THE MANAGEMENT OF POSTOPERATIVE PAIN

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The purpose of this review is to suggest methods of relieving acute postoperative pain. It will discuss how the use of peripherally-acting drugs (such as the non-steroidal anti-inflammatory drugs, centrally-acting agents (such as opioids) and local anaesthetics can achieve this. Guidelines are offered for pain relief in children and the elderly. Further suggestions are made about the route of administration of analgesic drugs and factors which may alter the complaint of pain following surgery. This review is not comprehensive but is intended to summarise current thought about the practical management of postoperative pain in an understandable and accessible fashion.

The effective relief of pain is of paramount importance to anyone treating patients undergoing surgery. This should be achieved for humanitarian reasons, but there is now evidence that pain relief has significant physiological benefit. Not only does effective pain relief mean a smoother postoperative course with earlier discharge from hospital, but it may also reduce the onset of chronic pain syndromes.

Pain serves a biological function. It signals the presence of damage or disease within the body. In the case of postoperative pain it is the result of the surgery, but the principles outlined in this article apply also to the management of other acute pains such as those following burns or injury. The goal for postoperative pain management is to reduce or eliminate pain and discomfort with a minimum of side effects as cheaply as possible. Postoperative pain relief must reflect the needs of each patient and this can be achieved only if many factors are taken into account. These may be summarised as clinical factors, patient-related factors and local factors. In the final analysis the ultimate determinant of the adequacy of pain relief will be the patient's own perception of pain.

Clinical factors

The site of the surgery has a profound effect upon the degree of postoperative pain a patient may suffer. Operations on the thorax and upper abdomen are more painful than operations on the lower abdomen which, in turn, are more painful than peripheral operations on the limbs. However, any operation involving a body cavity, large joint surfaces or deep tissues should be regarded as painful. In particular, operations on the thorax or upper abdomen may produce widespread changes in pulmonary function, an increase in abdominal muscle tone and an associated decrease in diaphragmatic function. The result will be an inability to cough and clear secretions which may lead to lung atelectasis (collapse of lung tissue) and pneumonia. Matters are made worse by postoperative bowel distension or tight dressings.

Pain causes an increase in the sympathetic response of the body with subsequent rises in heart rate, cardiac work and oxygen consumption. Prolonged pain can reduce physical activity and lead to venous stasis and an increased risk of deep vein thrombosis and consequent pulmonary embolism. In addition, there can be widespread effects on gut and urinary tract motility which may lead, in turn, to postoperative ileus, nausea, vomiting and urinary retention. These problems are unpleasant for the patient and may prolong hospital stay.

The choice of pain-relieving techniques may be influenced by the site of surgery. Equally, it may be influenced by drug availability and familiarity with different methods of analgesia. For example, although patient-controlled analgesia (PCA), has often been shown to be better than the intermittent delivery of intramuscular opioids it does not produce as much pain relief as epidural opioid analgesia. Equally, a local anaesthetic block can effectively relieve pain, but only for the duration of the particular agent used. Choice of technique will also be influenced by the degree of training and expertise of the staff.

For many years, the standard method of treating postoperative pain in the developed world has been intramuscular opioid (usually morphine). The effects of opioid drugs vary greatly among patients and thus individual responses cannot be predicted. Many studies have shown that under-treatment of acute postoperative pain occurs because doctors and nurses overestimate the length of action and the strength of the drugs and that they have fears about respiratory depression, vomiting, sedation and dependency.

Improvement can be achieved by better education for all staff concerned with the delivery of postoperative pain relief and by making the assessment and recording of pain levels part of the routine management of each patient. Ideally, a named individual should be responsible in each hospital for the delivery and teaching of acute pain management.

Patient-related factors

Although it may be possible to predict, to a degree, the amount of postoperative pain knowing the site and nature of the surgery, other factors may alter the amount of pain suffered by the individual patient. The nature and intended purpose of the surgery may be important. If the proposed operation will lead to a restoration of normal function, for example, a hernia repair or fixation of a fracture, it is likely to be seen in a positive way by the patient. Where the outcome is not clear, for example, an operation for cancer or to investigate an unknown pain, the patients' fear and anxiety may lead to high levels of postoperative pain being reported. Patients who are afraid of anaesthesia or surgery may report more pain and this can be very difficult to treat.

Adequate time must be allowed to explain the intended operation and the steps that will be taken to ensure pain relief afterwards. It is important to establish the expectations of the patient before surgery. Some may fear the unknown and others may have previous experience of surgery or have heard stories from friends and relatives that present the postoperative period in an unfavourable way. An adequate and friendly explanation in simple terms will often reduce anxiety and minimise misunderstandings about the nature and purpose of the proposed surgery.

Local factors

A major problem in some parts of the world is that certain drugs, such as morphine, which are the mainstay of postoperative pain relief in many places, are not available. In addition, economic factors may mean that techniques of pain relief such as patient-controlled analgesia (P.C.A.) are unavailable and that techniques of regional anaesthesia which employ continuous infusions through disposable catheters are impossible. It is no use advocating techniques such as these if they are beyond local resources. It is better to maximise the effective use of local anaesthetic techniques and intermittent delivery of such analgesic drugs as are available. This review will discuss the use of the more advanced techniques in broad terms with the hope that the availability of both drugs and equipment can be improved in the longer term.

In general, the introduction of new and potentially expensive techniques is resisted by administration and professions alike. However, the introduction of such techniques may yield increased benefits in the form of improved recovery and faster discharge from hospital with consequent reductions in the cost of health care. Effective postoperative pain management may be encouraged by education of politicians, administrators, professional colleagues and patients.

Assessment of pain severity

Assessment of pain is in two parts; before the operation to make a pain management plan and afterwards to see whether the plan is working. The preoperative assessment includes the factors mentioned previously, as well as variables such as age, sex, weight, degree of obesity, current drug intake or past history of drug-related problems. Potential difficulties caused by language or culture are also assessed. There may be problems related to age, and relief of pain in children and the elderly are considered under separate headings.

There is some evidence to suggest that the use of opioid premedication establishes a level of analgesic control from the outset. There is however no evidence to support the use of local anaesthetic blocks or peripherally acting drugs in this pre-emptive fashion.

Rating scales are the most commonly used method of assessing acute pain and its relief. In practice, these are either words or numbers. In addition, a numerical value can be derived from a visual analogue scale. All these methods are simple, can be readily understood and require little in the way of technology or resources.

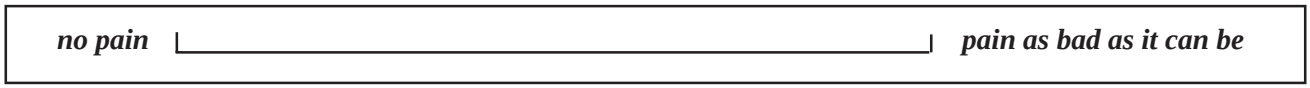
Words can be translated into any language and a simple five point scale is normally used. An example is shown on the next page.

Numbers can be assigned to each of the words for recording purposes (0-4). A simple numerical rating scale would require the patient to choose a number

no pain	*mild*	*moderate*	*severe*	*excruciating*

between 0 and 10 to represent their pain. Zero indicates that the patient has no pain and 10 means that the pain is as bad as can be imagined.

Visual analogue scales have a 10cm line which is marked as shown below. The patient is asked to make a vertical mark on the line to indicate the intensity of their pain.



There should be no other markings, numbers or words along the line as this tends to influence the results. It is most important to ensure that the patient understands the two end points. A small percentage of patients including the elderly and those with limited education have difficulty with visual analogue scales. Most can be trained by giving examples of familiar pain problems and relating these to positions along the line. If pain is being assessed regularly, then at the time of assessment the patient should not be able to see any other score as this may affect his decision. A visual analogue can be scored by measuring from the left side how far the patient marked towards the maximum pain end. This number can then be used to compare changes in the pain level.

Assessment of pain in infants or patients who cannot communicate can be difficult. Pain can be assessed with picture scales using varied facial expressions or by clinical observation (for example: sighing, groaning, sweating, ability to move). The latter method has the advantage that it does not rely on the patient to any great degree and can be carried out when other vital signs such as heart rate and blood pressure are being assessed. Asking the patient to take a deep breath or to cough or move will also provide useful information and it is important to emphasise that measurement of pain while the patient is at rest is unlikely to indicate the need for analgesia. Pain relief should be assessed when the patient is active.

Simple questions like "*where does it hurt?*" and "*what does it feel like?*" may allow a qualitative evaluation of pain after surgery. Pain distant from the operative site may indicate complications not associated with the procedure which may require separate treatment. Complaints of generalised pain all over the body may represent stress, anxiety, or in some cases fever. The description of the pain may indicate the cause. For example sharp, stabbing pain is associated with surgery, whereas numbness or tingling may mean nerve compression or ischaemia. Unusual or vague descriptions are more likely to be due to non-organic causes.

It may be difficult to assess pain in the early post-operative period by any of the methods described. It should be stressed that the assessment must be made at regular intervals and should form part of the routine postoperative observations. The progress of the patient is more easily assessed if results are charted in graphical form rather than as a number. Nursing, auxiliary and trainee medical staff should be encouraged to use assessment of pain routinely. Furthermore, they should be given training in the use of all forms of analgesic technique so they become confident in their use. Experience suggests that frequent assessment and delivery of analgesia whenever needed become a routine once the benefit to the patient is recognised.

PHARMACOLOGY

The World Health Organisation Analgesic Ladder was introduced to improve pain control in patients with cancer pain. However, it has lessons for the management of acute pain as it employs a logical strategy to pain management. As originally described, the ladder has three rungs. In the first instance peripherally acting drugs such as aspirin, paracetamol or non-steroidal anti-inflammatory drugs (NSAIDs) are given. If pain control is not achieved, the second part of the ladder is to introduce weak opioid drugs such as codeine or dextropropoxyphene together with appropriate agents to control and minimise side effects. If effective control is not achieved by this change, the final rung of the ladder is to introduce strong opioid drugs such as morphine. Analgesia from peripherally acting drugs may be additive to that from centrally-acting opioids and thus, the two are given together.

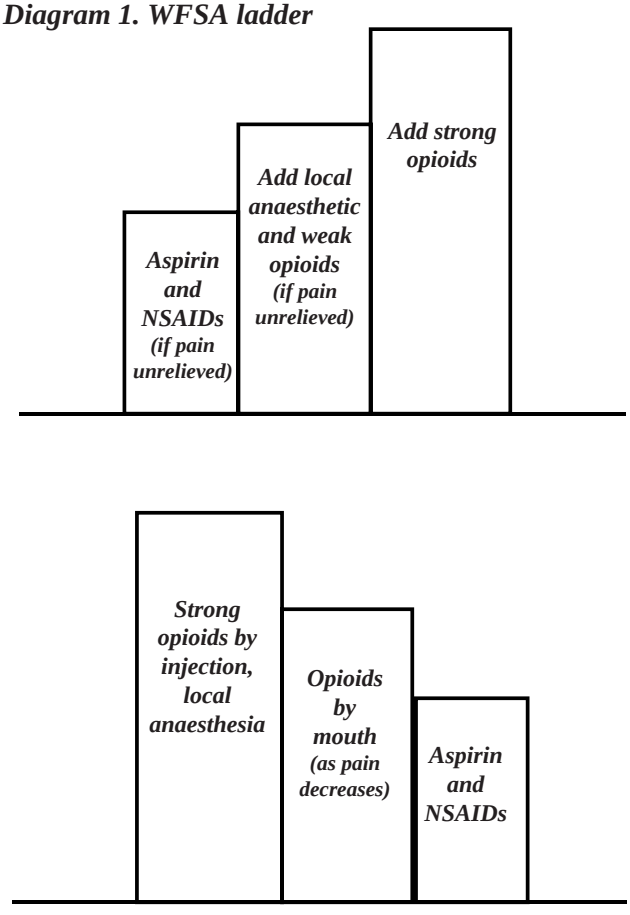
The World Federation of Societies of Anaesthesiologists (WFSA) Analgesic Ladder has been developed to treat acute pain. Initially, the pain can be expected to be severe and may need controlling with strong analgesics in combination with local anaesthetic blocks and peripherally acting drugs. The oral route for the administration of drugs may be denied because of the nature of the surgery and drugs may have to be given by injection. Normally, postoperative pain should decrease with time and the need for drugs to be given by injection should cease. The second rung on the postoperative pain ladder is the restoration of the use of the oral route to deliver analgesia. Strong opioids may no longer be required and adequate analgesia can be obtained by using combinations of peripherally acting agents and weak opioids. The final step is when the pain can be controlled by peripherally acting agents alone.

Local Anaesthetics

Regional anaesthetic techniques used for surgery may have positive respiratory and cardiovascular effects associated with reduced blood loss and excellent pain relief which can improve convalescence. Clearly, any technique that can be used for the surgical procedure will provide near perfect postoperative pain relief if it can be prolonged beyond the time of the surgery. There are many straightforward local anaesthetic techniques which can be continued into the postoperative period to provide effective pain relief. Most of these can be carried out with minimal risk to the patient and include local infiltration of incisions with long-acting local anaesthetics, blockade of peripheral nerves or plexuses and continuous block techniques peripherally or centrally. It is a mistake to expect 100% analgesia in every patient using a local anaesthetic technique alone as postoperative pain has many sources. The true place of local anaesthetic techniques is as part of a prepared plan for overall management that employs these techniques in conjunction with appropriate analgesic drugs. As pain is multifactorial in origin it is logical that management should consist of a combination of approaches in order to achieve the best results.

Infiltration of a wound with a long-acting local anaesthetic such as bupivacaine can provide effective analgesia for several hours. Further pain relief can be obtained with repeat injections or by infusions via a thin catheter. Blockade of plexuses or peripheral nerves will provide selective analgesia in those parts of the body supplied by the plexus or nerves. These techniques can either be used to provide anaesthesia for the surgery or specifically for postoperative pain relief. Depending upon the availability of drugs and equipment either single shot or continuous infusion techniques can be used to block brachial plexus, lumbar plexus, intercostal, sciatic, femoral or any nerves supplying the specific area of the surgery. These techniques may be especially useful where a sympathetic block is needed to improve postoperative blood supply or where central blockade such as spinal or epidural blockade is contraindicated.

Diagram 1. WFSA ladder



Spinal anaesthesia provides excellent analgesia for surgery in the lower half of the body and pain relief can last many hours after completion of the operation if long-acting drugs containing vasoconstrictors are used. Continuous analgesia using the spinal route has been tried but epidural analgesia is used more widely. The use of the epidural technique

requires experienced practitioners and specific training for nursing staff in the postoperative management of patients. In addition, great care must be taken to maintain sterility if a continuous technique is to be used. Epidural catheters can be placed in either the cervical, thoracic or lumbar regions but lumbar epidural blockade is the most commonly used. Although continuous infusions of

Fig 1. ***Local Anaesthetics for the Treatment of Acute Pain***

Agent	% solution for analgesic blocks	Duration (hours)	Max. single dose mg/kg. (Total mg in adults)*	% solution for infusion	Comments
Lignocaine					
Infiltration	0.5-1	1-2	7	——	Rapid onset
Epidural	1-2	1-2	(500)	0.3-0.7	Dense motor block
Plexus or nerve	0.75-1.5	1-3		0.5-1	
Mepivacaine					
Infiltration	0.5-1	1.5-3	7	——	Rapid onset
Epidural	1-2	1.5-3	(500)	0.3-0.7	Dense motor block
Plexus or nerve	0.75-1.5	2-4		0.5-1	Longer action than lignocaine
Prilocaine					
Infiltration	0.5-1	1-2	8.5	——	Rapid onset
Epidural	2-3	1-3	(600)	0.5-1	Dense motor block
Plexus or nerve	1.5-2	1.5-3		0.75-1.25	Least toxic amide agent Methaema-globinaemia >600 mg.
Bupivacaine					
Infiltration	0.125-0.25	1.5-6	3.5	——	Avoid 0.75% in obstetrics
Epidural	0.25-0.75	1.5-5	(225)	0.0625-0.125	
Plexus or nerve	0.25-0.5	8-24+	0.125-0.25		Mainly sensory block at low concen-trations. Cardiotoxic after rapid IV injection
Chloroprocaine					
Infiltration	1	0.5-1	14	——	Lowest systemic toxicity
Epidural	1.5-3	0.5-1	(1000)	0.5-1	of all agents Motor/sensory deficits may follow intrathecal injection

**for healthy patients with 1:200,000 adrenaline added to solutions. Maximum doses quoted should be reduced by 40% if solutions do not contain adrenaline. Much lower doses can be lethal if injected directly into a blood vessel*

local anaesthetic may produce very effective analgesia, they may also produce undesirable side effects such as hypotension, sensory and motor block, nausea and urinary retention. Combination of local anaesthetic drugs with opioids given centrally may reduce some of these problems (*see intrathecal and epidural opioids*)

The following table lists suggested concentrations, "safe" maximum doses and block characteristics of the most widely available local anaesthetics. All doses assume healthy adult patients and maximum permissible dosage should be calculated on the basis of body weight, particularly in the case of children (*see section on paediatric pain*).

Intravascular injection of local anaesthetic drugs can produce serious or life-threatening effects at much smaller doses than the maxima quoted.

Local anaesthetic injections at any site can form part of balanced analgesia where a mixture of techniques provides pain relief. This has the advantage of decreasing the dosage of each drug needed and diminishing the likelihood of side effects. The small delay that results from performance of the blocks is outweighed by the benefit to the patient.

Toxicity

The most important factor in the prevention of local anaesthetic toxicity is the avoidance of intravascular injection. Careful aspiration is vital especially if the needle is moved. However, a negative aspiration test is not an absolute guarantee of correct needle placement. Inject slowly and watch carefully for signs of toxicity such as buzzing in the ears, a feeling of numbness in the face and lips and a feeling of muscle twitching. If toxicity is suspected the injection should be stopped and the patient's respiration and circulation assessed. Provided hypoxia is avoided little other treatment is needed. Cardiovascular depression should be treated by raising the legs, giving intravenous fluids and administering a vasopressor such as ephedrine. Major collapse requires full resuscitation. Convulsions may occur and need management of airway, breathing and circulation as well as control of the fitting with diazepam or thiopentone.

Non-opioid analgesics

The most commonly used analgesic agents throughout the world are drugs in this group such as aspirin, paracetamol and the non-steroidal anti-inflammatory drugs (NSAIDs). These are the main analgesic treatment for mild to moderate pain.

Aspirin is an effective analgesic and is widely available throughout the world. It is active orally within a short period as it is rapidly metabolised into salicylic acid which has analgesic and, probably, anti-inflammatory activity. Salicylic acid has a half life of about four hours at therapeutic doses. Excretion is dose dependent and high doses will be excreted more slowly. The length of action may be reduced if aspirin is given with antacids.

Aspirin has major gastrointestinal side effects and may cause nausea, sickness or gastrointestinal bleeding because of antiplatelet effects which are irreversible. For this latter reason the use of aspirin after surgery should be withheld if alternatives are available. Diflunisal and Choline salicylate are related compounds without this latter problem.

Aspirin has an epidemiological association with Reye's syndrome and should not normally be used to provide analgesia in children under the age of 12 years.

Doses range from a minimum of 300mg orally, 4 hourly, to a maximum of 8g, orally daily.

Paracetamol has analgesic and antipyretic properties but little anti-inflammatory effect. It is well absorbed orally and is metabolised almost entirely in the liver. It has few side effects in normal dosage and is widely used for the treatment of minor pain. It causes hepatotoxicity in overdosage by overloading the normal metabolic pathways with the formation of a toxic metabolite.

Doses range from a minimum of 500mg, orally, 4 hourly to a maximum of 4g, orally daily.

NSAIDs have both analgesic and anti-inflammatory actions. Their mechanism of action is predominantly by inhibition of prostaglandin synthesis by the enzyme cyclo-oxygenase which catalyses the conversion of arachidonic acid to the various prostaglandins that are the chief mediators of inflammation. All NSAIDs work in the same way and thus there is no point in giving more than one at a time. In addition, there is a widespread individual variation in response to these agents and thus there is no drug of choice. NSAIDs are, in general, more useful for superficial pain arising from the skin,

buccal mucosa, joint surfaces and bone. They may be usefully combined with opioids due to their different modes of action.

The choice of a NSAID should be made on the basis of availability, cost and length of action. If pain is likely to be persistent over a long period of time it may be logical to choose an agent with a long half life and prolonged clinical effect. However, this group of drugs has a high incidence of side effects with prolonged use and caution should be exercised. All NSAIDs have antiplatelet activity leading to increased bleeding time. These drugs also inhibit prostaglandin synthesis in the gastric mucosa and may thus produce gastric bleeding as a side effect. Care should be exercised when using these drugs in patients with asthma or impaired renal function.

The following should be regarded as relative contraindications to the use of NSAIDs: Any history of peptic ulceration, gastrointestinal bleeding or bleeding diathesis; operations associated with high blood loss, asthma, moderate to severe renal impairment, dehydration and any history of hypersensitivity to NSAIDs or aspirin.

NSAIDs are available in a variety of formulations: tablet, injection, topical cream and suppository. The incidence of side effects and adverse reactions with an individual drug is similar regardless of the route of delivery.

Ibuprofen is the drug of choice if the oral route is available. It is clinically effective, cheap and has a lower side effects profile than other NSAIDs. Alternatives are diclofenac, naproxen, piroxicam, ketorolac, indomethacin and mefenamic acid. Where the oral route is not available the drug may be given by another route such as suppository, injection or topically. Aspirin and most of the NSAIDs are available as suppositories and are well absorbed.

NSAIDs

Drug Name	Forms Available	Daily Dose Range	Half Life (h)
Ibuprofen	tablet, syrup	600-1200 mg.	1-2
Diclofenac	tablet, suppository, injection, cream	75-150 mg.	1-2
Naproxen	tablet, suspension, suppository	500-1000 mg.	14
Piroxicam	capsule, suppository, cream, injection	10-30 mg.	35+
Ketorolac	tablet, injection	10-30 mg.	4
Indomethacin	capsule, suspension, suppository	50-200 mg.	4
Mefenamic Acid	tablet, capsule	1500 mg.	4

Weak opioids

Codeine is a weak opioid analgesic which is derived from opium alkaloids (as is morphine). Codeine is markedly less active than morphine, has predictable effects when given orally and is effective against mild to moderate pain. It may be combined with paracetamol but care should be taken not to exceed the maximum recommended dose of paracetamol when using combination tablets.

Doses range from 15 mg to 60mg 4 hourly with a maximum of 300mg daily. (If pain is not responding to maximum doses a stronger drug should be used if available)

Dextropropoxyphene is structurally related to methadone but is a relatively poor analgesic. It is often marketed in combination with paracetamol. and the same precautions should be observed. It offers few, if any, advantages over codeine.

Doses range from 32.5mg (in combination with paracetamol) to 60mg 4 hourly with a maximum of 300mg daily. (If pain is not responding to maximum doses a stronger drug should be used)

Combinations of weak opioids and peripherally acting drugs are useful in minor surgical procedures where excessive pain is not anticipated or for outpatient use:

Paracetamol 500mg/codeine 8mg tablets. 2 tablets 4 hourly to a maximum of 8 tablets daily.

If analgesia is insufficient - *Paracetamol 1g orally with Codeine 30 to 60mg 4 to 6 hourly to a maximum of 4 doses.*

Strong opioids

Severe pain arising from deep or visceral structures requires the use of strong opioids. Appropriate treatment begins with an understanding of the correct drug, route of administration and the mode of action. Early administration will achieve effective analgesic concentrations and make it easier to maintain the therapeutic level of the drug in the blood. Once a satisfactory level of pain relief has been achieved this can be sustained by regular administration of opioid regardless of whether the intramuscular, subcutaneous, intravenous, oral, sublingual or rectal route is chosen. Administration of adequate doses of analgesic may be inhibited because of side effects, notably nausea and vomiting.

The oral route of administration may not be available immediately after surgery. If gastrointestinal function is normal following surgery that has been superficial or minor in nature strong analgesia is not required. However, the oral route may be available as the patient recovers from major surgery and strong analgesics such as morphine are effective when taken by mouth. When the patient is unable to take drugs by mouth other routes of administration should be used. In general, effective analgesia can be provided by intramuscular injection despite the recognised drawbacks of this method. Conventional intramuscular delivery of opioid analgesics has the advantage of representing familiar practice and has inherent safety for this reason. The technique is inexpensive and the gradual onset of pain relief permits easy assessment of possible overdose. A disadvantage of the method may be that the dose is too large (side effects) or too small (no pain relief). In addition, the injections are painful and the onset of pain relief is delayed while the drug is absorbed.

Other factors affecting drug absorption. There may be enormous variations in the blood levels and rates of absorption of opioids after intramuscular injection. These may be influenced by the presence of hepatic or renal disease, the extremes of age and the presence of other drug therapy. Any condition that reduces peripheral blood flow can impair drug uptake and thus, reduced body temperature, hypovolaemia and hypotension will all result in lowered uptake from injection sites. Hypothermia and hypothyroidism may both lead to a reduction in metabolism causing an increased sensitivity to drugs.

Minimum effective analgesic concentration (MEAC) is the minimum plasma concentration at which analgesia occurs when a drug is given by constant infusion. The variation of MEAC level between different patients accounts for the vast difference in analgesic requirements that may be encountered. This can be illustrated by the large variations in drug demand seen when Patient Controlled Analgesia (PCA) systems are used. This varies between 13 and 44mg/h for pethidine (meperidine), 30 and 100mcg/h for fentanyl and 0.3 and 9mg/h for morphine in different patients.

Methods of using opioid drugs

The **oral** route of administration is the most widely used route and most acceptable for the patient. Disadvantages of the oral route to treat acute pain are that absorption of opioids may be reduced by the delay in gastric emptying that follows surgery. This has the dual disadvantage of non-absorption initially, followed by the possibility of a large dose being absorbed when gastrointestinal function resumes. Nausea and vomiting may prevent absorption of drugs administered orally and in addition, there is a reduced bioavailability after metabolism in the gut wall and the liver as the drug is absorbed (first pass metabolism). Thus the oral route may be unsuitable in many instances.

The **sublingual** route offers some theoretical advantages for drug administration. Absorption

occurs directly into the systemic circulation as there is no first pass metabolism. Tablets can be removed in the event of overdosage and, because of metabolism, they are unlikely to cause toxicity if they are swallowed. The drug that has been most commonly used by this route is buprenorphine which is rapidly absorped and has a long duration of action (6 h). It is associated with a high incidence of nausea, vomiting and sedation.

Rectal administration. Most opioid analgesics are subject to extensive metabolism if given by mouth. The rectal route is a useful alternative, particularly if severe pain is accompanied by nausea and vomiting. Opioids can be delivered successfully by suppository but it is not ideal for the immediate relief of acute pain because of the slow and sometimes erratic absorption, although it is ideally suited for the maintenance of analgesia. Rectal doses for most strong opioids are about half those needed by the oral route. Availability of preparations of opioids for rectal use is very variable throughout the world.

Strong analgesics

Drug Name	Route of Delivery	Dose (mg)	Length of Action (h)
Morphine	intramuscular/ subcutaneous	10-15	2-4
Methadone	intramuscular	7.5-10	4-6
Pethidine/meperidine	intramuscular	100-150	1-2
Buprenorphine	sublingual	0.2-0.4	6-8

(Intravenous - half the IM dose slowly over 5 minutes)

Intramuscular administration represents the optimum technique for the developing world where strong opioids are available. As stated previously, this method of analgesia may be associated with peaks and troughs in effect. A simple way of overcoming this problem is to administer the analgesic on a regular 4-hourly basis. In fact, it has been demonstrated that pain relief from intermittent intramuscular injection of opioids can be as good as that from PCA. To achieve this level of analgesia requires regular assessment and recording of pain scores and the development of treatment algorithms for automatic delivery of analgesia depending upon the level of pain recorded.

Intravenous administration. For many years it has been common practice to deliver small boluses of opioid both in theatre and the postoperative recovery area to produce immediate analgesia. This has the disadvantage of producing fluctuations in plasma concentrations of the injected drug, although when performed carefully intravenous injection brings more rapid pain relief than other methods. In general however intravenous techniques, by either intermittent injection or by infusion, are unsuitable except in high dependency and intensive therapy units as they are inherently dangerous if the patient is left unsupervised for even a short period.

Patient Controlled Analgesia (PCA) became popular when it was realised that individual requirements for opioids varied considerably. Therefore a system was devised whereby patients could administer their own intravenous analgesia and so titrate the dose to their own end-point of pain relief using a small microprocessor - controlled pump. A variety of commercial devices are now available for this purpose. When pain is experienced, the patient self-administers a small bolus dose of opioid and experiences the benefit of this action. Thus they can adjust the level of analgesia required, according to the severity of the pain. In theory, the plasma level of the analgesic will be relatively constant and side effects caused by fluctuations in plasma level will be eliminated.

To achieve successful and safe analgesia with PCA requires that the patient understands what is required and this should be explained in detail before the

operation. Almost every opioid drug has been used for PCA. In theory, the ideal drug should have rapid onset, moderate duration of action (to prevent the need for frequent demands) and have a high margin of safety between effectiveness and troublesome side effects. Choice usually depends upon availability, personal preference and experience. Once a selection has been made other parameters need to be set including the size of the bolus dose, the minimum time period between doses (the lock-out period) and the maximum dose allowed. Some devices permit the use of a continuous background infusion but for the reasons stated in the section on intravenous administration it will not be considered here.

Morphine is the most popular drug and will be used as an example. The ideal dose of morphine has been found to be 1mg. However, regular review is needed in every case to ensure that pain relief is adequate. The aim of the lock-out period is to prevent overdosage occurring because of over-enthusiastic demands for more analgesia. The lock-out time should be long enough for the previous dose to have an effect. In practice, lockout times of between 5 and 10 minutes are enough for most opioids. A maximum dose can be programmed into most PCA devices to prevent overdose. In practice, it is more logical to accept that the analgesic requirements of patients will vary considerably and some patients may require very large amounts to achieve adequate pain relief.

Guidelines for patient controlled intravenous opioid administration

Drug (concentration)	**Size of bolus (mg.)**	**Lockout interval (min)**
Morphine *(1mg/ml)*	0.5-2.5	5-10
Pethidine *(10mg/ml)*	5-25	5-1
Methadone *(1mg/ml)*	0.5-2.5	8-20
Fentanyl *(0.01mg/ml)*	0.01-0.02	3-10

PCA need not be administered intravenously and intramuscular, subcutaneous and epidural routes have all been employed. Patients using PCA usually titrate their analgesia to a point where they are comfortable rather than pain free. The reasons for this are not clear but are probably related to fears of overdosage, the need for contact with members of the hospital staff and the expectation of some pain after surgery. The normal pattern of use is for frequent demands to be made in the initial postoperative period and for these to decrease with time. The total amount of opioid used is less with PCA than with intramuscular delivery. The overall incidence of side effects is about the same with the two techniques but the incidence of respiratory depression is less with P.C.A. Where this has occurred it has usually been due to incorrect programming, device malfunction or inappropriate use by third parties. Because of this, devices should be tamperproof and activated only by the patient. The pump should normally be attached to a dedicated intravenous cannula. If it is attached to an existing intravenous infusion it must be through a one way valve to prevent increments of opioid collecting in the giving set which may be delivered later as a large bolus if the infusion rate is increased.

Intrathecal and epidural opioids have been used following a wide variety of surgical procedures and other acutely painful conditions. Intrathecal opioids are easy to administer either to provide surgical anaesthesia or as an additional technique when general anaesthesia is given. Many patients will remain comfortable for 24 hours or more after a single injection of intrathecal morphine. The epidural route has been used even more extensively although the reason for this is not clear. It may be that anaesthetists are more familiar with the epidural route for the delivery of long term analgesia and because of the potential advantages in terms of long term catheter use and freedom from post-spinal puncture headache.

Side effects are common using these routes of delivery. They include nausea, vomiting, itching (which is much more common with morphine than other drugs) and urinary retention. Of most concern however, as with any opioid, is the possibility of respiratory depression. Early respiratory depression may be caused by systemic drug absorption. Late respiratory depression is from rostral (towards the head) spread in the cerebrospinal fluid and the incidence is increased by factors such as dose, age, posture, aqueous solubility of the drug administered, positive pressure ventilation and increased intra-abdominal pressure

It should be assumed that all patients are at risk of this occasional complication and a high level of care and vigilance should be maintained. Many centres recommend that patients receiving analgesia by these methods should be in a high dependency or intensive therapy unit. Trained personnel should be present at all times to check on the rate and depth of respiration and level of consciousness of the patient at regular intervals, protocols should be available for immediate treatment of complications and

epidural catheter. These mixtures appear to produce a synergistic effect. Bupivacaine appears to be most suitable for this purpose as dilute solutions produce a very limited motor block. A mixture of bupivacaine 0.1% and morphine 0.01% infused at 3/4ml/h gives good pain relief and permits the patient to walk without the risk of hypotension.

Other routes of delivery Transdermal, inhaled and intranasal opioids are among the routes of drug delivery currently under development.

Intrathecal and epidural opioids for treatment of acute pain

Drug	Single dose (mg)	Onset(min)	Duration of single dose (h)
Epidural			
Morphine	1-6	30	6-24
Pethidine	20-150	5	4-8
Methadone	1-10	10	6-10
Fentanyl	0.025-0.1	5	2-4
Subarachnoid			
Morphine	0.1-0.3	15	8-24+
Pethidine	10-30	?	10-24+
Fentanyl	0.005-0.025	5	3-6

Note: lower dose levels may be effective in the elderly or when injected in cervical or thoracic regions. The duration of analgesia may be very varied. Higher doses tend to extend duration. Pethidine has local anaesthetic as well as analgesic actions.

medical staff have received appropriate training. Respiratory rate alone is insufficient to measure the status of respiration. A more global assessment is necessary particularly during the first 24 hours of treatment. Any patient receiving intrathecal or epidural opioids whose level of consciousness drops must be assumed to have respiratory depression until proved otherwise. Where available, the use of supple-mentary oxygen has been recommended.

It is particularly dangerous to prescribe other opioids to patients receiving intrathecal or epidural opioids as this increases the likelihood of clinically significant respiratory depression.

Opioid/local anaesthetic mixtures have been adopted in some centres in an attempt to reduce the frequency and severity of side effects seen with infusions of pure local anaesthetics. Dilute concentrations of these agents have been combined with opioids and delivered by infusion through an

Opioid analgesic agents (narcotics)

Opioid analgesic drugs act at receptors within the central nervous system. Initially three distinct receptor groups were described (mu, kappa and sigma) on the basis of their binding characteristics. The opioid drugs have differing affinities for these receptors and are described by their receptor affinities. Thus morphine and related compounds are known as mu agonists. Other analgesic agents have differing receptor affinities giving them different clinical properties.

Morphine remains the gold standard by which other analgesics are judged. Morphine has a short half life and poor bioavailability. It is metabolised in the liver and clearance is reduced in patients with liver disease, in the elderly and the debilitated. Major side effects include nausea, vomiting, constipation and respiratory depression. Tolerance may occur with repeated dosage but this is highly

unlikely to become apparent during the first week of continuous treatment.

Parenteral doses range from 2.5mg to a maximum of 20mg. Morphine may need to be prescribed as frequently as 2 hourly.

Pethidine is a synthetic opioid which is structurally different from morphine but which has similar actions. It has a short half life and similar bioavailability and clearance to morphine. Pethidine has a short duration of action and may need to be given hourly. Pethidine has a toxic metabolite (norpethidine) which is cleared by the kidney, but which accumulates in renal failure or following frequent and prolonged doses and may lead to muscle twitching and convulsions. Extreme caution is advised if pethidine is used over a prolonged period or in patients with renal failure.

Parenteral doses range from 25mg to a maximum of 150mg. Frequency of administration 1 to 4 hourly.

Methadone is different from morphine and pethidine but has the same actions. It differs from the other agents in that it is well absorbed by mouth and undergoes little metabolism. It is slowly metabolised in the liver and has a very long half life. The resultant prolonged duration of action makes it more suitable for use in chronic pain rather than acute postoperative pain although it has been used successfully for this purpose.

Oral doses range from 2.5mg to 25mg given 6 to 12 hourly.

Fentanyl is used chiefly for intraoperative analgesia because of its relatively short duration of action. It has similar actions and side effects to morphine and is metabolised in the liver. Postoperatively it has been used intrathecally or epidurally as described earlier.

Buprenorphine is described as a partial agonist, which, in practical terms, means that it has different properties from drugs which work mainly at the mu receptor. Buprenorphine appears to have some action at all the major opioid receptors. Its most useful attribute is that it can be delivered by the sublingual route. It is rapdly absorbed and has a prolonged duratiuon of action (6 h) but is associated with a high incidence of nausea, vomiting and sedation. Of the opioids, buprenorphine poses the least risk to patients with renal failure as the metabolites are virtually inactive and if accumulation does occur it is of no significance.

Sublingual doses range from 200-400mcg 8 hourly

Nalbuphine and Butorphanol are known as agonist/antagonists as unlike conventional opioids, they act at the kappa receptor rather than the mu receptor. Both have been used to provide postoperative analgesia by intermittent, continuous and PCA techniques. They exhibit a ceiling effect for analgesic activity (which has limited their popularity) and also for respiratory depression which should make clinical use safer. They are alleged to have a lower abuse potential than conventional opioid agents.

Side effects and toxicity

Opioid analgesics share many side effects though the degree may vary between agents. The most common include nausea, vomiting, constipation and drowsiness. Larger doses produce respiratory depression and hypotension. The specific antidote naloxone is indicated if there is coma or very slow respiration. Because of its short action, repeated injections of 200 - 400mcg intravenously may be necessary. Alternatively, it may be given by continuous intravenous infusion, the rate of administration being adjusted according to response.

Pain Relief In Children

Management of pain in children is often inadequate and there is no evidence to support the idea that pain is less intense in neonates and young children due to their developing nervous system. Children tend to receive less analgesia than adults and the drugs are often discontinued sooner. Furthermore, it is simply not true that potent analgesics are dangerous when used in children because of the risks of side effects and addiction. As with all pain, successful management depends upon the identification and treatment of all the factors which contribute, in particular fear and anxiety. In this context, careful explanations to child and parents can be helpful. A major problem in treating pain in children is associated with the difficulty in assessment

Assessment presents a major challenge, especially in those patients who cannot explain how they feel and who cannot understand the relationship between the treatment and the pain. The worst response is to

ignore the presence of pain and the best is to assess the pain and the patients response to treatment as thoroughly as possible. In very young children observational measures may be helpful, but absence of these signs does not rule out the existence of pain. Assessing simple factors such as whether or not the child is asleep, crying, relaxed, tense or are responding to their parents may be used to create a cumulative pain score.

Pain assessment for children under four years If the patient is asleep, no further assessment is needed. If the patient is awake check the following:

		Score
1. Cry	not crying	0
	crying	1
2. Posture	relaxed	0
	tense	1
3. Expression	relaxed or happy	0
	distressed	1
4. Response	responds when spoken to	0
	no response	1

Score 1 as slight pain, 2 as moderate pain, 3 as severe pain and 4 as the worst pain possible.

Children over four are better able to report pain and are able to use colour scales, pictures of varying facial expression and often visual analogue scales.

Management of pain in children needs to be handled more actively than in adults. Greater effort should be made to anticipate pain as children cannot be relied upon to ask for analgesia as might an adult. It may be better to establish a schedule of regular analgesia. The route of administration will depend on the drug to be used, the severity of the pain and the likely side effects. Drugs are best given by mouth if possible but the rectal route may be tolerated better if vomiting is a problem. The parenteral route (by injection) should only be used if the drug selected can only be given by that method or where other methods have failed. Intramuscular injections should be avoided as they may be very painful themselves and subcutaneous or intravenous routes are to be preferred.

Local anaesthetic creams are available that can be applied under an occlusive dressing to produce anaesthesia of the underlying skin for up to an hour. These may enable painless placement of venous catheters or allow infiltration of the area with local anaesthetic. These creams should not be used rectally, directly on the wound or on mucous membranes.

Many procedures associated with the relief of pain can themselves be painful. The performance of regional blockade, wound infiltration and the placement of intravenous or subcutaneous lines and catheters may be carried out without discomfort or resistance whilst the patient is anaesthetised.

Infiltration of local anaesthetic agent into the wound before wakening can reduce postoperative pain for long periods. Equally, regional anaesthesia undertaken while the child is under general anaesthesia can give prolonged control of pain and avoid the use of opioids. It is particularly suitable where early discharge from hospital is required. Extradural anaesthesia by the caudal route will provide excellent analgesia for any surgery below the waist such as herniorrhaphy, orchidopexy or circumcision. Children and their parents should be warned of the possibility of urinary retention and of transient weakness or numbness. Hypotension does not seem to be a problem in children under the age of six, but can be anticipated in older children and adults.

Dose schedule for caudal block with bupivacaine in children. 0.25% solution is satisfactory for blocks requiring a volume of 20ml or less. **A more dilute solution (0.2% bupivacaine) should be used where volumes of 20ml or more are required.**

For short cases 1% lignocaine will be effective and the required volume can be calculated in a similar fashion.

Type of block	Volume (ml/kg)
Lumbosacral	0.5
Thoracolumbar	1.0
Mid-thoracic	1.25

Maximum doses of bupivacaine in any four hour period are 2-3mg/kg and for lignocaine 3mg/kg (without adrenaline), 6mg/kg (with 1:200,000 adrenaline)

Non-opioid analgesics

Paracetamol is effective for mild to moderate pain. It can be given as an oral suspension in a dose of 15mg/kg to a maximum of 60mg/kg in 24 hours. Slightly higher doses (20mg/kg) are needed if this drug is used rectally as absorption is less reliable.

NSAIDs

Aspirin should not be given to children under 12 years old because of the association with Reye's syndrome. There is little experience with the use of NSAIDs in children except in the case of ibuprofen. This is available as a suspension or a syrup and should be given up to a dose of 20mg/kg/day. Diclofenac is available as a suppository (12.5mg or 25mg) for paediatric use and can be used as a premedicant or administered at induction of anaesthesia. Dosage can be up to 3mg/kg/day.

Opioids

Opioids can be used in the same way for children as for adults. The chief concern is that of respiratory depression when larger doses are being used. Suggested dose guidelines given here will minimise the possibility of this and yet still give effective pain relief.

Codeine is effective by mouth for mild to moderate pain and is usually taken in combination with paracetamol. Caution is needed when using this drug with neonates who may be more liable to respiratory depression. Codeine can be given by subcutaneous or intramuscular injection to provide pain relief for babies or children who are outpatients. Doses are similar whichever route is chosen. Codeine is effective when given by suppository. However, children between the ages of 2 and 12 may not always appreciate the virtues of giving the drug by this method.

Codeine is not suitable for intravenous use as it can produce severe falls in blood pressure and apnoea.

Doses of codeine syrup range from 0.5-1mg/kg 4 hourly given orally or by intramuscular injection. Codeine given as a suppository: 1mg/kg 4 hourly.

Morphine is the drug of choice for children who are inpatients. The preferred route of injection is intravenous but other routes can be used. Intramuscular injection is painful and unpopular with patients and nurses, however, this route may be used during the operation to provide analgesia at the time the child awakens from anaesthesia. The subcutaneous route can be useful when venous access is difficult. Intravenous morphine is painless once access has been established and if an infusion is to be used the same precautions must be taken to prevent accumulation as were outlined earlier. Normally a loading dose is infused over 30 minutes followed by a background infusion, titrated against the child's pain and the presence of side effects. If staff are experienced in looking after children postoperatively, there is no need for high dependency or intensive care facilities whilst these techniques are employed.

Doses of morphine orally are 200-400mcg/kg 4 hourly.

Subcutaneous or intramuscular routes 100-150mcg/kg 4 hourly. Intravenous doses 50-100mcg/kg over 30 minutes as a loading dose and then 5-40mcg/kg hourly.

Children as young as five years can use PCA satisfactorily. This is one of the rare circumstances where a background infusion may be of some benefit, as children rarely remember preoperative instructions immediately upon waking. Great care must be taken to ensure that parents do not use the device on behalf of the child. PCA may be of value when dealing with other acute pains such as may accompany sickle cell crisis or the mucositis associated with chemotherapy.

PCA Doses; background infusion 4mcg/kg/h. Additional doses 10-20mcg/kg and a 5-15 minute lock-out. A four hour dose limit is advisable and should be calculated after the patient's response is assessed (usually around 400mcg/kg).

Intrathecal and epidural opioids have been used in children. There is a very high incidence of nausea and vomiting, itching, urinary retention and late (up to 24 hours) respiratory depression. Although analgesia is good, the potential for unpleasant and serious side effects limits the use of these approaches in children.

Pain Relief in the Elderly

The elderly also present special problems in the provision of analgesia. There may be great difficulty in communication and assessment and the choice of analgesic techniques should reflect this. As a general rule the elderly report pain less frequently and require smaller doses of analgesic drugs to achieve adequate pain relief. Many patients are anxious, however, and this may correlate with increased pain postoperatively.

Assessment of pain may be carried out by normal methods and conventional numerical or graphical methods work well. However, impairment of higher intellectual functions may mean that observational techniques similar to those described earlier be needed. When analgesic drugs are given they may not be absorbed as well or metabolised as efficiently. In practical terms, doses of drugs such as NSAIDs and opioids should be reduced because of a decrease in liver metabolism. In addition, since the metabolites of drugs such as morphine and pethidine are excreted by the kidneys, any decrease in renal function may lead to accumulation with repeated doses. The elderly are more likely to be receiving more than one drug for underlying medical conditions and the possibility of drug interaction is greater.

Local anaesthetics. Nerve blocks are a most effective way of giving postoperative pain relief. Intercostal nerve block can aid pulmonary function after chest or upper abdominal surgery and pain below the waist can be abolished by epidural blockade aiding the return of gastrointestinal function after surgery. However, blocks spread more widely in the elderly and there may be compromise of respiratory function due to intercostal paralysis. In addition, a greater sympathetic block may occur with a consequent fall in blood pressure. With care, local anaesthetic blocks can be very useful in the elderly and give excellent pain relief whilst permitting mobilisation and rehabilitation.

NSAIDs are often undervalued. However, gastrointestinal disorders are more common and care should be taken in patients with compromised hepatic or renal function.

Opioids. Self-medication with opioids is not always wise in elderly patients and thus the role of PCA may be limited. It is probably better to use conventional intravenous and intramuscular methods of delivery which will give an immediate effect which can be assessed by those caring for the patient. The elderly may be particularly sensitive to opioids and side effects such as confusion, sedation and respiratory depression assume greater importance. Because of changes in hepatic and renal function lower doses of opioids are needed and the expected length of action may be longer.

Only one drug should be used at a time. In general about half the normal adult dose should be given at first, especially if the drug is being given intravenously. Small doses should be given regularly to anticipate pain where appropriate.

Pain from other Acute Causes

Many of the principles of pain relief contained in this survey apply to the management of other pain conditions; burns and trauma are obvious examples. A difference is that pain as a symptom may last longer than when seen in association with surgery. The initial pain of the injury will require treatment in the normal fashion, but there are subsequent

Drug interactions with local anaesthetics (drugs competing for plasma cholinesterases, phenobarbitone, (β–blockers, calcium channel blockers, cimetidine, tricyclic antidepressives and antiarrhythmic agents)

Drug interactions with NSAIDs (Most relate to the antiplatelet and gastrointestinal effects. Oral anticoagulants, tricyclic antidepressives, phenytoin, (β–blockers, and the ACE inhibitor captopril)

Drug interactions with opioids (Morphine: tricyclic antidepressives, metoclopramide, H2-blockers. Pethidine/meperidine: H2-blockers, barbiturates, phenothiazines, MAOIs, phenytoin. Methadone: tricyclic antidepressives, diazepam, anticonvulsants.

phases of healing and rehabilitation which may be long and painful.

The healing phase may take many weeks depending upon the nature of the injury and the length of the rehabilitation phase. It is important to provide adequate analgesia for the performance of procedures such as dressings, physiotherapy and skin grafts. Emotional consequences and tissue damage from the burn or injury, such as nerve damage, may require additional treatment. In these circumstance use of short-acting drugs is inappropriate. In addition, it is better to establish regimens of regular pain relief. Combined techniques to address all aspects of the pain problem are best carried out by a multidisciplinary team.

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