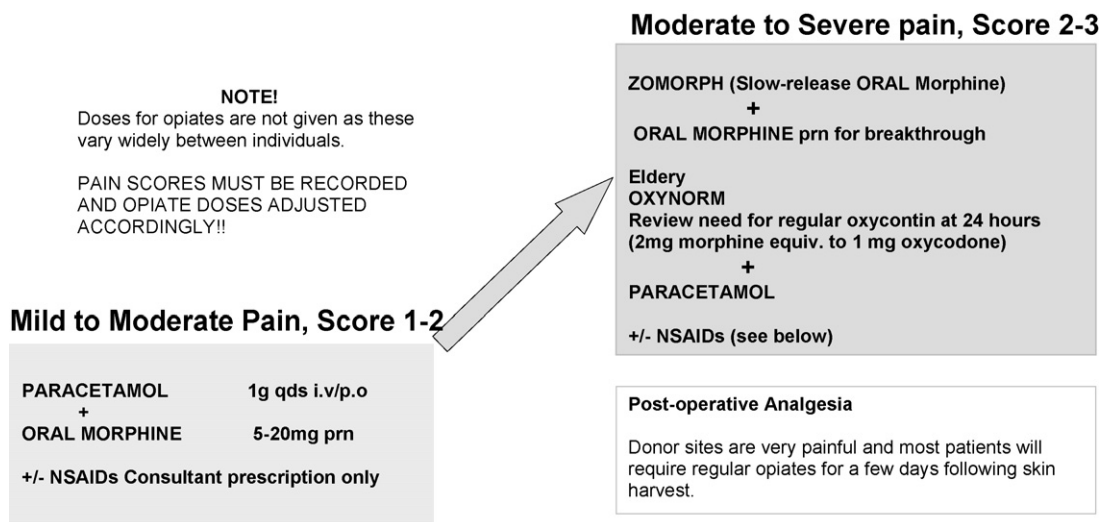
Operative procedures will alter levels of pain experienced, whether the procedure is one of simple debridement, reconstruction or skin grafting. The pain may worsen, or improve following the application of a padded or movement limiting dressing. The baseline pain control will require a review in view of the surgery undertaken and the frequency of pain assessment should increase in the post-operative period to optimise the likelihood of achieving adequate analgesia promptly.

Analgesic techniques	Example of drugs to be considered	Example of suitable procedure
General anaesthesia administered by anaesthetist		Wound debridement and grafting Unable to tolerate steps below
Conscious sedation administered/supervised by trained practitioner	i.v opiates +/- sedative as infusion or PCA  i.v/ po ketamine/midazolam*	Large area dressing change in stable patient Large area staple removal
Analgesia administered by nurse	Opiates orally, lozenge or intranasal +/- oral anxiolytic +/- entonox	Small area dressing change Bath
Short-acting analgesia	Entonox	Short burst of pain

↑  
Assess for suitable starting point and step up or down ladder according to pain outcome  
↓

Non-pharmacological techniques to be considered in addition, in all cases.

Fig. 3 – Procedural analgesic step-ladder.



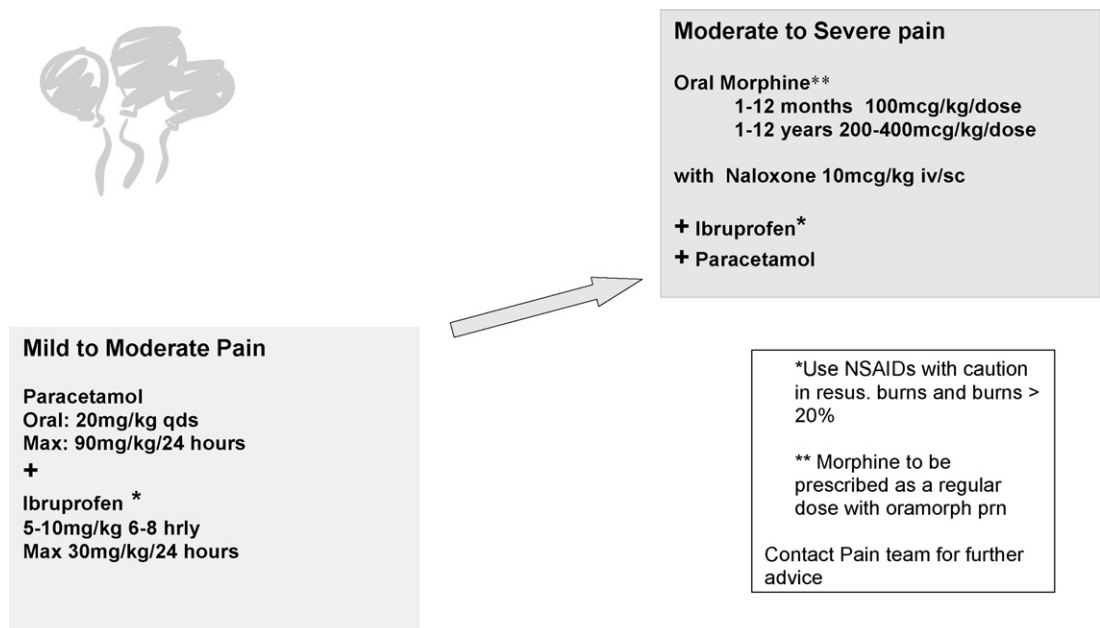
**ASSESS, EVALUATE & REVIEW REGULARLY**

**Fig. 4 – Acute pain guidance for adult burn inpatients.**

Autograft skin donor sites, often harvested from the anterior thigh, are well recognised as being a source of considerable pain for 10–14 days, and this frequently exceeds that from the burned area. Appropriate regional nerve blockade, such as of the femoral nerve, lateral cutaneous nerve of the thigh plus a 3 in 1 and fascia iliac compartment blocks can be highly effective [116,117]. Topical application of local anaesthetic directly to the dressing directly covering the wound is a useful adjunct technique [118]. The need for regular opiates should be anticipated, and NSAID use is suitable in patients without contra-indications.

Some painful areas may lend themselves to management with regional or local anaesthetic blocks. The use of central blockade such as epidural analgesia is limited by concerns of catheter colonisation and infection. Additionally the ongoing ward care needs to be attended to by appropriately trained staff.

A pro-active approach to procedure related pain is of benefit intra-operatively. Staples used to secure skin grafts have a role in surgical procedures, but will be require with a potentially painful removal procedure. The use of sutures or skin glues may be more appropriate in selective patients, particularly children.



**ASSESS, EVALUATE & REVIEW REGULARLY**

**Fig. 5 – Acute pain step-ladder for paediatric burn inpatients aged (1 month–12 years).**

## 8. Standardisation and guidance

The input of pain specialists is, in our experience, a positive addition to the care of the burn patient. This allows co-ordination of the multidisciplinary pain management, the development of local guidelines for all common situations, and continuous education of all staff contributing to the service. The service should aim to provide leadership and be cautious not to deskill other practitioners [119].

Analgesic guidelines are useful in managing burn pain [120,121], and those used at St. Andrews Centre in Chelmsford are shown in Figs. 4 and 5. Successful implementation of protocols and algorithms is dependent on comprehensive introduction of these as evidence-based tools [122]. Following an audit on pain during the first 48 h at our institution the pain team introduced a protocolised approach to managing pain during this period, see Fig. 6. The use of a simple algorithm and pre-printed prescriptions allows application of effective doses of opioids to be established early in the burn patient's stay [123].

The importance of ongoing education for all staff caring for burns patients cannot be overemphasised. Knowledge and attitudes of nurses have been identified as causative factors of deficient practice in pain management [27-29,124], and similar problems are attributed to the lack of education for undergraduate and newly qualified doctors [125,126]. Worryingly a local self-evaluation questionnaire audit showed high levels of confidence prescribing and converting opioid doses, but no correlation between the prescribers' level of confidence and their actual knowledge of the action and properties of opioid drugs.

We addressed staff education in the following ways:

1. Integration of the pain team into the burns team.
2. Weekly consultant led pain rounds.
3. Teaching session provided for all newly appointed staff, medical and nursing.
4. Rolling programme of training and education in place.
5. Problems, poor practice or changes in patient management discussed with staff involved at the time.

### Adult admission pain assessment programme ( 24-48hrs)

Mid Essex Hospital Services NHS Trust      St Andrews Burns Unit

Hospital No.....		Surname.....		First Name.....	
Date.....					
Prescribe analgesia as	*oramorph po (reg 4hrly)	<input type="checkbox"/> (tick)	Dose ____mg		
PLUS	oramorph po (prn 1hrly)	<input type="checkbox"/> (tick)	Dose ____mg		
PLUS	paracetamol 1g qds (reg)	<input type="checkbox"/> (tick)			
PLUS	naloxone 200-400mcg iv prn	<input type="checkbox"/> (tick)			

\*Suggested doses:      66 – 100kg = 15mg x 4hrly, 15mg prn 1hrly  
 45 - 65.5kg = 10mg x 4hrly, 10mg prn 1hrly  
 Consider reduced dose for the elderly (>70 yrs)

**Pain scores: 0 none, 1 mild, 2 moderate, 3 severe**

**Sedation scores: 0 awake, 1 easy to rouse, 2 drowsy but rousable, 3 difficult to rouse**

First 24 hours (2 hourly assessment)

Time													
Pain													
Sedation													

Second 24 hours (2 - 4 hourly assessment)

Time													
Pain													
Sedation													

**Review pain scores and patient's need for rescue (prn) opiates at 24 hours.. Total dose of oramorph required to achieve a of pain score 0-1 to be prescribed as appropriate either as prn only or regularly with prn (most likely).**

**Moderate/Severe**  
 Zomorph (or oxycontin) bd  
 Paracetamol 1g qds  
 PRN oramorph/oxynorm 1 hrly

**Mild/Moderate**  
 Paracetamol 1g qds  
 PRN oramorph /oxynorm 1hrly

### AFTER 24 HOURS START STANDARD PAIN ASSESSMENT CHART

Fig. 6 – Adult admission pain assessment programme (0–48 h).

6. Link nurses appointed and provided with specialist training.

Re-audit has shown some promising data reflecting improvements in pain assessment records and provision of analgesia.

## 9. Summary

Burn pain is a unique and complex challenge for all specialist staff and their patients. Understanding the pathophysiology of burns and the pharmacological and non-pharmacological treatment of burn pain should improve the patient experience. The fundamental goal is to give pain control a high clinical priority through comprehensive training, education and support across all disciplines, and to strive for consistently evolving best practice. Staff should be aware of all the available options, and individual units should have locally generated guidelines available such that all staff can contribute to high quality care, regardless of their level of experience, resources or their speciality.

Good pain control for the individual with pain from a burn depends on assessment, prompt analgesia titrated to effect, and regular evaluation as a continuous cycle of care.

## Conflict of interest

As authors of this review article, we confirm that we have no conflict of interest to declare.

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