Pain is a common problem in patients being managed on a critical care unit (CCU). In recent large multicentre studies, 49–64% of patients reported severe pain. However, only 14.9% were unhappy with the pain management they had received. The International Association for the Study of Pain defines pain as ‘an unpleasant sensory or emotional experience that is associated with actual or potential tissue damage, or which can be described in terms of such damage’. Therefore, pain perception is influenced by many factors such as personality, cultural background, unfamiliar surroundings and fear. This makes the assessment of pain difficult, especially in CCUs because patients may be sedated, intubated, frightened, confused or at the extremes of age.

Patients in critical care areas (ICU and HDU) may have pain not only arising from their primary disease but also from therapeutic procedures (e.g. endotracheal tube suctioning, line insertion). Disrupted sleep and anxiety can increase pain perception and prolonged immobility can cause painful joints, contractures or decubitus ulcers. Notwithstanding humanitarian considerations, failure to manage pain effectively may result in increased sympathetic drive leading to cardiovascular instability, vasosconstriction, diaphragmatic splinting, basal atelectasis, increased oxygen consumption and tissue ischaemia.

Assessment of pain in critical care

Assessment is influenced by past medical history; in particular, past pain experiences. Previous chronic analgesic use may alter a patient’s requirements in an acute situation. If a patient is able to speak and communicate, verbal report is naturally most important. Furthermore, analogue scores (visual or numerical) or verbal descriptor scales (e.g. mild, moderate, severe) may be used. The visual analogue can also be presented as a thermometer or as Wong Baker faces. Although it is ideal to evaluate pain in many dimensions, and should be possible in the HDU setting, it is less likely that patients on ICU would be able to complete the McGill Pain Questionnaire or Brief Pain Inventory. A review of these techniques was published recently in this journal (see key references).

Analgesia should be considered in conjunction with sedation which may be required to help patients tolerate the endotracheal tube or the ventilator. The ideal situation is a patient who is co-operative and able to control his/her own analgesia, environment and position. Analgesic and sedative agents should not be used as an automatic response to an unhappy patient. There is need to consider other factors such as environment, positioning and boredom.

It is more common for critical care clinicians to evaluate pain in patients who are unable to communicate. Naturally, one would look for physiological signs of sympathetic overdrive. However, in critically ill patients on inotropic support, this may not be easy. Behavioural clues may be helpful (e.g. posture, vocalization). The various sedation scoring systems that have been developed do not specifically address pain. Whipple and colleagues found that doctors and nurses underestimated pain. In their study of critically ill patients, 95% of doctors felt that their patients had received adequate pain relief; however, 74% of these patients stated that their pain was moderate or severe. The use of a detailed, standardized pain assessment and intervention algorithm that incorporates physiological and behavioural indicators may assist ICU staff in

Key points

Assessment and management of pain in the critically ill is difficult but standardised assessment and an intervention algorithm improves results.

A multidimensional approach should be adopted, including pharmacotherapy, regional analgesia, sedation and environmental considerations.

Drugs other than opioids can be used.

Regional analgesia has an important role in some patients and may reduce length of stay.

In the critically ill, pain during hospitalisation is the variable most commonly associated with persistent pain after discharge.

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relatively accurate assessments of pain intensity. Scales have been developed for neonatal and paediatric practice along these lines (e.g. CHEOPS, COMFORT, Riley Infant Pain Scale). The implementation of systematic practices for assessment of pain has been shown to decrease pain intensity scores in cardiac surgery patients. It is possible to adapt some paediatric objective pain scales for adult use.

### Methods of analgesia

#### Systemic opioids

It has become routine to administer opioids intravenously on a CCU because the bioavailability of intramuscular or subcutaneous opioids is unpredictable in critically ill patients with poor perfusion. They can be administered by continuous infusion or via a patient-controlled analgesia (PCA) device, which requires a conscious and coherent patient. Protocol-based therapy has been shown to improve analgesia and sedation on the ICU. Table 1 shows typical dose ranges when used in adults.

Continuous infusions are simple and the choice of opioid varies between different critical care units. Nurse-directed adjustment of the infusion rate to achieve a set pain (or sedation) score is now common practice, especially for ventilated patients.

Morphine is a common choice and easy to use. However, its metabolites are excreted by the kidneys and care should be taken to reduce the dose in patients with renal dysfunction. Morphine is not removed by haemodialysis. It has been noted that there is an inhibition of water and electrolyte excretion after morphine administration, possibly because morphine increases the secretion of antidiuretic hormone. However, this effect has also been seen in hypophysectomized rats. Morphine may promote histamine release and consequent bronchoconstriction and/or pruritus. Diamorphine is a pro-drug and has no benefits over morphine as an intravenous infusion. It requires reconstitution from its powdered form.

Fentanyl is metabolised in the liver and approximately 70% of the administered dose is excreted in the urine. Extraction during haemodialysis is not known precisely; it does not increase antidiuretic hormone secretion.

Alfentanil has a shorter duration of action than fentanyl (terminal half-life 1.6 h). However, more than 90% is metabolised in the liver; hence its action is prolonged in patients with liver failure. The clearance of alfentanil is not affected by renal dysfunction.

Meperidine (pethidine) has no benefits over morphine or fentanyl and has several drawbacks. Its duration of action is longer than fentanyl and marginally less than morphine. Furthermore, its metabolite (normeperidine) causes convulsions. Meperidine has anticholinergic properties and may cause tachycardia. It is not removed by haemodialysis. It is traditionally taught that meperidine is the opioid of choice in pancreatitis because morphine causes spasm of the sphincter of Oddi. However, there are no studies comparing morphine and meperidine in this situation.

Remifentanil is a very short acting synthetic opioid (metabolised by plasma and tissue esterases). Its elimination half-life is 10–20 min and offset of action is predictable, even after prolonged infusion. Although it is now being marketed for the critical care setting, it is very expensive if used routinely.

#### Patient-controlled analgesia

PCA requires an awake and co-operative patient who is able to press the demand button. Children as young as 8 years of age have used PCA successfully. The commonest choice of opioid for PCA is morphine. However, fentanyl and meperidine are also used. Analgesia should already be established when a PCA device is started. The use of a background infusion has been shown to increase opioid use and increase side-effects, including sedation and respiratory depression. Hence, the routine use of background infusions with PCA is discouraged. However, there may be role for a background infusion in patients who are not opioid naïve.

#### Local analgesia

**Neuroaxial block**

Epidural and, less commonly, subarachnoid catheters are used frequently on the CCU. The use of epidural catheters for analgesia following major surgery has been shown to decrease pulmonary, gastrointestinal, cardiovascular and thrombo-embolic complications in the postoperative phase. Epidural analgesia has also been shown to be superior to systemic narcotics in critical care patients in terms of analgesia and recovery. In a study comparing

| Table 1 Typical dose ranges for intravenous opioid infusions for ventilated adult patients |
|------------------|------------------|
| Morphine         | 1–5 mg h⁻¹        |
| Fentanyl         | 1–4 mcg kg⁻¹ h⁻¹  |
| Alfentanil       | 25–50 mcg kg⁻¹ h⁻¹|
| Remifentanil     | 0.1–0.25 mcg kg⁻¹ min⁻¹|
epidural and intravenous morphine for oesophagectomy, patients in the epidural group had a reduction in intensive care stay of 2.5 days and total hospital stay of 7 days. A more recent study has shown that carefully titrated epidural analgesia and physiotherapy in oesophagectomy patients was associated with earlier extubation and discharge. A retrospective study of case mix adjusted mortality in critically ill patients showed a reduction in standardised mortality from 1.41 to 0.46 in those patients receiving central neuroaxial blockade.

Epidural catheters should ideally be placed close to the relevant dermatomal segments. Although the risks increase with thoracic catheter placement, this has several benefits. First, less drug is required. Second, the block of only thoracic segments will allow mobilization of the patient and may reduce the risk of venous thrombosis or decubitus ulcers. Intrathecal catheters are placed in the lumbar region but offer rate dependent analgesia to T6.

The main concerns in a critically ill patient are risks of infection and epidural haematoma formation.

**Infection**
The epidural catheter site should be checked everyday for erythema or discharge. Darchy and colleagues studied the risk of epidural catheter infection in 75 patients who received epidural analgesia for more than 48 h on an intensive care unit. Four patients (5.3%) had epidural catheter infection but in no patient was spinal space infection diagnosed. Local inflammation (erythema or local discharge) was seen in 27 patients and 9 of these had infection. The presence of both erythema and local discharge was a good predictor of infection. There was no positive epidural culture in patients with erythema alone or no local signs. Epidural catheter infections were not increased by concomitant infection at other sites, antibiotics, duration of epidural insertion or level of catheter placement. However, this study may have lacked sensitivity as the number of patients was small. To our knowledge, there are no reports suggesting that the placement of an epidural catheter in a patient with sepsis (e.g. septicaemia) increases the risk of epidural sepsis. However, it would seem prudent not to do so.

The maximum duration for the insertion of an epidural catheter is debatable. A commonly accepted duration is 3 days. In patients with chronic pain, such catheters have been left for weeks; however, they are tunnelled and the patients are usually not septic and immunocompromised.

**Coagulation status**
Coagulation is often deranged in the critically ill and neuroaxial blockade should be avoided under these circumstances. In our unit, we expect the coagulation tests (activated partial thromboplastin time, international normalised ratio) to be normal and platelets to be > 100,000 per ml.

Care should also be taken with patients who are receiving fractionated or unfractionated heparins. Certainly, neuroaxial blockade should only be undertaken at least 4 h (unfractionated, standard heparin) and 12 h (fractionated or low molecular weight heparin) after administering the dose. Similar care should be taken for removal of the epidural catheter. As many as 60% of clinically important spinal haematomas occur after removal of epidural catheter. Neurological examination is often difficult in a sedated intensive care patient. Insertion should ideally take place with the patient awake to rule out direct neural damage and return of movement confirmed as soon as possible. Although it is possible to measure levels of anti-Factor Xa activity (for low molecular weight heparin), the current American guidelines do not recommend this as the risk of bleeding cannot be accurately predicted (Table 2).

**Peripheral nerve blocks**
Analgesia can be provided with peripheral nerve blocks in some patients on the intensive care unit (e.g. femoral nerve infusions for lower limb problems, interscalene for the upper limb). In some institutions, paravertebral blocks are maintained with a catheter; this has the benefit of avoiding sympathetic block. Intrapleural catheters infusing local anaesthetic have been utilised for unilateral thoracic analgesia. However, its placement can be difficult in patients who are ventilated and a chest drain on the ipsilateral side might complicate matters.

**Non-opioid analgesics**
It is important to remember the use of other non-opioid analgesics on the ICU. In recent years, the α2-agonist dexmedetomidine has been used. It has both analgesic and sedative properties and is associated with cardiovascular stability, morphine sparing and minimal effects on the respiratory system. Regular paracetamol can be of benefit and is easily administered via a nasogastric tube. Its suppository preparation may also be useful. NSAIDs should
be used with caution in the critically ill; their effects on renal function and the gastrointestinal tract are well documented. They may also interfere with platelet function. COX-2 selective inhibitors (celecoxib, rofecoxib, parecoxib) are as effective as regular NSAIDs. They are less likely to cause gastric ulceration and have little effect on platelet function. However, there is no suggestion as yet that these agents are safer with respect to renal function; the same precautions apply.

Treatment of neuropathic pain
Neuropathic pain on the intensive care unit is not an area that has been studied in detail. The incidence of critical illness polyneuropathy in long-term intensive care patients has been reported as 58–96%. Some of these neurophysiological changes are seen 2 weeks after CCU admission. Sensory nerves can be involved in critical illness neuropathy and Leitjen has found that 83% of patients had sensory symptoms in their feet which lasted longer than their motor problems. Motor or mixed (motor and sensory) neuropathy can be demonstrated up to 5 years after ICU discharge in more than 90% of long-stay patients.

Neuropathic pain may be associated with conditions such as traumatic or surgical nerve damage and nerve compression. It does not respond well to analgesics used for nociceptive pain. Amitriptyline (10–25 mg) can be very useful and is unlikely to cause arrhythmias at this dose. However, its onset of action may be slow and is administered orally. Gabapentin is renally excreted and has very few drug interactions. Its major side effects are dizziness, ataxia and drowsiness. Carbamazepine is effective in neuropathic pain but induces liver enzymes and has several drug interactions and side-effects.

Non-pharmacological treatment
Pharmacotherapy and nerve blocks form only one dimension of pain management on the ICU. Care must be taken to make the patients as comfortable as possible (e.g. sedation, noise levels and temperature of the unit). We should also predict activities that may cause pain (e.g. turning, physiotherapy) and administer analgesia beforehand.

Long-term follow up
The prevalence of chronic pain following admission to the ICU is not an area that has been studied in detailed. Of patients who reported severe pain during hospitalisation, 40% report pain 6 months after discharge. There is a 38% increase in the incidence of chronic pain in survivors of acute respiratory distress syndrome when compared with control groups. In a large study of 5000 critically ill patients, it was found that pain during hospitalisation was the variable most strongly associated with chronic pain after discharge. Of further interest was the fact that this was reported in patients who had conditions not normally associated with pain such as chronic obstructive pulmonary disease or heart failure. Therefore, it is likely that good pain management on the ICU will reduce the likelihood of chronic pain after discharge.

Key references
Buggy DJ, Smith G. Epidural anaesthesia and analgesia: better outcome after major surgery? BMJ 1999; 319: 530–1

See multiple choice questions 130 and 131.