ACE-Inhibitors, Beta(β)-Blockers

Definition
Drugs used to lower blood pressure and relieve heart failure.
▶ Postoperative Pain, Acute Pain Management, Principles

Acetaminophen

▶ Paracetamol
▶ Postoperative Pain, Paracetamol
▶ Simple Analgesics

Acetylation

Definition
The acetyl group of acetylsalicylic acid (aspirin) binds to serine 530 in the active site of COX–1, or serine 516 in the active site of COX–2. This prevents the access of arachidonic acid to the catalytic site of the cyclooxygenase.
▶ Cyclooxygenases in Biology and Disease

Acetylcholine

Synonyms
Ach; ACh

Definition
Acetylcholine is a neurotransmitter synthesized from choline and acetyl coenzyme A. It is localized in large reticular formation neurons, and is the chemical mediator in the synapse of a motor endplate. The electrical signal of the motor nerve terminal causes release of many packets of acetylcholine. The packets are released into the synaptic cleft, where receptors in the postjunctional membrane of the striated muscle fiber membrane convert the chemical signal to an electrical signal (a propagated action potential), which can produce muscle contractile activity. Normally, an occasional acetylcholine packet is released spontaneously by the nerve terminal without a nerve signal. Each packet produces a miniature endplate potential in the muscle fiber, but its amplitude is too small to be propagated. Myofascial trigger points are associated with excessive spontaneous release of acetylcholine packets in affected endplates.
▶ Myofascial Trigger Points
▶ Thalamic Neurotransmitters and Neuromodulators

Acetylcholine Receptors

Definition
Receptors for the neurotransmitter acetylcholine, which can be distinguished into muscarinic (G protein coupled) and nicotinic (ion channel) receptors.

Ach, ACh

▶ Acetylcholine

Acidosis

Definition
Acidosis is the disturbance of the acid-base balance, characterized by acidity (decreased pH) by accumulation of protons, caused by injury, inflammation or ischemia. Acidosis is an important source of pain. In humans, it produces non-adapting nociceptor excitation and contributes to hyperalgesia and allodynia in inflammation.
▶ Acid-Sensing Ion Channels
▶ TRPV1, Regulation by Protons

Acid-Sensing Ion Channels

NICHOLAS VOILLEY, MICHEL LAZDUNSKI
Institut de Pharmacologie Moleculaire et Cellulaire, Valbonne, France
voilley@ipmc.cnrs.fr

Synonyms
ASIC; ASIC1a; brain sodium channel 2 (BNC2, BNaC2); ASIC1b: ASICβ; ASIC2a: mammalian degenerin 1 (MDEG1), brain sodium channel 1 (BNC1, BNaC1); ASIC2b: mammalian degenerin 2 (MDEG2); ASIC3: dorsal-root acid-sensing ion channel (DRASIC)

Definition
Acid-Sensing Ion Channels (ASICs) are membrane protein complexes that form depolarizing ion channels present on peripheral and/or central neurons. These channels are opened by extracellular protons. Their activation induces action potential triggering on neurons after an extracellular pH decrease to acidic values. Such tissue ▶ acidosis occurs during ▶ inflammation or ▶ ischemia, and is a major source of pain.
Characteristics

ASICs are membrane protein complexes formed by four subunits among the six characterized isoforms (Fig. 1). The isoforms are coded by four different genes, two of them spliced in two variants: ASIC1a and ASIC1b, ASIC2a and ASIC2b, ASIC3 and ASIC4 (Chen et al. 1998; Garcia-Anoveros et al. 1997; Grunder et al. 2000; Lingueglia et al. 1997; Waldmann et al. 1997a; Waldmann et al. 1997b). Each subunit is 510 to 560 amino-acids long, with two transmembrane domains and a large extracellular loop, and belongs to the ENaC/DEG/ASIC family (Fig. 2) (Waldmann and Lazdunski 1998). The properties of the channels (i.e., activation and inactivation kinetics, pH sensitivity, ion selectivity) vary according to their subunit composition. For example, ASIC1a opens transiently for pH values from 7.2 and under with a pH₅₀ of 6.2, and is sodium selective (Waldmann et al. 1997b) (Fig. 3). ASIC3 generates a biphasic current: the transient current is followed by a sustained current that lasts as long as the pH is low (Waldmann et al. 1997a) (Fig. 3). It has been associated with cardiac ischemic pain (Sutherland et al. 2001), and ASIC3-deficient mice display alterations in the modulation of high-intensity pain stimuli (Chen et al. 2002). Some isoforms have no activity when expressed alone: the isoform ASIC2b modifies the properties of the other subunits when present in heteromeric complexes (Lingueglia et al. 1997); the isoform ASIC4 has absolutely no activity, either alone or with other isoforms (Grunder et al. 2000). The association of ASIC3 and ASIC2b forms a channel with an ion selectivity and a pH sensitivity that is similar to those of an endogenous native current widely expressed on sensory neurons (Benson et al. 2002; Lingueglia et al. 1997), and that can participate in the sustained neuronal activity observed in lasting acidic pain states such as inflammatory and ischemic pain.

ASIC isoforms can be localized exclusively in sensory neurons and particularly nociceptors (ASIC1b and ASIC3), or in both sensory and central neurons (ASIC1a, ASIC2a and 2b). Their role as pH-sensors on sensory neurons occurs particularly in pathophysiological situations when tissue pH decreases. During inflammation, ischemia, around a fracture or a tumor, the extracellular pH can be lower than 6. This acidosis is directly responsible for pain feelings, and bicarbonate solutions used to be infused in arthritic joints to diminish pain.

ASIC currents are sensitive to amiloride but with relatively low affinities (around 10 μM). ASIC1a is also potently inhibited by a peptidic toxin isolated from tarantula venom (Escoubas et al. 2000). It has been shown that NSAIDs directly block recombinant and native ASIC currents (Voilley et al. 2001). Ibuprofen and flurbiprofen inhibit ASIC1a-containing channels, and aspirin, salicylate and diclofenac inhibit ASIC3-containing channels. The blocking action of these NSAIDs is direct on ASICs and is independent of cyclo-oxgenase inhibition (Voilley 2004). It prevents sensory neurons from triggering action potentials when submitted to acidic pH (Voilley et al. 2001). The effective concentrations are in the same range as the therapeutic doses necessary for analgesic effect. This pharmacology can explain some of the pain release observed with NSAIDs in experimental tissue acidosis and inflammation (Steen et al. 1996). During inflammation, the mRNA levels of the ASICs are increased 6–15 fold, and this in vivo increase is completely abolished by treatments with glucocorticoids or NSAIDs (Voilley et al. 2001). This increase is correlated to a higher level of ASIC currents on sensory neurons, and leads to a greater excitability of these cells under pH variations (Mamet et al. 2002). Some pro-inflammatory mediators, and particularly NGF, are directly responsible for the observed increase in ASIC expression and activity. Indeed, NGF controls the expression and the transcriptional regulation of the ASIC3 encoding gene (Mamet et al. 2002; Mamet et al. 2003). Moreover, ASICs are also expressed de novo by a greater number of neurons, and participate in the recruiting of sensory fibers that become nociceptive neurons (Mamet et al. 2002; Voilley et al. 2001).

ASICs can also undergo post-translational regulations. Pro-inflammatory mediators like prostaglandins and bradykinin activate protein kinase cascades, which participate in sensory neuron sensitization. ASIC2a protein can be directly phosphorylated by protein kinase C (PKC). This phosphorylation, which is facilitated by an interaction with the PICK–1 protein, has a positive effect on the activity of the channel (Baron et al. 2002).
Acid-Sensing Ion Channels, Figure 2 Phylogenic tree of the ENaC/DEG/ASIC family. The family is constituted mainly by the vertebrate epithelial sodium channel subunits (ENaC), the small FMRF-amide activated sodium channel (FaNaC), the mammalian acid-sensing ion channels (ASICs) and the nematode Caenorhabditis elegans degenerins (MEC and DEG). The proteins share homologies in sequence and structure. Each member protein has a simple structure consisting of 2 transmembrane domains and a large extracellular loop.

Acid-Sensing Ion Channels, Figure 3 Measurement by electrophysiology of the currents generated by ASIC cDNAs transfected in mammalian cells when an acidic stimulus is applied. ASIC1a, ASIC1b and ASIC2a display a transient activation. ASIC3 displays a transient current followed by a sustained phase. ASIC2b and ASIC4 do not bear any activity. In heteromers, ASIC2b confers a plateau phase with a cationic non-selective permeability. For each current type, the half-activation pH (pH$_{50}$) and the sodium over potassium selectivity ($P_{Na}/P_{K}$) are given; when the current is biphasic, both values (peak-plateau) are given.
ASICs present on sensory neurons are thus implicated in acidic pain sensing, neuron sensitization, and onset and maintenance of inflammatory hyperalgesia and allodynia.

References

Acinar Cell Injury

- Visceral Pain Model, Pancreatic pain

Acrylamide

An acrylic chemical used in industry and also in the laboratory (gel electrophoresis), with intoxication resulting in peripheral nerve disease (acrylamide neuropathy).

- Toxic Neuropathies

Action

A readiness to change stage, in which a person is taking concrete steps to change his or her behavior and/or environment.

- Motivational Aspects of Pain

Action Potential

Definition

Electrical potential actively generated by excitable cells. In nerve cells, the action potential is generated by a transient (less than 1 ms) increase in Na+ and K+ conductances, which brings the membrane potential to the equilibrium potential of Na+. Immediately afterwards, the membrane repolarizes and becomes more negative than before, generating an action potential.

- Demyelination
- Molecular Contributions to the Mechanism of Central Pain
- Nociceptor Generator Potential

Action Potential Conduction of C-Fibres

- Mechano-Inensitive C-Fibres, Biophysics

Action Potential in Different Nociceptor Populations

- Nociceptors, Action Potentials and Post-Firing Excitability Changes
**Actiq®**

**Definition**

Actiq® is a transmucosal fentanyl system that produces more significant pain relief at 15, 30, 45, and 60 minutes following administration (over a recommended 15 minutes) in opioid tolerant cancer patients.

▶ Postoperative Pain, Fentanyl

---

**Activa®**

**Definition**

The Brand name (Medtronic, Minneapolis, USA) of a system of electrodes, connectors, and implantable pulse generators for the treatment of movement disorders, pain and epilepsy, by stimulation of the basal ganglia, midbrain and thalamus.

▶ Pain Treatment, Spinal Cord Stimulation

---

**Activation Threshold**

The current level needed to initiate an action potential in a nerve fiber.

▶ Pain in Humans, Electrical Stimulation (Skin, Muscle and Viscera)

---

**Activation/Reassurance**

**GEOFFREY HARDING**  
Sandgate, QLD, Australia  
geoffharding@uq.net.au

**Synonyms**

Reassurance and Activation

**Definition**

Activation and reassurance are interventions that have been used for the treatment of acute low back pain. They involve having the practitioner gain the patient’s confidence that they do not have a serious cause of pain, and that remaining active, or restoring activity, is beneficial for their recovery.

---

**Characteristics**

Systematic reviews have shown that bed rest is neither appropriate nor effective for acute low back pain (Koes and van den Hoogen 1994; Waddell et al. 1997). Bed rest offers no therapeutic advantages, and is less effective than alternative treatments in terms of rate of recovery, relief of pain, return to daily activities, and time lost from work. By inference, these results support keeping patients active. Nevertheless, patients may harbour fears or misconceptions about their pain, which may inhibit their resumption of activities. Explanation and reassurance are required to overcome these fears.

---

**Evidence**

The study of Indahl et al. (1995) constitutes a landmark in the management of non-specific musculoskeletal conditions. It was the first rigorously controlled trial to demonstrate long-term efficacy for an intervention based on reassurance and activation, with no passive interventions. Patients were provided with a biological model of their painful condition. They were assured that light activity would not further injure the structures that were responsible for their pain, and was more likely to enhance the repair process. The link between emotions and musculoskeletal pain was explained as a muscular response. Patients were told that increased tension in the muscles for any reason would increase the pain and add to the problem. It was explained how long-standing pain and associated fear could create vicious cycles of muscular activity that caused pain to persist. It was strongly emphasised that the worst thing they could do would be to act in a guarded, over-cautious way.

Regardless of clinical and radiographic findings, all patients were told to mobilise the affected parts by light, non-specific exercise, within the limits of intense pain exacerbation. No fixed exercise goals were set, but patients were given guidelines and encouraged to set their own goals. Great emphasis was placed on the need to overcome fear about the condition and associated sickness behaviour. Misunderstandings about musculoskeletal pain were dealt with.

The principal recommendation was to undertake light, normal activities, moving as flexibly as possible. Activities involving static work for the regional muscles were discouraged. No restrictions were placed on lifting, but twisting when bending was to be avoided. Acute episodes of pain in the affected region were to be treated as acute muscles spasm, with stretching and further light activity. Instruction was reinforced at three months and at one year.

The actively treated patients exhibited a clinically and statistically significant difference from the control group with respect to decrease in sickness-leave. At 200 days, 60% in the control group, but only 30% in the intervention group, were still on sick-leave. A five-year follow-
up demonstrated that these differences were maintained (Indahl et al. 1998). Only 19% of the intervention group were still on sick-leave at five years, compared with 34% in the control group.

The results of Indahl et al. (1995) were corroborated by another study (McGuirk et al. 2001). The intervention was based on the principles set by Indahl, and focused on identifying the patient’s fears, providing explanation, motivating patients to resume activities, and helping them maintain those activities. This approach achieved greater reductions in pain than did usual care, with fewer patients progressing to chronic pain, less use of other health care and greater patient satisfaction.

**Principles**

Providing reassurance and motivating patients into activity are skills that have to be learnt. It is not enough to simply give information in the form of test results, diagnoses, prognoses or proposed treatments. The manner of the consultation and the doctor’s ability to empathize with the anxious patient is a pre-requisite to any “motivational interview” (McDonald and Daly 2001). In order to develop empathy, a long consultation may be required. However, reassurance can nevertheless be achieved through a systematic series of shorter consultations (Roberts et al. 2002).

Interviewing techniques can be adapted to achieve an “educational outcome” (Arborelius and Bremberg 1994). The process of consulting or interviewing in a motivational way has been detailed (Kurtz et al. 2005), and is quite different from a normal medical interview that is geared towards collecting and collating information in as short a time as possible. Naturally, the educational (or motivational) interview demands more time from the practitioner. However, it is more effective in terms of changing behaviour towards self-motivation (Miller and Rollnick 2002). The doctor must establish an initial rapport with the patient. In general, one should greet each patient as if they were a friend of a friend, not a complete stranger. The doctor should not give the impression of rushing. The concerns with which patients present can be encapsulated by Watson’s quartet (Watson 1999): “I hurt”, “I can’t move”, “I can’t work”, and “I’m scared”. The latter can be expanded to encompass: what has happened?; why has it happened?; why me?; why now?; what would happen if nothing were done about it?; what should I do about it, and who should I consult for further help?

It is useful to ask patients what they think has caused their problems – the answers given to this question are often surprising, and can sometimes hold the key to guiding patients through a complex biopsychosocial landscape. There are no routine responses to these issues and questions. The practitioner must be prepared to respond in an informed, convincing, and caring manner. One example of an explanation might be:

“Well, we don’t actually know why you have developed this but there are many reasons, and some of them come down to just bad luck. It might be related to an event or an injury, but these are often hard to track down. At the end of the day I can say that there doesn’t seem to be anything that you could have avoided, and the problem is one that is not serious – it is painful, but not harmful. It might happen again and it might not.

There are lots of people who will tell you that it’s “this” or “that” which has caused it, but frankly this is speculation in most cases. Some people will tell you that it’s because you have weak muscles, but you know that the fittest athletes in the world get injured from time to time, and there are many people out of condition who never get injuries. Others might say that it is your posture. But you have presumably not altered your posture in many years and you have never had the problem before. So trying to fix your posture in a major way might be pointless at this stage. I can say that there is no disease process going on and there are no broken bones or things that the surgeons have to fix. It’s not something that you will pass onto your children and it will not shorten your lifespan. It might be that you will have to look at the type of work you do, but we will get more of an idea about that as time goes on.”

This sort of explanation takes an enormous amount of time; but short-changing the patient will result in a less-than-effective consultation. The paradox of appearing to have shortage of time will result in no change accomplished, whereas appearing to have “all day” often results in a change occurring in a matter of minutes (Miller and Rollnick 2002).

As the patient raises issues, their narrative should be expanded, with the use of phrases such as: “tell me more about that”. Terms and expressions used by the patient should be checked for meaning, so that the doctor understands what the patient is communicating. Developing rapport relies on the appropriate use of eye contact, expressing concern and understanding, and dealing sensitively with the patient during the physical examination.

A thorough examination is a necessary pre-requisite for gaining the satisfaction (and thus the confidence) of the patient (McCracken et al. 2002). The reasons for examination procedures should be explained. The practitioner can reassure patients by developing an “educational enterprise” (Daltroy 1993). Printed material is an effective reinforcer of tuition (see ▶ Patient Education). Models and pictures serve to explain concepts about normal structure and pathology. The language used should be appropriate to the patient and understood by them. Alarming and distressing terms should be avoided.

When recommending exercises, those exercises should be demonstrated, and the patient’s ability to reproduce them should be observed and confirmed. The same confirmation should be obtained when advice is given about
how the patient will undertake their desired activities. Checking their understanding is what converts the consultation from one in which instructions are simply issued, to one in which the patient is confident about that instruction.

References


Active

This refers to movement of a body part using power generated from one’s own muscle action.

▶ Cancer Pain Management, Orthopedic Surgery

Active Inhibition

Definition

Active inhibition implies that nociceptive processing during the interphase of the formalin test is suppressed by specific inhibitory mechanisms, as opposed to simply reflecting the absence of excitatory input.

▶ Formalin Test

Active Locus

Synonyms

EPN locus

Definition

The motor component of a Myofascial Trigger Point is the active locus, or endplate-noisy locus (EPN locus). From this locus, spontaneous electrical activity, known as endplate noise (EPN), can be recorded. It is related to taut band formation in skeletal muscle fibers.

▶ Dry Needling

Active Myofascial Trigger Point

Definition

An active trigger point is a myofascial trigger point that is causing, or contributing to, a clinical pain complaint. When it is compressed, the individual recognizes the induced referred pain as familiar and recently experienced.

▶ Dry Needling
▶ Myofascial Trigger Points

Activities of Daily Living

Definition

Activity: The execution of a task or action by an individual. Activities of daily living refers to normal physical activity such as getting out of bed, walking (initially with support), sitting, and personal toileting.

▶ Physical Medicine and Rehabilitation, Team-Oriented Approach
▶ Postoperative Pain, Importance of Mobilisation

Activity

Definition

Activity is described as the execution of a task or action by an individual. It represents the individual perspective of functioning. Difficulties an individual may have in executing activities are activity limitations.

▶ Disability and Impairment Definitions
Activity Limitations

**Definition**
Difficulties an individual may have in executing activities.
- Impairment, Pain-Related
- Physical Medicine and Rehabilitation, Team-Oriented Approach

Activity Measurement

**Definition**
A measure of personal activities of daily living (e.g. showering, dressing, toileting, feeding), independent activities of daily living (e.g. cleaning, cooking, shopping, banking), and discretionary activities of daily living (e.g. driving, visiting, leisure activities).
- Pain Assessment in the Elderly

Activity Mobilization

**Definition**
Strategies aimed at maximizing a chronic pain patient’s participation in activities of daily living.
- Catastrophizing

Activity-Dependent Plasticity

**Definition**
This is an alteration in neuronal structure or function due to activation of the neurons.
- Spinothalamic Tract Neurons, Role of Nitric Oxide

Acupuncture

**Definition**
A system of healing that is part of traditional Chinese medicine. It consists of the insertion of thin solid needles into specific points, usually into muscles, on the body that lie along channels or meridians, in order to treat different symptoms.
- Acupuncture Mechanisms
- Alternative Medicine in Neuropathic Pain
- Acupuncture Efficacy

Acupuncture Efficacy

**EDZARD ERNST**
Complementary Medicine, Peninsula Medical School, Universities of Exeter and Plymouth, Exeter, UK
edzard.ernst@pms.ac.uk

**Definition**
- Acupuncture can be defined as the insertion of needles into the skin and underlying tissues at specific sites (acupuncture points) for therapeutic or preventative purposes (Ernst et al. 2001). Sometimes other forms of point stimulation are used, electrical current (electroacupuncture), pressure (acupressure), heat (moxibustion) or laser light (laser acupuncture). Acupuncture is part of the ancient Chinese medical tradition. In recent years, a new style (Western acupuncture) has emerged, which no longer adheres to the Taoist philosophies underpinning Chinese acupuncture but seeks explanations for its mode of action from modern concepts of neurophysiology and other branches of medical science.

**Characteristics**
The evidence for or against the efficacy (or effectiveness) of acupuncture is highly heterogeneous and often contradictory. Thus single trials, even of good quality, may not provide a representative picture of the current evidence. The following section is therefore exclusively based on systematic reviews of controlled clinical trials, i.e. on the totality of the available trial data rather than on a possibly biased selection of it. Whenever more than one such publication is available, the most up to date one was chosen.

**Any Chronic Pain**
One landmark paper summarised the results of 51 randomised clinical trials testing the efficacy of acupuncture as a treatment of all forms of chronic pain (Ezzo et al. 2000). Any type of acupuncture was considered. The studies were rated for methodological rigour using the Jadad score (Jadad et al. 1996). The results revealed a significant association between lower quality studies and positive outcomes. There was no clear evidence to demonstrate that acupuncture is superior to sham acupuncture or to standard treatment. Good evidence emerged that it is better than waiting list (i.e. no acupuncture). The quality of the review was rated “good” by independent assessors (Tait et al. 2002). Depending on one’s viewpoint, one can interpret these findings differently. Acupuncture ‘fans’ would claim that they demonstrate acupuncture to be as good as standard treatments, while sceptics would point out that the data suggest that acupuncture has no more than a placebo effect. Pooling the data for all types of chronic pain is perhaps an approach too insensitive to tease out effects on more defined types of pain. Other
systematic reviews have therefore focussed on more specific targets.

**Dental Pain**

Sixteen controlled trials were available, 11 of which were randomised (Ernst and Pittler 1998). All studies of manual or electroacupuncture were included. Their methodological quality was assessed using the Jadad score (Jadad et al. 1996). The overall results support the role of acupuncture for recurrent headaches but not for migraine or other types of headache. The conclusions were limited through the often low methodological quality of the primary studies. The review was independently rated to be of good quality (Tait et al. 2002).

**Headache**

A Cochrane Review summarised the evidence from 26 randomised or quasi-randomised trials of any type of acupuncture (Linde et al. 2001). Their methodological quality was assessed using the Jadad score (Jadad et al. 1996). The overall results support the role of acupuncture for recurrent headaches but not for migraine or other types of headache. The conclusions were limited through the often low methodological quality of the primary studies. The review was independently rated to be of good quality (Tait et al. 2002).

**Neck Pain**

Fourteen randomised clinical trials of all types of acupuncture were included in a systematic review (White and Ernst 1999). Their rigour was evaluated using the Jadad score (Jadad et al. 1996) and found to be mixed. About half of the trials generated a positive result while the other half could not confirm such a finding. Thus the efficacy of acupuncture was not deemed to be established. The quality of the review was rated “good” (Tait et al. 2002).

**Back Pain**

A Cochrane Review assessed the effectiveness of manual acupuncture or electroacupuncture for non-specific back pain (van Tulder et al. 2001). Eleven randomised trials were included and evaluated according to the Cochrane Back Review Group criteria. The results were mixed, but overall acupuncture was not found to be of proven effectiveness, not least because the quality of the primary studies was found to be wanting. This review was rated as of good quality (Tait et al. 2002). Other systematic reviews of these data have drawn different conclusions, e.g. (Ernst and White 1998). An updated review on the subject including many new studies is now being conducted.

**Fibromyalgia**

A systematic review included 4 cohort studies and 3 randomised clinical trials of any type of acupuncture (Berman et al. 1999). Their methodological quality as assessed using the Jadad score (Jadad et al. 1996) was mixed, but in some cases good. The notion that acupuncture alleviates the pain of fibromyalgia patients was mainly based on one high quality study and thus not fully convincing. The quality of the review was rated as “satisfactory” (Tait et al. 2002).

**Osteoarthritis**

A systematic review of controlled acupuncture trials for osteoarthritis of any joint included 13 studies (Ernst 1997). Their methodological quality was evaluated using the Jadad score (Jadad et al. 1996) and found to be highly variable. The methodologically sound studies tended to yield negative results. Sham-acupuncture turned out to be as effective as real acupuncture in reducing pain. Thus it was concluded that acupuncture has a powerful placebo effect. Whether or not it generates specific therapeutic effects was deemed uncertain.

**Conclusion**

These systematic reviews collectively provide tantalising but not convincing evidence for acupuncture’s pain reducing effects. The evidence is limited primarily by the paucity of studies and their often low methodological quality. The scarcity of research funds in this area is likely to perpetuate these problems. Since acupuncture is a relatively safe therapy (Ernst and White 2001), it deserves to be investigated in more detail and with more scientific rigour, e.g. using the novel sham needle devices (Park et al. 2002; Streitberger and Kleinhenz 1998) that have recently become available.

**References**


**Acupuncture Mechanisms**

Acupuncture Mechanisms

CHRISTER P.O. CARLSSON
Rehabilitation Department, Lunds University Hospital, Lund, Sweden
akusyd@swipnet.se

Definition

▶ Acupuncture is a traditional Chinese therapeutic method for the treatment of different symptoms including pain. Thin, solid needles are inserted into proposed specific points on the body, called acupuncture points. The needles are inserted through the skin to varying depths, often into the underlying musculature. The needles are often twirled slowly for a short time, 30–60 s and may be left in place for a varying time, 2–30 min. Many modifications of the method have been described and the concept of acupuncture is not well defined. The method of applying electrical stimulation via acupuncture needles, ▶ electro-acupuncture (EA), was introduced in 1958. The treatments are usually applied in series of 8–12 sessions, each treatment lasting 20–30 min and separated by ½–2 weeks. Needling is often performed with some needles near the source of pain (called local points), and some other needles on the forearms and lower legs (called distal points).

Common Clinical Observations
Concerning Therapeutic Acupuncture for Chronic Pain

After the first few acupuncture treatments there may be some hours of pain relief or nothing at all happens. Often pain relief starts 1–2 days after treatment. Some patients even get worse and have a temporary aggravation of their symptoms for some days before they start to improve. This aggravation can be seen for 2–3 days or even for a week. For those responding to acupuncture, usually both the degree and duration of the pain relief increase after each treatment, a clinical observation that has gained some experimental support (Price et al. 1984).

Acupuncture Is a Form of Sensory Afferent Stimulation

As acupuncture needles are inserted into the tissue and mostly down to the muscular layer, they excite receptors and nerve fibres, i.e. the needles mechanically activate somatic afferents. Other forms of afferent sensory stimulation are trigger point needling or dry needling and transcutaneous electrical nerve stimulation (▶ TENS) as well as vibration. These methods may share some common features concerning mechanisms of action. A special method is painful sensory stimulation, which has been used through the centuries, an idea that a short but very painful stimulus would reduce pain.

The term ▶ acupuncture analgesia (AA) was used for electro-acupuncture (EA) used to get powerful and immediate pain relief during surgery, first used in China in 1958 but not described until 1973 (Foreign Languages Press, Beijing 1973). A success rate of 90% was claimed among those selected for the method. However, it soon became clear that only a minority of patients could develop so strong an analgesia as to tolerate surgery. Less than 10% of the patients showed a satisfactory response in acupuncture trials (Bonica 1974). Among these 10%, only one third had acceptable analgesia according to Western standards. Even so, patient selection and psychological preparations were crucial and often combinations with local anaesthetics or other drugs were used.

Felix Mann (1974) reported 100 observations on patients receiving AA. In only 10% of the experiments was the resulting analgesia considered adequate for surgery. He emphasised, that in ▶ therapeutic acupuncture (TA) to treat different symptoms, a mild stimulus was all that was usually required. This was in contrast to that needed to obtain AA where the stimulation had to be continued for at least 20 min and had to be painful to the maximum level the patient could tolerate. He concluded that usually, the stimulus required to achieve AA was so intense that the resulting pain would be unacceptable to most Western patients. For the main differences between AA and TA, see Table 1.

Characteristics

The proposed AA effect on surgical pain initiated physiological research where the goal was to find an explanation for immediate and very strong analgesia. Consequently, physiological research during the last 25–35 years has concentrated on explaining a phenomenon that may only exist in about 3–10% of the population and that may have little in common with therapeutic acupuncture.
Differences between acupuncture analgesia and therapeutic acupuncture

<table>
<thead>
<tr>
<th>Acupuncture Analgesia</th>
<th>Therapeutic Acupuncture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate and strong hypoalgesia is the goal.</td>
<td>Immediate hypoalgesia is not the goal.</td>
</tr>
<tr>
<td>Fast onset (minutes)</td>
<td>Slowly induced symptom relief after a number of treatments. The effects gradually increase after additional treatments.</td>
</tr>
<tr>
<td>Short-term = minutes</td>
<td>Long-term = days-weeks-months</td>
</tr>
<tr>
<td>The stimulation is felt very strongly. It is often painful and uncomfortable.</td>
<td>The stimulation is felt rather weakly. It is rarely painful and often relaxing.</td>
</tr>
<tr>
<td>Used most often in different physiological experiments and for surgical hypoalgesia. Often electro-acupuncture and pain threshold experiments on humans or animals.</td>
<td>Used for clinical pain relief and other symptom relief. Most often manual acupuncture but can also be electro-acupuncture.</td>
</tr>
</tbody>
</table>

The experimental acupuncture research has concentrated on very short-term effects (after a single treatment of EA) where pain thresholds and / or central neurochemicals (mostly endorphins) have been measured. The research groups have mostly used conscious animals where no special care has been taken to rule out stress-induced analgesia (SIA) (Akil et al. 1984). In some studies it is explicitly noted that the animals showing obvious signs of discomfort during EA also had pain threshold elevations, but that this was not the case for those who were not distressed (e.g. Bossut and Mayer 1991; Galeano et al. 1979; Wang et al. 1992).

Conclusions from the Existing Acupuncture Experimental Data

Most acupuncture research on animals has been performed using (strong) EA, even though human therapeutic acupuncture is most often performed with gentle manual acupuncture. Much of the animal research on acupuncture probably only shows the consequences of noxious stimulation and the activation of SIA and DNIC. When manual acupuncture has been used in animal research, no pain threshold elevation has been described.

Pain threshold elevation in humans only seems to occur if the stimulation is painful and does not correspond at all with the clinical outcome after therapeutic acupuncture. Endorphins are partially involved in acupuncture analgesia in humans. Thus, AA in humans is believed to rely both on opioid and non-opioid mechanisms. However, whether endorphins are involved both locally (in the tissues) and within the central nervous system is not known (Price and Mayer 1995). Thus, the hitherto performed experimental acupuncture mechanism research is really only valid for acupuncture analgesia and not for therapeutic acupuncture.

Acupuncture Mechanisms – the Standard Neurophysiological Model

Several physiological mechanisms have been suggested to account for the pain relieving effect of acupuncture. Spinal and supraspinal endorphin release has been proposed, as has the activation of DNIC (diffuse noxious inhibitory control) through bulbospinal paths. The involvement of neurochemicals like serotonin, noradrenaline and different endorphins as well as hormones like ACTH and cortisone has been studied in detail. Acupuncture physiology is often summarised in the following manner (Han 1987; Pomeranz 2000):

For acupuncture needles inserted within the segment of pain:
- Spinal gate-control mechanism (involving enkephalin and dynorphin)

For extrasegmental acupuncture:
- Activation of midbrain structures (PAG) and the descending pain relieving system (involving endorphins, serotonin and noradrenaline).
- Diffuse noxious inhibitory control (DNIC) is sometimes claimed to be involved.
- Activation of the HPA-axis (hypothalamic-pituitary-adrenal) with increased levels (in the blood) of β-endorphin and ACTH / cortisone.

Problems with the Standard Neurophysiological Model to Explain Clinical Observations

The model can only explain very short-term pain relief after each stimulation period. The gate-control mechanism is only active during stimulation and the descending inhibitory system for up to perhaps 8 h. The model cannot explain why, in some patients, pain relief starts some days after the treatment whether the patient is first worse or not. The gate-control does not start some days after the stimulation and that does not hold for the descending pain inhibitory systems either. The model cannot explain why there seems to be more prolonged pain relief after additional treatments and why there seems to be long-term pain relief after a course of 8–12 treatments. Probably, the standard neurophysiological model can explain AA, but even so it should be realised that AA is mostly painful stimulation – and, if the gate-control mechanisms are implicated, then the stimulation should be non-painful. For a summary of probable acupuncture mechanisms for both TA and AA see Table 2 below.

Acupuncture Efficacy

In chronic pain patients the improvements are often incomplete with symptom relief for weeks or months. From the first Western descriptions of acupuncture, efficacy was claimed for a lot of different conditions, but mainly for musculoskeletal pain, headaches and nausea. Depending on the technique and the criteria employed,
Acupuncture Mechanisms, Table 2

<table>
<thead>
<tr>
<th>Summary of probable mechanisms for acupuncture</th>
<th>Therapeutic acupuncture: mostly gentle manual Usual clinical use</th>
<th>Acupuncture Analgesia: high intensity electro-acupuncture Physiological experiments and surgical analgesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local events in the tissue (Local needles)</td>
<td>Axon reflexes in the tissue around needles and deeper through dichotomising fibres giving increased circulation and neuropeptide release. These can act as trophic factors (e.g., regeneration of glands). They can also have anti-inflammatory effects (like low dose of CGRP). Perhaps also release of local endorphins to local receptors.</td>
<td>Tissue trauma around the needles giving rise to more local pain (CGRP in higher doses has pro-inflammatory actions). Increased local pain for some days.</td>
</tr>
<tr>
<td>Segmental mechanisms and somato-autonomous reflexes (Regional needles)</td>
<td>Gate mechanism and perhaps long term depression (LTD). Sympathetic inhibition with increased segmental circulation. (Gate mechanism) and perhaps LTD.</td>
<td>Sympathetic stimulation with decreased segmental circulation.</td>
</tr>
<tr>
<td>Central mechanisms (Distant, regional and some local needles)</td>
<td>Sympathetic inhibition. Decreased levels of stress hormones, adrenaline and cortisol in plasma. Probably oxytocin is involved and induces long-term pain threshold elevations and anti-stress effects.</td>
<td>Sympathetic stimulation. Increased levels of the stress hormones, ACTH, adrenaline and cortisol in plasma. DNIC is activated. Descending pain inhibition from PAG with endorphins, serotonin and noradrenaline.</td>
</tr>
</tbody>
</table>

20–40% of patients in pain clinics have been said to benefit from acupuncture. In primary care or private clinics, where experienced practitioners choose who and what they treat, 60–70% of the patients have been reported to benefit. Because of inherent study design problems, especially with double blinding and the use of a proper placebo, the meta-analyses and systematic reviews are very difficult to interpret. However, from clinical research, in which the author has been involved, the conclusion has been drawn that clinically relevant long-term (> 6 months) pain relief from acupuncture can be seen in a proportion of patients with chronic nociceptive pain (Carlsson and Sjölund 1994; Carlsson and Sjölund 2001). For a full reference list to all sections of this chapter see (Carlsson 2002).

References
7. Foreign Languages Press (1973) Acupuncture anaesthesia. Foreign Languages Press, Beijing

Acupuncture-Like TENS

Definition
The delivery of TENS to generate activity in small diameter Group III muscle afferents, leading to the release of opioid peptides in a similar manner to that suggested for acupuncture. TENS is administered using low frequency train (1–4 Hz) bursts (5–8 pulses at 100Hz) at a high, but non-painful, intensity to stimulate selectively large diameter muscle efferents. This results in a ‘strong but comfortable’ muscle twitch that elicits Group III muscle afferent activity.

- Transcutaneous Electrical Nerve Stimulation Outcomes
- Transcutaneous Electrical Nerve Stimulation (TENS) in Treatment of Muscle Pain

Acute Backache

- Lower Back Pain, Acute
Acute Experimental Monoarthritis
▶ Arthritis Model, Kaolin-Carrageenan Induced Arthritis (Knee)

Acute Experimental Synovitis
▶ Arthritis Model, Kaolin-Carrageenan Induced Arthritis (Knee)

Acute Inflammatory Demyelinating Polyneuropathy
▶ Guillain-Barré Syndrome

Acute Ischemia Test
▶ Tourniquet Test

Acute Knee Joint Inflammation
▶ Arthritis Model, Kaolin-Carrageenan Induced Arthritis (Knee)

Acute Lumbago
▶ Lower Back Pain, Acute

Acute Pain in Children, Post-Operative
JOLENE D. BEAN-LJEWISKI
Department of Anesthesiology, Scott and White Memorial Hospital, Temple, TX, USA
jbean-ljewiski@swmail.sw.org

Synonyms
Pediatric Post-Surgical Pain; Acute Post-Operative Pain in Children

Definition
Children who have surgery experience significant postoperative pain for several days. Appropriate pain management should be initiated in the immediate post-operative period and continue until the pain resolves, whether the child is at home or in the hospital. Surgical trauma results from tissue destruction and musculoskeletal strain that causes the release of vaso- and immuno-reactive substrates that promote inflammation, hyperpermeability and pain.

Ineffective pain management increases the incidence of postoperative behavioral disorders in children and the risk of developing persistent or neuropathic pain. In preterm infants and neonates, this effect may be compounded by the lack of descending inhibitory pathways and enhanced neuroplasticity resulting in more extensive, persistent effects (Tachibana et al. 2001). Despite advances in the management of post-operative pain, nearly 70% of patients experience moderate or severe pain after surgery (Apfelbaum et al. 2003). Effective post-surgical pain management reduces the stress response to surgery, promotes respiratory function, improves wound healing and permits faster return to normal functioning. Surgical invasiveness correlates with the intensity and duration of postoperative pain and analgesic requirements. As surgical invasiveness increases, the interventions employed to manage it escalate.

Characteristics
Good pain management begins with informative preoperative teaching regarding the nature of the surgery, the anticipated level and duration of discomfort and strategies for reducing pain. This is particularly important as more children experience ambulatory surgery that requires parents to manage pain at home. Parents may fail to administer prescribed analgesics due to fear of side effects, addiction or difficulty with administration. Preoperative teaching, improves parental compliance with prescribed analgesic dosing and patient comfort postoperatively (Greenberg et al. 1999). Complementary, non-pharmacological techniques taught preoperatively also reduce anxiety and postoperative pain (Huth et al. 2004).

Postoperative Pain Management Following Ambulatory Surgery
▶ Local anesthetics improve immediate postoperative comfort and hasten transition through the recovery process. A ▶ field block, ▶ installation block or direct peri-neural infiltration (▶ peri-neural injection) are the safest and easiest analgesic techniques available. Common peripheral nerve blocks employed in children include the ilioinguinal and iliohypogastric nerve block for inguinal herniorrhaphy, ▶ penile block for circumcision or phallic surgery, femoral, or the ▶ fascia iliaca
Why Should We Aim to Optimise the Management of Acute Pain?

Post-operative pain is a major marker of peri-operative morbidity and mortality and its effective treatment should be a goal in every hospital and institution. We should all aim to control pain, not only for humanitarian reasons, but also to attenuate the psychological and physiological stress with which it is associated following trauma or surgery. While it is now recognised that adequate pain control alone is not sufficient to reduce surgical morbidity, it remains an important variable and one that is perhaps more readily controlled (Kehlet and Holte 2001).

Adequate management of post-operative pain is vital to attenuate the stress response to surgery and the accompanying pathophysiological changes in metabolism, respiratory, cardiac, sympathetic nervous system and neuro-endocrine functions. These effects (summarised in Neuroendocrine and metabolic responses to surgery after NH&MRC 1999) are wide ranging and have significant impact on homeostasis. Effects on the respiratory system are most prominent, as persistent pain will result in a reduction in respiratory effort that then leads to hypoxaemia from significant ventilation/perfusion mismatching. Continuing hypoventilation predisposes to collapse of lung segments and the supervening infection that follows carries significant morbidity. Psychological and behavioural changes (e.g. yellow flags) also accompany pain states and may need to be recognised and managed. Not only will proper management of post-operative pain result in greater patient comfort and earlier discharge home, but the improved earlier mobilisation and return to function will also reduce serious post-operative complications such as venous thromboembolism.

However, despite the emergence of pain management as a specialty and the availability of a wide range of guidelines and templates for effective analgesia, pain continues to be poorly managed. Why this should be the case is a difficult question to answer, although there is clearly a wide range of possibilities (Cousins and Phillips 1986; Macintyre and Ready 1996).

As can be seen from “Reasons for ineffective analgesia (after NH & MRC 1999)”, in some cases it may be simply the result of inadequate knowledge or equipment, but sometimes there can be more disturbing reasons. Macintyre (2001) has pointed out that some health service personnel are still concerned that pain relief can be ‘too efficacious’ and thereby mask post-operative complications such as urinary retention, compartment syndrome or even myocardial infarction. Another barrier to providing effective analgesia is a view held in some quarters that maintaining the patient in pain is somehow a useful way to aid diagnosis – a concept that with no valid scientific basis (Attard et al. 1992; Zolte and Cust 1986).

**Reasons for Ineffective Analgesia (After NH & MRC 1999)**

- The common idea that pain is merely a symptom and not harmful in itself
- The mistaken impression that analgesia makes accurate diagnosis difficult or impossible
- Fear of the potential for addiction to opioids
- Concerns about respiratory depression and other opioid related side effects such as nausea and vomiting
- Lack of understanding of the pharmacokinetics of various agents

**Neuroendocrine and Metabolic Responses to Surgery (after NH & MRC 1999)**

**Endocrine**

- Catabolic – Due to increase in ACTH, cortisol, ADH, GH, catecholamines, renin, angiotensin II, aldosterone, glucagon, interleukin-1
- Anabolic – Due to decrease in insulin, testosterone

**Metabolic**

- Carbohydrate – hyperglycaemia, glucose intolerance, insulin resistance
- Due to increase in hepatic glycogenolysis (epinephrine, glucagon) – gluconeogenesis (cortisol, glucagon, growth hormone, epinephrine, free fatty acids)
- Due to decrease in insulin secretion / action
- Protein – muscle protein catabolism, increased synthesis of acute-phase proteins
- Due to increase in cortisol, epinephrine, glucagon, interleukin-1
- Fat – increased lipolysis and oxidation
- Due to increase in catecholamines, cortisol, glucagon, growth hormone
- Water and electrolyte flux – retention of H2O and Na+, increased excretion of K+, decreased functional extracellular fluid with shifts to intracellular compartments
- Due to increase in catecholamines, aldosterone, ADH, cortisol, angiotensin II, prostaglandins and other factors
Lack of appreciation of variability in analgesic response to opioids
Prescriptions for opioids, which include the use of inappropriate doses and/or dose intervals.
Misinterpretation of doctor’s orders by nursing staff, including use of lower ranges of opioid doses and delaying opioid administration.
The mistaken belief that patient weight is the best predictor of opioid requirement.
The mistaken belief that opioids must not be given more often than 4 hourly.
Patients’ difficulties in communicating their need for analgesia.

Mechanisms in Acute Pain

The manner in which pain signals are processed and modulated is a complex topic that is covered in detail elsewhere. However, the following brief overview is provided as a background to the sections that follow.

The traditional view of the processing of pain inputs is that they are first detected through non-specific polymodal nociceptors that respond to a range of stimuli, including thermal, chemical and mechanical alterations. It is a process designed to alert us to tissue damage.

These peripheral nerves terminate in the dorsal horn of the spinal cord where they undergo considerable modulation both via neurotransmitters present at that site and through the action of descending tracts from higher centres, which usually have an inhibitory role. Following modulation, the nociceptive impulse is finally transmitted through tracts to supraspinal sites. Although a number of links are involved, the spinohalamic tract is perhaps the most prominent.

Having given this outline, it is now accepted that our nervous system is a “plastic” environment where stimuli or trauma in any one part of the body can invoke change within other body systems, especially that of the nervous system (Cousins and Power 1999). Changes in nerve function are particularly important and this plasticity can lead nerve fibres whose physiological role is not normally to transmit pain signals to act as nociceptors. For example, while A delta and C fibres are traditionally seen as primary nociceptive fibres, A beta fibres can become nociceptive under certain circumstances.

Coincident with this is the development of peripheral sensitisation. Trauma or other noxious stimuli to tissue result in a neurogenic inflammatory response that in turn leads to vasodilation, increased nerve excitability and the eventual release of a range of inflammatory mediators such as serotonin, substance P, histamine and cytokines—the so-called sensitising soup. This altered environment leads to a modification in the way that input signals are processed with innocuous stimuli being sensed as noxious or painful stimuli, leading to the phenomena of hyperalgesia.

The Scope of Acute Pain Management

Acute pain management has developed into a subspecialty in its own right during the last decade with an ever-increasing range of activities. In the hospital setting, the major role of the acute pain team is in the area of post-operative pain management in the surgical patient, although their involvement must not be limited to these patients. In patients with burns, appropriate pain management will help in optimising pain control both in the early stages where skin grafting and debridement are being carried out and later when the patient requires assistance to undergo physiotherapy. In the patient with spinal cord injury, the initial phase following the injury is often complicated by acute neuropathic pain where early intervention is critical, while in the oncology patient, acute pain can complicate therapy, as in the patient who develops mucositis as a complication of treatment.

Providing Comprehensive Acute Pain Management

Acute and post-operative pain is best managed by an acute pain team and there are a number of structural models of how these are best set up and operated (Rawal and Allvin 1998). While many are headed by consultant anaesthetists, this is not always the case and often the day to day running of the team is managed by a specialist pain nurse, with medical staff used only for back up when necessary. Acute pain teams need to have clearly defined guidelines and major goals, which will be dictated in part by their institution and circumstances (see Clinical practice guidelines for Acute Pain teams, Cousins and Power 1999). Irrespective of how the team is organised there must be an efficient method of referral of patients either from the operating theatre or from the various surgical teams.

Clinical Practice Guidelines for Acute Pain Teams (Cousins and Power 1999)

Guidelines

A collaborative, interdisciplinary approach to pain control, including all members of the healthcare team and input from the patient and the patient’s family, when appropriate. An individualised proactive pain control plan developed proactively by patients and practitioners (since pain is easier to prevent than to treat)

Assessment and frequent reassessment of the patient’s pain.
Use of both drug and non-drug therapies to control and/or prevent pain

A formal, institutional approach, with clear lines of responsibility

Major Goals

- Reduce the incidence and severity of patients’ post-operative or post-traumatic pain
- Educate patients about the need to communicate regarding unrelieved pain, so they can receive prompt evaluation and effective treatment
- Enhance patient comfort and satisfaction
- Contribute to fewer postoperative complications and, in some cases, shorter stays after surgical procedures

Where possible, the pain team should also be involved in pre-operative education of the elective surgical patient. At such a meeting, the patients’ fears and anxieties about pain should be addressed, as there is considerable evidence to suggest that patients who have the opportunity to speak about their concerns about post-operative pain prior to surgery do better and use less medication that control groups. A number of studies have consistently pointed out that pain is usually the major fear of patients undergoing surgery. During preoperative assessment, at least in the elective patient, it is important to obtain a full medical history especially in relation to use of analgesic agents and the duration of such therapy. Tolerance to opioids can develop quickly and identifying patients who attend for surgery with a history of oral opioid use is important, as they will most likely have different analgesic requirements when compared to the opioid-naïve individual. The acute pain team also needs to be responsible for the overall post-operative management of the patient. This includes ensuring that regular monitoring and recording of physiological parameters occurs. Details such as oxygen saturation, respiratory rate and pain status need to be recorded regularly and reviewed. Pain scores can be recorded either numerically or by descriptors. It is important to record pain levels both at rest and on movement, since treatment strategies for these problems will differ. Movement pain in particular is better treated with adjuvant agents rather than opioids.

Accurate recording of physiological data in patients being treated for acute pain is mandatory. Sedation scores and respiratory rate are important in reducing the incidence of opioid-induced toxicity. Pain management records or electronic data apparatus should also allow for the recording of any associated adverse events (such as nausea and vomiting) and record data in a form allowing regular or on-going audit. Such audits of acute pain patients should, where possible, allow not only for examination of the parameters already described but also for outcome measures. The acute pain team should supervise the transition from a parenteral to an oral analgesic regime. Likewise, members of the acute pain service must recognize when a patient might be suffering a Persistent Acute Pain state or undergoing transition from an acute to a chronic pain state and need referral to chronic pain specialists.

Post-operative care also involves being alert for warning signs, so called “red flags” that might indicate developing complications of the surgery or trauma. In patients previously well controlled using a particular analgesic regime, continuing episodes of unexpected pain requiring increasing doses of medication should alert the practitioner. Under these circumstances, an investigation should be made to elicit the cause of these events, which might be a result of complications of surgery or trauma. This should be diagnosed and treated directly, rather than merely increasing doses of analgesic drugs (Cousins and Phillips 1986).

Pre-emptive Analgesia

Much has been made of the usefulness of pre-emptive or preventive analgesia. The concept of providing analgesia prior to a surgical stimulus and thus reducing central sensitisation seems to be a logical and useful proposition and generated a great deal of initial enthusiasm (Dahl and Kehlet 1993; Woolf and Chong 1993). Unfortunately, subsequent controlled trials have failed to consistently demonstrate that any of the commonly used strategies are effective in reducing post-operative pain or analgesic use. These include the pre-operative administration of opioids, non-steroidal anti-inflammatory drugs and the provision of local analgesic neural blockade (Gill et al. 2001; Podder et al. 2000; Uzunkoy et al. 2001). Much research has been conducted in an effort to ascertain the reasons for this (Charlton 2002; Kehlet 1998; Kissin 1996). Some hypotheses that have been advanced include the suggestion that when local anaesthesia is employed in a pre-emptive setting, any failure to provide complete blockade will still allow sensitisation to occur (Lund et al. 1987). Another possibility is the timing between placement of the blockade and the commencement of surgery is critical, with a time interval of at least 30 min being required between drug administration and surgery (Senturk et al. 2002). One question that has not been fully answered is whether the use of pre-emptive analgesia might lead to a reduction in the number of patients progressing from acute to chronic pain states. Early studies such as that of Bach et al. (1988) suggested that this may well be the case and this has been supported by more recent reports (Obata et al. 1999).
**Treatment Strategies – General**

The principles of management of acute nociceptive pain are generally called **multi-modal**. This implies using a number of agents, sometimes given by different routes, to maximise pain control. While pain control after some minor procedures can be controlled by non-opioids alone, opioids remain the mainstay of moderate to severe pain management. The use of combinations of **adjuvant analgesics** also known as **balanced analgesia**, allows for a reduction in opioid dosage and thus side effects, which can be useful in managing some aspects of pain that can be less responsive to opioids alone.

With regard to the selection of a route of drug administration, whilst the use of the oral route might initially seem easiest, it is rarely used in the first instance. The variable bioavailability of oral products coupled with post-operative attenuation of gastrointestinal function and the possibly of superimposed vomiting, makes this route a poor choice initially. Parenteral administration is usually called for and the intravenous route is the preferred route of administration, often using **patient controlled analgesia** (PCA) devices.

**Patient Controlled Analgesia**

PCA, as a means of drug administration has to a degree revolutionised modern pain management. Although purchase of the devices represents a significant financial outlay, there are savings to be made in terms of medical and nursing staff time, as well as less tangible benefits, such as reducing the number of needle stick injuries for example. Importantly, patients generally feel positive about using PCAs (Chumbley et al. 1999), with most studies suggesting that the feeling of “being in control” was the most common reason for the high level of satisfaction (Albert and Talbott 1988). However, despite a number of inbuilt safety mechanisms, overdosage can still occur with these devices, and strict post-operative monitoring is imperative (Macintyre 2001). While the intramuscular route can be used for intermittent analgesia, the pharmacokinetics are often unattractive, requiring repeated injections. Furthermore, intramuscular analgesia is most often prescribed on a prn or “as required” basis, which perforce implies that the patient must be in a pain state before they request the medication – a situation that should be avoided. Finally, every intramuscular (or indeed subcutaneous) injection given presents a possibility for a needlestick injury to occur – another situation best avoided.

**Epidural Analgesia**

Much has been written about the risks and benefits associated with the use of epidural analgesia in the post-operative period and interpreting the results of these myriad studies conducted under varying circumstances is extremely difficult. There is no doubt that epidural analgesia provides a number of real advantages. It allows the use of drug combinations, which can be delivered close to appropriate receptor sites in the spinal cord (Schmid et al. 2000), it reduces the requirements of opioid analgesics (Niemi and Breivik 1998) and generally allows for a faster return of physiological function, especially gastrointestinal and respiratory status in the post-operative period. The degree to which this occurs appears to be dependent, at least in part, on the nature of surgery performed (Young Park et al. 2001). However, more recently, despite the fact that there are considerable benefits associated with the use of epidural infusions, attention has focussed on the nature and incidence of complications associated with epidural infusions (Horlocker and Wedel 2000; Rigg et al. 2002; Wheatley et al. 2001). These complications can range from local or systemic infection through to haematoma formation and local or permanent neurological sequelae. The rates of the most serious complications of permanent nerve defects or paraplegia are quoted as between 0.005 and 0.03% (Aromaa et al. 1997; Dahlgren and Tornebrandt 1995). Again analysis of these data is difficult because of the number of variables involved. For example there is growing evidence that those people who develop epidural neurological complications frequently have significant pre-existing pathologies, which may predispose them to such complications. Lastly, there has been considerable debate about guidelines for epidural placement and removal in patients undergoing peri-operative anticoagulation. This is especially so when fractionated or low molecular weight heparin products are employed, because of the possibility of increased risk of development of epidural haematoma under these circumstances. Again, the evidence is conflicting (Bergqvist et al. 1992; Horlocker and Wedel 1998). Patient controlled epidural analgesia is a means of pain management that combines the efficacy of epidurally administered drugs with the convenience of patient control.

**Intrathecal Analgesia**

The intrathecal route of drug administration can be useful both as a means of providing anaesthesia and for post-operative analgesia. Both opioids and local anaesthetic agents have been administered by this route. While the use of low doses of less lipophilic agents such as morphine is popular and gives prolonged post-operative care, the use of this route is not without risk, as there has been a rise in the number of cases of transient neurological symptoms following lignocaine use (Johnson 2000).
Pharmacotherapies

Opioids

With regard to the opioids, there has been an increase both in the range of drugs available and in their routes of administration. The traditional range of opioids such as morphine, pethidine and fentanyl has been augmented by drugs such as oxycodone and hydromorphone. None of these drugs are actually “new”, having been synthesised in some cases almost 100 years ago, but rather they have been re-discovered by a new generation of prescribers. Oxycodone in particular is available in a sustained release form that exhibits a useful biphasic pharmacokinetic profile. The role of pethidine (meperidine) in modern pain management continues to be problematic. While it still has a place under certain circumstances, it should be avoided as an agent for long-term use, owing to its apparently increased abuse potential and the risk of accumulation of the excitatory metabolite norpethidine. The increased opioid armamentarium has also given scope for opioid rotation. Although this is a strategy primarily associated with chronic pain management, patients can develop a degree of tolerance to opioids even after a few days. Where continued opioid treatment is needed for whatever reason, switching opioids often results in enhanced pain control, often together with a reduction in dosage. Methadone is an interesting drug, which has generated some recent interest. Its unusual pharmacokinetic profile, with a long and unpredictable half-life of up to 72 h, makes it impracticable for use in the very early stages of acute pain. However it can be used in later stages where a long acting oral product is preferable. That the drug has activity at the NMDA receptor as well as the mu opioid receptor is well known. However it has always been difficult to assess to what, if any, extent this contributes to its analgesic effect and the fact that it has been shown to be of benefit in the treatment of other pain states such as phantom limb pain (Bergmans et al. 2002).

Non-Opioids

The non-opioids are a diverse group of drugs with differing modes of action and means of administration. Most show clear synergism with the opioids. Members of this group include tramadol, the non-steroidal anti-inflammatory drugs (NSAIDS), COX-2 inhibitors and ketamine.

Paracetamol

Paracetamol should be almost the universal basis of acute and post-operative pain control. A number of well controlled trials have clearly demonstrated that regular paracetamol, when given in a dose of 1 gm q.i.d. clearly reduces opioid requirements by up to 30%. Side effects are minimal and the drug is very well tolerated. In most countries it is available in both oral and rectal forms and in a small number a parenteral pro-drug propacetamol is also available.

The only real contraindication to the prescribing of paracetamol is impaired hepatic function, where the drug is probably best avoided. Much work has also been done on the efficacy of other drugs given in combination with paracetamol. In general, the analysis of trial data suggests that while the combination of codeine phosphate (60 mg) has benefits over paracetamol alone, the use of paracetamol with lower quantities seems to confer little benefit. Likewise, although the combination of paracetamol with dextropropoxyphene is widely used to treat more severe pain, many trials suggest that it too has little to offer above paracetamol alone.

Tramadol

Tramadol is unique amongst analgesic agents in having a dual action. Its main activity probably lies in enhancing the action of noradrenaline and 5-hydroxytryptamine at the spinal cord level, while it also has a very weak agonist activity at the mu receptor at supraspinal sites. Tramadol is a very useful drug for the management of mild to moderate pain and the fact that it can be given orally or by the intravenous or intramuscular routes further adds to its versatility. Its low addiction potential makes it a good choice for long-term use. Because of risk of precipitating serotonin syndrome, tramadol is probably best avoided in combination with many of the different anti-depressant medications, especially the SSRIs, although in clinical practice the real risk seems quite low. Recent studies have confirmed that it possesses significant synergy when combined with paracetamol and indeed a combination product is now available in some countries (Friac et al. 2002). There are few studies available on the usefulness of combination of tramadol with opioids, although initial results appear encouraging (Webb et al. 2002).

Tramadol is also attractive because of its low abuse potential. Certainly in comparison to strong opioids, the incidence of abuse, dependence and withdrawal is considerably lower (Cicero et al. 1999). However a number of such cases have been reported, almost all of which were in patients with a pre-existing history of drug or substance abuse (Brinker et al. 2002; Lange-Asschenfeldt et al. 2002).

In the management of post-operative pain, all efforts should be made to reduce the incidence of post-operative nausea and vomiting, which is not only uncomfortable for the patient, but an can also lead to fluid imbalance, impaired respiratory function and electrolyte disturbances. In this regard the use of tramadol is somewhat problematic, as the incidence of nausea and vomiting is at least as high as with opioids (Sil-
recent studies suggest that. However, some strategies have been suggested to attenuate this response including administration of an intra-operative loading dose (Pang et al. 2000) and slow IV administration (Petrone et al. 1999). Should management of tramadol induced nausea and vomiting require pharmacological intervention, recent studies suggest that members of the butyrophenone class such as droperidol might be a better choice than 5HT3 antagonists such as ondansetron, which might not only be less effective, but also antagonise tramadol’s analgesic effects.

Non-Steroidal Anti-Inflammatory Drugs

- NSAIDs. Survey (NSAIDs) are widely used in acute pain management (Merry and Power 1995). While they may be used as the sole agent in mild pain, they are primarily employed as adjunctive medications in combination with opioids in moderate to severe pain states. Here their action both at central and peripheral sites complements opioid activity and they are especially useful in the management of pain associated with movement. There have always been concerns associated with the use of NSAIDs in the surgical patient because of the risk of the development of serious complications, especially renal impairment. However, careful patient selection and monitoring, the use of a product with a short half-life and restricting the duration of treatment to about 3 days greatly reduces the danger. The discovery of the two isoforms of the cyclooxygenase (COX) enzyme has more recently led to the development of COX-2 specific inhibitors such as celecoxib and rofecoxib, with the aim of developing a potent NSAID without significant associated gastrointestinal side effects. The majority of studies on these drugs have been conducted in outpatient populations and whether they offer any advantage over traditional NSAIDs in the management of post-operative pain is unclear. Even more recently, a parenteral COX-2 inhibitor (parecoxib) has been developed specifically for the management of post-operative pain and initial results of studies are encouraging.

Unfortunately, the cardiovascular safety of these products has recently come under scrutiny that has resulted in at least one (rofecoxib) being withdrawn from the market, owing to an increase in thrombo-embolic events associated with its use (Solomon et al. 2004). There is considerable discussion at present as to whether this constitutes an individual drug effect or a class effect. These setback have not however prevented the development and release of other members of this group with improved safety profiles.

Ketamine

- Ketamine is an important second line drug in the pain physician’s armamentarium. Well known as an anaesthetic agent, it has in the last decade or so found use as an analgesic product when used in sub-anaesthetic doses. The drug has some useful N-methyl-D-aspartate (NMDA) receptor antagonist activity and can also augment the action of opioids in the treatment of nociceptive pain. The usual psychomimetic effects of the drug are not usually a problem in the dosages employed, although the development and release of the S(+) might signal a resurgence in the interest of this drug.

Neuropathic Pain

Comprehensive acute pain management also entails the recognition and management of acute neuropathic pain. Neuropathic pain is most frequently seen as a sequela of long-term pathological states such as diabetes or herpes zoster infection (Bowsher 1991). However this is not always the case and acute neuropathic pain can be seen immediately following surgical procedures where peripheral nerves have been disrupted, such as in the post-thoracotomy syndrome, following specific events such as acute spinal cord injury or as evidenced by phantom limb pain following amputation. It is important to be alert for the signs or symptoms of neuropathic pain in the acute or post-operative phase (see Features suggestive of neuropathic pain after NHMRC 1999). Failure to diagnose such a condition will result not only in prolonged pain, but also most probably in the patient being given increasing doses of opioid medication in a futile effort to control the condition (Hayes and Molloy 1997).

Features Suggestive of Neuropathic Pain (After NH & MRC 1999)

- Pain can be related to an event causing nerve damage
- Pain unrelated to ongoing tissue damage
- Sometimes a delay between event and pain onset
  - The pain is described as burning, stabbing, pulsing or electric-shock like
  - Hyperalgesia
  - Allodynia (indicative of central sensitisation)
  - Dysaesthesia
- Poor response to opioids
- The pain is usually paroxysmal and often worse at night
- Pain persists in spite of the absence of ongoing tissue damage

Management of neuropathic pain can be complex and much has been written on the usefulness of various pain strategies. A wide range of drugs with differing pharmacological targets such as anti-convulsant medications, notably gabapentin and carbamazepine,
Specific Acute Pain States

There are some acute pain states that have been subject to more extensive research and whose symptomatology and pathogenesis follows recognised patterns. These include acute lower back pain, pain following chest trauma or thoracic surgery, compartment syndrome and the acute presentation of visceral or somatic (deep or superficial) pain.

Summary

There have been a number of significant improvements in the management of acute and post-operative pain management during the past decade. To some degree this has been helped by the emergence of new drugs or, in some cases, whole new drug groups. However in the main, advances in acute and post-operative pain management have come about by recognising how to manage pain better with existing drugs, focussing on the use of drug combinations to maximise outcomes. There has also been a greater appreciation of the importance of diagnosing acute neuropathic pain, requiring a different approach. Those involved in pain management have embarked on a virtual crusade in an effort to convince health professionals that acute and post-operative pain can be and must be appropriately and successfully managed. Perhaps the most important lesson of all is an appreciation that all chronic pain must start as acute pain. Appropriate management of acute pain will therefore have the additional bonus of eventually reducing the worldwide burden of patients having to suffer debilitating chronic pain states.

References

compartment block for lower extremity procedures and digital nerve blocks for toe or finger procedures. Peripheral nerve blocks provide analgesia of similar duration compared to plexus or epidural injections. The duration of the block is determined by the choice of local anesthetic, regional blood flow and use of vasoconstrictor (Table 1). Bupivacaine produces higher peak local anesthetic, regional blood flow and use of vasoconstrictor (Table 1). Bupivacaine proves the safety of the technique by providing an indicator for inadvertent intravascular or intraosseous injection. The addition of clonidine 1–2 mcg kg\(^{-1}\) to the solution significantly prolongs the block but may delay discharge due to excessive duration (Farrar and Lerman 2002). Neuraxial morphine or hydromorphone should not be used for ambulatory patients due to the risk of delayed respiratory depression. Systemic analgesic therapy must be initiated in order to prevent severe pain (prior to resolution of a local anesthetic block). Nonsteroidal anti-inflammatory agents (NSAIDs) and acetaminophen are the most commonly employed analgesics for children following ambulatory surgery. NSAIDs should be included in the analgesic regimen unless contraindicated (see Contraindications for the Use of NSAIDs) because they reduce the incidence of opioid related side effects and improve recovery characteristics and patient well being (Farrar and Lerman 2002; Gan et al. 2004; Watcha et al. 2003). In addition, they have been associated with a lower incidence of post-surgical behavioral disturbances in children (Kokki 2003).
Acute Pain in Children, Post-Operative, Table 1

<table>
<thead>
<tr>
<th>Drug</th>
<th>Concentration</th>
<th>Usual Duration</th>
<th>Usual Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Without epinephrine</td>
<td>w/o epinephrine</td>
<td>w/ epinephrine</td>
</tr>
<tr>
<td>Chloroprocaine</td>
<td>1–2%</td>
<td>8</td>
<td>½–1</td>
</tr>
<tr>
<td>Procaine</td>
<td>1–2%</td>
<td>7</td>
<td>½–1</td>
</tr>
<tr>
<td>Bupivacaine</td>
<td>0.25–0.5%</td>
<td>2</td>
<td>4–12 (peripheral Nn)</td>
</tr>
<tr>
<td>Levo-bupivacaine</td>
<td>0.25–0.5%</td>
<td>2</td>
<td>2–4 (s.c. / epidural)</td>
</tr>
<tr>
<td>Ropivacaine</td>
<td>0.2–0.5%</td>
<td>2</td>
<td>2–4 (s.c. / epidural)</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>0.5–2%</td>
<td>5</td>
<td>1–2</td>
</tr>
<tr>
<td>Mepivacaine</td>
<td>1–1.5%</td>
<td>5</td>
<td>1.5–3</td>
</tr>
</tbody>
</table>

Contraindications for the Use of NSAIDs

- Renal Impairment
- Liver Dysfunction
- Hypovolemia
- Hypotension
- Coagulation Disorder
- Active Bleeding
- Hypersensitivity / Asthma precipitated by aspirin or other NSAID

A variety of NSAIDs are available for oral, intravenous and rectal administration (Table 2). Comparative trials in children are lacking, however when administered in appropriate doses little variation in their analgesic efficacy is expected with the exceptions of ketorolac and rofecoxib that appear to have stronger analgesic properties (Kokki 2003; Watcha et al. 2003). The volume of distribution and clearance of the NSAIDs are higher in children necessitating slightly higher or more frequent dosing regimens. A ceiling effect limits effectiveness of all NSAIDs. Children are less susceptible to the gastrointestinal side effects of NSAIDs. Caution is advised with renal impairment, asthma, dehydration and bleeding diatheses (Kokki 2003).

Acute Pain in Children, Post-Operative, Table 2

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Frequency [h]</th>
<th>Max Daily Dose [mg kg(^{-1})]</th>
<th>Preparations Available</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diclofenac</td>
<td>1 mg kg(^{-1})</td>
<td>8–12</td>
<td>3</td>
<td>i.v. / pr / PO</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>10 mg kg(^{-1})</td>
<td>6–8</td>
<td>4</td>
<td>PO</td>
</tr>
<tr>
<td>Flurbiprofen</td>
<td>1 mg kg(^{-1})</td>
<td>8–12</td>
<td>5</td>
<td>PO / i.v.</td>
</tr>
<tr>
<td>Ketoprofen</td>
<td>1–2 mg kg(^{-1})</td>
<td>6–8</td>
<td>5</td>
<td>PO / i.v.</td>
</tr>
<tr>
<td>Ketorolac</td>
<td>0.3–0.5 mg kg(^{-1})</td>
<td>6–8</td>
<td>2</td>
<td>i.v.</td>
</tr>
</tbody>
</table>
and severity of postoperative nausea and vomiting (PONV) than morphine and permits the early initiation of oral analgesics so that the adequacy of pain relief can be assessed prior to discharge. Intravenous morphine 0.05–0.2 mg kg\(^{-1}\) is employed when pain is more severe or persistent. When larger doses are required, inadequate pain relief after discharge is increasingly likely.

Codeine, the most common oral opioid for mild to moderate postoperative pain, is less popular due to the high incidence of side effects. Codeine metabolism to morphine is responsible for its analgesia. Conversion to morphine is impaired in 10% of patients and absent in fetal liver microsomes, rendering it ineffective in 10% of the population and infants <1 month. The usual dose is 1 mg kg\(^{-1}\) every 4 h and is limited by the high incidence of side effects including nausea, vomiting, sedation, urinary retention and constipation.

Hydromorphone, a synthetic opioid agonist, is available alone and in combination with acetaminophen and ibuprofen as an elixir or tablet. Twenty-five percent of the administered dose is converted to active metabolites including hydromorphone. Following ambulatory surgery, the incidence and severity of side effects is reduced when compared to codeine. Analgesia begins within 20–30 min of oral administration and lasts 3–6 h. The usual dose is 0.1–0.15 mg kg\(^{-1}\) / dose or 0.6 mg kg\(^{-1}\) day\(^{-1}\) administered every 4–6 h. The safety of oxycodone in children following ambulatory surgery has not been established but it is useful during transition from PCA or continuous epidural after major surgery as is hydromorphone.

**Adjunctive Analgesics for Ambulatory Surgery**

Post-tonsillectomy and genitourinary pain is significantly reduced by ▶ dexamethasone, 1 mg kg\(^{-1}\) up to a maximum 20 mg, intravenously after induction of anesthesia. ▶ Clonidine is employed preoperatively at a dose of 1–2 mcg kg\(^{-1}\) to reduce analgesic requirements. It has limited usefulness in outpatient surgery due its side effects of sedation, bradycardia and hypotension. ▶ Tramadol offers no advantage in the management of acute pediatric postoperative pain.

**Postoperative Pain Management Following Major Surgery**

Insertion of a catheter into the ▶ epidural space permits continuous infusion of opioid or local anesthetics. This provides patients with a baseline, prophylactic analgesic strategy. Studies in adults and most pediatric studies indicate that active pain following major thoracoabdominal, genitourinary, spinal and orthopedic surgeries is more effectively managed by neuraxial analgesia than PCA (Bozkurt 2002; Kokinsky and Thornbert 2003). In infants, catheters are frequently placed caudally and may often be threaded to the desired dermatomal level in most infants younger than 6 months. Caudally inserted catheters are at greater risk of dislodgement and contamination than those placed at the lumbar or thoracic levels. Infection rates can be reduced and catheter longevity improved by tunneling the catheter to a separate exit site (Kost-Byerly 2002).

When epidural catheters are inserted in anesthetized patients, as in most pediatric situations, the risk of spinal cord or neural injury may be increased. Controversy exists over the safety of anesthetized placement, however, when inserted by experienced anesthesiologists in children, the risk appears to be acceptably low (Krane et al. 1998). Catheters can be placed under direct visualization during spinal instrumentation, so that the catheter tip is located at the level of injury. In addition, two catheter techniques have been employed for extensive spinal surgeries. Bupivacaine 0.125% at 0.0625% and ropivacaine 0.1–0.2% are the most common solutions employed although 1% lidocaine or 0.125% levobupivacaine are employed in some hospitals. The addition of opioids like fentanyl, 2–10 mcg ml\(^{-1}\), acts synergistically to improve analgesia. At the recommended doses, these solutions provide a band of analgesia. Their safety is quite acceptable but high plasma concentrations can cause seizures and cardiac depression. Neonates are at increased risk of local anesthetic toxicity due to decreased ▶ alpha-1-acid glycoprotein binding and the accumulation of ▶ amide local anesthetics. Therefore, infusions should be terminated in infants younger than 3 months after 48 h unless lidocaine is employed and blood levels of lidocaine assessed daily to guide therapy (Kost-Byerly 2002). Motor blockade responds to dose reductions. Dosing guidelines are presented in Table 3. When neurosensory evaluation is necessary, e.g. following spinal instrumentation, where risk for compartment syndrome exists, or when the catheter tip cannot be located near the surgical site, neuraxial infusions of...
morphine or hydromorphone provide effective analgesia. Improvement of pain after rate adjustment or bolus requires ca. 45 min. Short-acting local anesthetics can be administered when prompt analgesia is needed. The incidence of nausea, pruritus and sedation are comparable to that of intravenous opioids (Kokinsky and Thornbert 2003). The risk of respiratory depression following neuraxial morphine ranges from 0.09–1.1% (Bozkurt 2002).

**Patient Controlled Analgesia**

When neuraxial techniques are not employed following major surgery, opioids should be administered intravenously whenever possible. Intramuscular injections are painful and result in slow onset of analgesia that cannot be titrated. Nurses should be encouraged to seek painful behavior or elicited pain scores regularly to detect escalation of pain. Early treatment reduces the duration of severe pain, the dose of opioid required to achieve comfort and the risk of inadvertent overdose.

> PCA improves pain relief when compared to intermittent, scheduled dosing. Standard dosing regimens are provided in Table 4. Careful assessment of respiratory function is essential to the safety of this technique since the incidence of serious respiratory depression is between 0.1–1.7% (Bozkurt 2002). The inclusion of a basal infusion rate is associated with a higher incidence of hypoxemia and lower respiratory rates (McNeely and Trentadue 1997). Consideration should be given to provision of a basal infusion at night to improve sleep. Continuous infusion of opioids is recommended for infants and young children. Nurse or family member activation of the PCA pump for children who cannot activate it due to cognitive impairment or physical limitations is an innovation that circumvents the main design feature that insures safety. Appropriate monitoring for opioid-induced respiratory depression is mandatory. Nurses trained to assess pain and opioid related side effects can safely employ PCA pumps as an alternative to intermittent bolus dosing. This promotes faster availability of the analgesic, lower incremental doses and improved pain relief. Monitoring protocols following bolus dosing and rate changes are required to maximize safety (Bozkurt 2002; Kokinsky and Thornbert 2003).

### Acute Pain in Children, Post-Operative, Table 4

<table>
<thead>
<tr>
<th>Medication</th>
<th>Loading Dose</th>
<th>Continuous / Basal Rate</th>
<th>PCA Bolus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine 1 or 5 mg ml-1</td>
<td>0.03 mg– 0.05 mg kg⁻¹</td>
<td>0.01– 0.03 mg kg⁻¹ h⁻¹</td>
<td>0.03 mg kg⁻¹</td>
</tr>
<tr>
<td>Hydromorphone 100 mcg ml-1</td>
<td>5 mcg kg⁻¹ 3–5 mcg kg⁻¹ h⁻¹ 2–5 mcg kg⁻¹ h⁻¹</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fentanyl 50 mcg ml-1</td>
<td>0.3 mcg kg⁻¹ 0.5–1 mcg kg⁻¹ h⁻¹ 0.2–1 mcg kg⁻¹ h⁻¹</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Caregivers can be trained to administer intermittent doses of parenteral opioids. Well-designed, training programs for caregivers and an appropriate level of nursing supervision are required to insure the safety of this innovation (Kost-Byerly 2002). Research regarding the safety of this approach in the acute, post-surgical setting is lacking.

The inclusion of NSAIDs, in particular ketorolac, reduces analgesic requirements and improves analgesia in children with epidurals or PCA (Kokki 2003). The use of NSAIDs following major orthopedic procedures remains controversial since prostaglandins induce lamellar bone formation and animal studies suggest that NSAIDs impair bone healing and fracture repair. No difference in the incidence of curve progression, hardware failure or back pain was found in adolescents following spinal fusion (Farrar and Lerman 2002). Since NSAIDs can result in renal dysfunction they are best avoided during the initial 24 h following major surgeries if ongoing third space losses are anticipated.

### References

Acute Pain in Children, Procedural

CHRISTINA LIOSSI
School of Psychology, University of Southampton and Great Ormond Street Hospital for Sick Children, London, UK cliossi@soton.ac.uk

Synonyms

Pediatric Pharmacological Interventions; Pediatric Psychological Interventions; Pediatric Integrated Care for Painful Procedures; Acute Procedural Pain in Children

Definition

Acute procedural pain refers to the pain that infants and children experience as a result of necessary invasive diagnostic and therapeutic procedures. Procedural pain management refers to the pharmacological, psychological and physical interventions used to prevent, reduce or eliminate pain sensations in children arising as a result of an invasive or aversive medical procedure.

Characteristics

Acute procedural pain is a significant problem for infants and children and, regrettably, is currently undertreated in many centers. A recent survey of institutions in the Pediatric Oncology Group (Broome et al. 1996) found that 67% of institutions routinely used local anesthesia, 22% used systemic premedication and 11% used different relaxation techniques for management of painful procedures such as lumbar punctures (LPs) and bone marrow aspirations (BMAs). Children (this term refers to all individuals in the pediatric age range, i.e. neonates, infants and adolescents) and their families experience significant emotional and social consequences as a result of pain and the effects of inadequately managed procedure-related pain can be severe and long lasting (Kazak et al. 1997; Young et al. 2005).

The aims of pain management are to 1) optimize pain control during the procedure, recognizing that a pain-free procedure may not be achievable, 2) enhance the patient’s physical well-being, 3) enhance the patient’s self-esteem and self-efficacy and 4) minimize the short and long term psychological distress of the patient and his / her family.

Invasive Procedures

Children undergo a variety of painful procedures in varied settings such as venipunctures, lumbar punctures, bone marrow aspirations, fracture reduction and orthodontic procedures. Painless procedures (such as CT scanning, MRI positioning for radiotherapy and ultrasonic examination, pelvic examination in young girls) that require patients to lie still, often on a cold, hard surface, may still be aversive and indirectly provoke pain and distress.

Factors that Affect Procedural Pain

Acute procedural pain in children is the result of a dynamic integration of physiological processes, psychological factors and sociocultural context embedded within a developmental trajectory. Consequently, procedural pain management is most probably effective when all components of the child’s pain experience are evaluated and addressed. Depending on the nature of the procedure and the characteristics and preferences of the child and his / her family, optimal pain control strategies will range from general anesthesia to psychological strategies. In all cases, a multimodal approach may reduce the potential for adverse effects arising from either escalating frequency or dosage levels of a single pharmacological modality (Lang et al. 2000).

In order to address all relevant factors, health care providers must assess the factors that affect a child’s pain. A standard nomenclature and a multidimensional approach are essential components of a comprehensive procedural pain assessment. The description of the pain should include its temporal features, intensity, quality and exacerbating and relieving factors. Treatment strategies should be based on the findings of the assessment and should address the inciting and contributing factors. The specific approach to procedural pain is shaped according to the anticipated intensity and duration of expected pain, the type of procedure, the context and meaning as seen by the child and family, the coping style and temperament of the child, the child’s history of pain and the available family support system (Liossi 2002; McGrath 1990; Zeltzer et al. 1989).

Procedures that cause pain in a child should be performed by health care professionals with high technical competence, so that pain is minimized to the greatest possible extent. The child and his / her family should be included in the planning and decision-making process regarding the treatment plan. This provides families with control and health care providers with valuable insights into how the child understands and copes with pain. Children and parents should receive appropriate information about what to expect and appropriate preparation about how to minimize distress (Blount et al. 1994). A quiet environment, calm adults and clear, confident instructions increase the likelihood that the specific pain management strategy selected will be effective (McGrath 1990; Zeltzer et al. 1989).
Pharmacological Interventions for Procedural Pain in Children

Local anesthesia is the standard analgesic intervention whenever tissue injury is involved. Topical anesthetics such as EMLA (eutectic mixture of local anesthetics) and amethocaine have recently revolutionized analgesic care but infiltration and regional nerve blocks with lidocaine, bupivacaine and ropivacaine remain in wide use (Finley 2001; Schechter et al. 2003). For procedural pain that is predictably severe and for which local measures give inadequate relief, such as for bone marrow aspirations, the use of systemic agents is required to reduce or eliminate pain. The use of anxiolytics or sedatives (such as benzodiazepines, propofol, chloral hydrate or barbiturates) alone for painful procedures does not provide analgesia but makes a child less able to communicate distress. The child still experiences pain during the procedure and there are no data on the short- or long-term sequelae of this strategy. These agents are adequate as sole interventions only for nonpainful procedures such as CT or MRI scans (Finley 2001; Schechter et al. 2003).

When it is necessary to use sedation and analgesia for painful procedures, the guidelines issued by the AAP (American Academy of Pediatrics, Committee on Drugs 1992) should be followed. These AAP guidelines recommend that skilled supervision is necessary whenever systemic pharmacologic agents are used for conscious sedation (i.e. the patient maintains a response to verbal and physical stimuli), that sedation should be conducted in a monitored setting with resuscitative drugs and equipment available and that agents should be administered by a competent person. The guidelines further recommend that one person is assigned to monitor the child’s condition and another qualified person is present to respond to medical emergencies. After the procedure, monitoring should continue until the patient is fully awake and has resumed the former level of function. Discharged patients should be accompanied by an adult for a time at least as long as two half-lives of the agents used. In contrast to conscious sedation, deep sedation (i.e. when the patient is not responsive to verbal or physical stimuli) is equivalent to general anesthesia and should be performed only under controlled circumstances by a professional trained in its use and skilled in airway management and advanced life support. Despite careful titration of sedative doses, individual responses are variable and patients may occasionally have respiratory compromise or loss of airway reflexes (Zeltzer et al. 1989). Nitrous oxide offers one more analgesic pharmacological option in the management of procedural pain. Its use requires availability of trained personnel and appropriate monitoring procedures. Administered by a mask or tent, nitrous oxide is a potent, short-acting inhalant analgesic. A significant drawback is the high degree of room air contamination, making occupational exposure a serious concern.

Psychological Interventions for Procedural Pain in Children

Psychological interventions for procedural pain management include preparation, deep breathing, distraction, relaxation, play therapy, guided imagery, cognitive therapy and hypnosis. Of these interventions, cognitive therapy and hypnosis have achieved status as empirically validated, efficacious and possibly efficacious interventions respectively, in the management of pediatric procedure-related cancer pain (Liossi 1999; Liossi 2002; Powers 1999), according to the framework developed by the American Psychological Association Division 12 Task Force on Promotion and Dissemination of Psychological Procedures (Chambless and Hollon 1998). The focus in cognitive therapy is on the child’s behavior, emotions, physiological reactions and cognitions (i.e. thoughts and visual images). The rationale for cognitive therapy is that a person’s understanding of the pain or the illness / procedure causing their pain determines their emotional reactions; therefore it is possible by modifying negative and maladaptive cognitions to reduce pain and distress. Hypnosis is a psychological state of heightened awareness and focused concentration, in which critical faculties are reduced and susceptibility and receptiveness to ideas is greatly enhanced. In all studies conducted to date, cognitive therapy and hypnosis were effective in reducing the pain and anxiety of young patients during procedures (Liossi 2002; Hilgard and LeBaron 1982).

Psychological strategies alone, however, often do not reduce pain sufficiently. A combination of psychological with pharmacological interventions is necessary. To this end, in 1998, the World Health Organization (WHO) developed and published guidelines for the management of pain in children with cancer. For all medical procedures, the use of a combination of a psychological with a pharmacological approach is supported and aggressive, preemptive approaches are emphasized. Preliminary empirical evidence for these guidelines has been offered in a recent randomized controlled clinical trial combining self-hypnosis with local anesthesia (Liossi et al. 2006) and in the development and evaluation of a multidisciplinary psychological and pharmacological protocol for procedure pain in childhood leukemia (APPO) at the Children’s Hospital of Philadelphia (Kazak and Kunin-Batson 2001). The general principles for pediatric procedural pain management are as follows:

Before the Procedure
- As far as possible treat procedure-related pain preemptively.
- Provide information regarding the time, frequency, and “clustering” of procedures, if more than one is to be required. For procedures that will be repeated, maximize treatment for the pain and anxiety of the first procedure to minimize the anticipatory anxiety before subsequent procedures.
• Provide the patient and his / her family with education regarding pain and pain management
• Tailor treatment options to the patient’s and the family’s needs and preferences, to the procedure and to the context.
• Provide adequate preparation of the patient and family. For children, discuss with the child and parents what can be expected and how the child might respond.
• Explore and address concerns regarding the procedure and pain management interventions.
• Minimize delays to prevent escalation of anticipatory anxiety.

During the Procedure
• Integrate pharmacological and nonpharmacological approaches in a complementary style.
• Allow parents to be with the child during the procedure, if parents choose to remain. Parents should be taught what to do, where to be and what to say to help their child through the procedure.

After the Procedure
• Debrief the patient and his / her family
• Encourage the use of coping skills
• Review with the patient and family their experiences and perceptions about the effectiveness of pain management strategies.

The list below provides an example of how psychological and pharmacological interventions can be integrated in the management of lumbar puncture pain for an older child (>6 years old):

Before the Procedure
• Teach the child self-hypnosis.
• Teach parents how to support their child in the use of self-hypnosis.
• Apply EMLA 60 min before the procedure.

During the Procedure
• Encourage the child to use self-hypnosis and their parents, if they wish, to coach them.

After the Procedure
• Encourage the use of self-hypnosis for the management of possible post lumbar puncture headache.

Summary
Innovations in acute pediatric procedural pain management do not need to be “high tech” In most cases, excellent analgesic results can be achieved through application of standard pharmacological and psychological approaches, continuous patient assessment and patient and family participation in treatment planning. Although financial pressures may slow the adoption of pain control as a priority in acute patient care (and in this regard integrated care is particularly expensive), equally strong social trends demand treatments that enhance patient and family-centered outcomes. Education of the public will increase societal awareness and support of children in pain and shape appropriate public policy, which in turn will speed up the bridging of the gap between theoretical developments, research evidence and current clinical practice in acute pediatric procedural pain management.

References