Part 2   DRUGS IN LABOUR

For myriad reasons, very few deliveries take place without some form of pharmacological intervention. Ideally, all labours would require no more than inhalational analgesia, but, in practice, such labours are the minority, and even Entonox® is not without its hazards. Administration of analgesia would appear to be linked with use of anti-emetics and possibly oxytocics. This core section of the book describes the drugs regularly administered to healthy women in labour. We aim here to present the evidence base for these interventions, which, in some centres, have become routine practice.

Chapter 4    PAIN RELIEF IN LABOUR

Sue Jordan

This chapter describes the analgesics commonly administered to labouring women, starting with the least invasive and progressing to the most technically complicated. This ordering has entailed dividing the discussion of the opioids, in accordance with their routes of administration.

Chapter Contents:

• Pathophysiology of Pain

• Inhalational analgesia (mainly nitrous oxide)
• Opioids (mainly meperidine/pethidine)
• Local Anaesthetics (bupivacaine and lignocaine)
• Spinal and Epidural Analgesia (both local anaesthetics and opioids)

Many women request pain relief during labour and a wide range of pharmacological and non-pharmacological options exist. These options should be carefully discussed with the woman during ante-natal visits so that she is able to choose a method of pain relief appropriate to her individual needs. This decision should then be documented in the case notes. Nevertheless, it is recognised that women’s requirements for pain relief are not always predictable and may change during labour and therefore the midwife should be able to discuss with the woman the specific advantages and disadvantages of all the pharmacological options available (Dickersin 1989, Simpkin 1989).

**Pathophysiology of Pain**

Most authorities define pain as: ‘an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage’ (IASP 1986 p.S217). The experience of pain is individual and contextualised; there is not always a clear relationship between tissue damage and pain experience. Pain scores offer a useful communication tool to assist in assessing the need for analgesia (Fairlie et al 1999).

**Practice point**

*Analgesia should be monitored using a ‘pain scale’, such as a visual analogue scale.*
The individual’s learnt experience is an important determinant of pain perception and the development of pain syndromes (see Loeser & Melzack 1999). Therefore, experience in previous deliveries will influence each woman’s analgesic requirements.

The anatomy of the pain (or nociceptive) pathways is outlined in figure 1. Aspects most relevant to pharmacology include:

- The passage of pain impulses depends on action potentials in the neurones of the pain pathways. These are blocked by local anaesthetics.

- The integration of pain fibres, touch fibres and descending analgesic tracts occurs in the dorsal horn of the spinal cord, the ‘pain gate’ (see Melzack and Wall 1996). This is one site of opioid action.

- The pain pathways synapse in the reticular formation in the brain stem. Here they activate the sympathetic nervous system and increase:
  - Level of arousal and consciousness
  - Respiration
  - Heart rate
  - Blood pressure
  - Emesis
  - Sweating/ perspiration
Anaesthetic gases (e.g. nitrous oxide) and opioids act in the brain stem.

- The pain pathways can overwhelm the cerebral cortex, to the exclusion of other considerations. The cerebral cortex is one site of opioid action.

Severe, unrelieved pain may not only provide the woman with a very negative experience of childbirth, but can also have adverse physiological consequences:

**Increased rate and depth of respirations (see nitrous oxide)**

Hyperventilation rapidly reduces the carbon dioxide in the body, leading to vasoconstriction of the maternal and placental circulations, jeopardising the foetus.

Between contractions, the lack of carbon dioxide reduces the respiratory drive and decreases respirations. This can lead to hypoxia of mother and foetus.

**Tachycardia**

The increase in heart rate increases the work and oxygen needs of the heart, while simultaneously reducing coronary blood flow. Ischaemic changes in the ECG are not uncommon in labour.

Tachycardia can reduce cardiac output. In labour, cardiac output must increase to meet the work requirements of the muscles. If cardiac output declines, insufficient oxygen will
be delivered to the muscles for aerobic respiration to take place. Therefore, lactic acid will accumulate, making the woman acidotic.

**Hypertension**

Any sudden rise in blood pressure can threaten the cerebral circulation. The physiological changes of pregnancy render cerebral blood vessels especially vulnerable to hypertensive episodes.

**Gastric stasis and emesis**

Pain causes gastric stasis and disturbances of the autonomic nervous system. Intense pain may lead to nausea and vomiting.

*Practice Point*

*Even if a woman has received no analgesia, close observations of vital signs must be maintained.*


**INHALATION ANALGESIA**

**Introduction**

Inhalation analgesia is achieved by the use of anaesthetic gases in sub-anaesthetic concentrations. The widespread use of inhalation analgesia in childbirth for over 100
years has established its relative safety. Nevertheless, the administration of inhalation agents requires close supervision (Clyburn and Rosen 1993). (See Implications for Practice). In the UK, only nitrous oxide is in regular use for inhalation analgesia in childbirth, although other anaesthetic agents may be employed for Caesarean section and surgical procedures. Therefore, the principles of inhalation anaesthetics, relevant to all gaseous agents, will be outlined in this chapter, with a more detailed review of nitrous oxide analgesia as Entonox® (a mixture of 50% nitrous oxide and 50% oxygen).

**USES OF INHALATION AGENTS**

Nitrous oxide, as Entonox®, is normally available to women in all delivery settings and provides intermittent analgesia during uterine contractions (Clyburn and Rosen 1993). Reynolds (1993a) suggests that it is most effective when reserved for use during transition, the second stage of labour, perineal suturing and while awaiting epidural analgesia. Studies have shown that women have found it to be a more effective analgesic than meperidine (pethidine) or TENS machines, but less effective than epidural analgesia (Reynolds 1993a). The pharmacology of nitrous oxide described here is directly applicable to Entonox®, used in the UK.

**ACTIONS OF INHALATION AGENTS**

The precise mechanism of action of the anaesthetic gases remains uncertain. Although the chemistry of these agents is diverse, they share the properties of lipid solubility and the ability to bind to cell membranes at certain sites. This interaction with cell membranes affects the release of neurotransmitters at synapses and the transmission of nerve impulses in the central nervous system. Anaesthetics potentiate the actions of
inhibitory neurotransmitters (Kennedy and Longnecker 1996). The reticular activating system in the brain stem is an important site of action for inhalational agents. This is a network of neurones which transmits sensory input to the cerebral cortex, in a non-specific manner, to control states of arousal and consciousness. Gradual suppression of the reticular activating system results in the four stages or depths of anaesthesia: analgesia; delirium; surgical anaesthesia; and finally depression of the vital centres of the medulla.

**Practice Point**

*It is important to realise that an incorrect dose of an inhalation agent may produce a stage of anaesthesia which is not clinically desirable.*

**How the Body Handles Inhalation Agents**

The effect of an inhalation agent depends on not only how much is absorbed, but also on the concentration of gas reaching the brain. This is determined by:

- the concentration of the inspired gaseous mixture
- the pulmonary ventilation delivering the gas to the lungs
- the transfer across the respiratory (alveolar) membrane into the bloodstream
- the solubility of the gas in blood
- the loss of the gas into other body tissues
- the cardiac output (glossary) and the blood supply to the brain.

**Concentration of inspired gas**
Nitrous oxide is not sufficiently powerful to produce surgical anaesthesia when used alone. Concentrations of 50% nitrous oxide are needed for effective analgesia. If this is administered with air, rather than oxygen, hypoxia will ensue. Should high concentrations be administered (for example, following improper storage, see below) hypoxia is an urgent consideration. When nitrous oxide was inhaled with air from the pre-1965 standard obstetric analgesic machine, oxygen concentrations as low as 1.8% were inhaled and the women were so hypoxic they became cyanosed (Cole 1975). Nitrous oxide is now administered as Entonox®, using pre-mixed cylinders of 50% nitrous oxide in 50% oxygen as a homogenous gas (BOC 1996).

**Practice point**

_Improper storage of cylinders could allow administration of concentrations of nitrous oxide greater than 50%, reducing the percentage of oxygen available. If this is suspected, oxygen saturation should be assessed._

**Pulmonary ventilation**

Increases in ventilation (glossary) will increase the delivery of gas to the blood, and hasten the effects of gaseous analgesia and anaesthesia. Women given nitrous oxide tend to over-ventilate in order to maximise pain relief. The inherent danger is that they will exhale too much carbon dioxide, lowering the CO₂ concentration in the blood, which causes:

- vasoconstriction of the placental bed and hypoxia in the foetus
- maternal hypoventilation between contractions, leading to foetal hypoxia
• cerebral vasoconstriction, making the woman dizzy
• alkalosis (glossary), which may induce tetany.

Practice Points

• It is important that the respirations of all women are supervised during the administration of inhalation agents and instructions are given to breathe slowly and fairly deeply (Clyburn and Rosen 1993 p.180).
• Tetany usually begins as painful involuntary spasms of the muscles of the hands and feet. If the early signs go unnoticed, it may develop into spasm of the larynx and obstruction of the airway.
• Any reports of dizzines, tingling or twitching in the woman’s hands or feet should be an indication to monitor breathing patterns very closely for signs of over-breathing.
• The prolonged use of nitrous oxide from early labour should be avoided (Reynolds 1993a).
• Women with diseases of nerves or muscles (such as disseminated sclerosis) may be unable to benefit fully from nitrous oxide inhalation.

Transfer across the respiratory membrane

This will be compromised in women with lung disease (such as severe asthma or cystic fibrosis), resulting in delays in both the absorption and elimination of the gas (Kennedy and Longnecker 1996).

Solubility of the gas in blood
This determines the rate at which the gas is absorbed and eliminated from the body. Gases such as nitrous oxide, which dissolve in blood to a minimal extent, act on the brain very quickly giving rapid analgesia (within 20-60 seconds) and are excreted rapidly. Due to its relatively low solubility in lipids (fats), nitrous oxide is rapidly eliminated from the blood and tissues with high blood flow, including the brain.

**Transfer into tissues**

The amount of gas transferred into different tissues depends on the flow of blood, the concentration of the gas and the nature of the tissue, since gases dissolve more readily in some tissues than in others. Anaesthetics have a tendency to accumulate in fat.

**Practice Points**

- *Wome with generous deposits of adipose tissue will require more anaesthetic agent than thin women.*

- *Recovery from all anaesthetics is delayed in obese people (Rang et al. 1999).*

The blood/brain barrier (glossary) is freely permeable to anaesthetics and the brain is well perfused, therefore, the concentration of gas in the brain is approximately equal to that in the blood. The analgesic effects of nitrous oxide are experienced some 25-35 seconds after administration.

**Practice Point**
Ideally, nitrous oxide should be inhaled some 20 seconds before a contraction. There is a 15 second interval between a contraction becoming palpable to the midwife and the onset of pain. Therefore, palpation assists in the timing of administration of nitrous oxide (Beischer et al 1997).

Cardiac output is important in determining blood flow to lungs and tissues; the distribution of inhalation agents may be impaired in women with pre-eclampsia or a compromised cardiovascular system (Nagelhout 1992).

**Elimination of inhalation agents**

Being lipid soluble, inhalation agents cross the placenta, and accumulate in the foetus. They are eliminated via the lungs after delivery. This is an advantage over other analgesics, which depend on the immature liver and kidneys for removal (Clyburn and Rosen 1993). In both mother and neonate, it is estimated that the effects of Entonox ® have worn off after 2-3 minutes (BOC Gases 1996) although removal from tissues with low blood flow, such as fat, takes longer (Kennedy and Longnecker 1996).

**Practice Point**

*Opioids depress ventilation in mothers and neonates, and therefore, may retard the recovery from inhalational agents if co-administered (Rang et al 1999).*

When high concentrations of nitrous oxide have been administered for some time, ‘diffusion hypoxia’ may occur on abrupt discontinuation and resumption of breathing air.
This is due to large volumes of nitrous oxide entering the alveoli and diluting the available oxygen. Therefore, for a brief period, the woman and neonate are inhaling a concentration of oxygen below 20%.

**Practice Point**

_The resulting hypoxia can be prevented by administration of supplementary oxygen when nitrous oxide is discontinued, to both the neonate at birth and the woman in the early recovery period (Clyburn and Rosen 1993, Kennedy and Longnecker 1996, Marshall and Longnecker 1996)._  

**NITROUS OXIDE**

Nitrous oxide is colourless, odourless, heavier than air and non-explosive. It strongly supports combustion, and should not be allowed to contact lighted cigarettes, oils, greases, tars or many plastics. Should a fire occur, normal fire extinguishers are effective (BOC 1995). It is available at concentrations of 50% or 70% in oxygen.

**SIDE EFFECTS of NITROUS OXIDE**

The side effects of nitrous oxide impact in 2 areas (See Implications for Practice):

- The central nervous systems of the woman and foetus/neonate
- The bone marrow and reproductive systems of staff

Nitrous oxide is not a muscle relaxant and unlike other anaesthetic gases, it has no effect on smooth muscle, including the uterus (Marshall and Longnecker 1996).
Central nervous system

All anaesthetic gases depress the nervous system. This involves both the higher functions and the vital centres of the medulla and brain stem.

Central nervous system depression (obtunding)

Nitrous oxide produces some maternal sedation. Self-administration provides some safeguard against overdosage: as the woman becomes drowsy, the mask or mouthpiece falls away. The manufacturers suggest that administration will cease before the laryngeal (gag) reflex is lost (BOC 1996). However, overuse of inhalation agents can result in depression of the central nervous system, including the laryngeal reflex. If the laryngeal reflex is suppressed, and unable to protect the airway, there is a danger of aspiration of stomach contents, should any vomiting occur (Zelcer et al 1989, Clyburn and Rosen 1993).

Practice Point

Close observation of the woman for any signs of sedation is extremely important.

Central nervous system depression, dizziness and confusion are usually mild, although it is recommended that no-one should drive a motor vehicle or use machinery for at least 12 hours following the use of Entonox ® analgesia (BOC 1995). Only in very high concentrations, does medullary paralysis (stage 4 of anaesthesia) occur, depressing respiratory and cardiovascular systems (Rang et al 1999, Malseed et al 1995).
Neonatal CNS depression is a potential hazard with all inhalational agents, including prolonged administration of nitrous oxide (Capogna and Celleno 1993). In normal doses, nitrous oxide is eliminated so rapidly that neonates do not suffer adverse effects (Brownridge 1991).

**Hallucinations**

Vivid dreams and hallucinations represent the delirium stage (stage 2) of anaesthesia and women should be warned that these may occur transiently, since the feelings of dissociation produced may be very unpleasant (Bushnell and Justins 1993). Some of the analgesic properties of nitrous oxide are attributed to its effect on the affective and cognitive dimensions of pain (Carstoniu et al 1994). Some people may find inhalation pleasurable, and over-use Entonox® in early labour.

**Nausea**

Nausea is a common side effect of nitrous oxide and vomiting may occur (Reynolds 1993a).

**Hypoxia**

Hypoxia is a particular danger if nitrous oxide is used without adequate supervision. All anaesthetics tend to depress the vital centres, but the effects of nitrous oxide are subtle and may be easily overlooked (Marshall and Longnecker 1996). The use of nitrous oxide may worsen any existing foetal hypoxia and exacerbate any placental insufficiency. Zelcher et al (1989) suggest that if the foetal heart rate is abnormal, the use of nitrous oxide is ill-advised. In one study (n=40), inhalation of Entonox® throughout the first
and second stages of labour resulted in a higher incidence of maternal hypoxia than did epidural anaesthesia (Arfeen et al 1994). Pulse oximeters were used to detect hypoxia in this study.

**Practice Points**

- A pulse oximeter assists in assessing the situation, since it provides continuous measurement of maternal haemoglobin saturation without causing discomfort. However, it cannot detect changes in carbon dioxide concentrations.

- Use of a pulse oximeter is advised if administration of nitrous oxide has been prolonged, the woman has dark skin, opioids are co-administered or any uncertainty exists (DoH. 1996, Marshall and Longnecker 1996).

**Side Effects related to Prolonged Exposure (mainly staff)**

**Vitamin B_{12} inactivation**

Nitrous oxide inactivates vitamin B_{12}. The effect persists for several days. After brief exposure, this is rarely clinically significant. However, nitrous oxide should be avoided if pre-existing vitamin B_{12} deficiency exists, for example, in pernicious anaemia (Rang et al 1999).

BOC (1995) recommend that the administration of Entonox for longer than 24 hours (which is unlikely to occur in labour) should be accompanied by routine examination of the red and white blood cells for evidence of B_{12} deficiency.

**Effect on reproduction**
There is a possibility that prolonged occupational exposure to nitrous oxide may impair male or female fertility and increase the incidence of spontaneous abortions and preterm delivery (BOC 1995, Reynolds et al 1996, Rang et al 1999). Nitrous oxide in low analgesic doses is teratogenic in rodents, but these findings have not been confirmed in humans (Rice 1993). Use of, or exposure to, nitrous oxide during the first trimester may be harmful to the foetus, but is not absolutely contra-indicated, for example, following trauma (BOC 1995).

**Practice point**

*Because of the possible effects on staff, the concentration of nitrous oxide in the atmosphere, should be maintained below a specified level.*

The literature offers conflicting advice on the precise concentration considered safe:-

- BOC (1995) recommend that the concentration of nitrous oxide should not exceed 100 parts per million (ppm.).

- Marshall and Longnecker (1996) state that the atmosphere of the delivery / operating room should not contain more than 50 ppm.

- Exposure limits given by the US National Institute of Occupational Safety and Health indicate that the maximum permissible dose for nitrous oxide is 25 ppm time-weighted average (West 1993).

These concentrations may be achieved by effective ventilation and the scavenging of waste gases.
**Practice point**

*Health care workers should protect themselves by ensuring all gas cylinders are functioning correctly (not leaking) and avoiding the area within one foot of the client’s face while the client is exhaling or administering nitrous oxide (McKenry and Salerno 1998).*

**Storage**

Entonox® may separate into nitrous oxide and oxygen if the temperature falls below -6°C (for example if it is stored outside). It is unsafe to administer in this condition. To ensure homogenisation, cylinders should be stored horizontally above 10 °C for 24 hours before use; if this is not possible, the manufacturers should be contacted to suggest alternatives (BOC 1995). Incorrectly stored cylinders may administer insufficient oxygen (vi.).

**DRUG INTERACTIONS**

- The respiratory depressant action of opioids may be compounded by nitrous oxide, causing transient maternal hypoxia (Clyburn and Rosen 1993).

Most gaseous anaesthetics sensitishe the heart to the action of adrenaline / epinephrine, risking cardiac dysrhythmias, but nitrous oxide is free from this effect.
CAUTIONS

Nitrous oxide has the capacity to enter any pockets of gas trapped within the body and expand them. Therefore, it is contra-indicated in any situation where abnormal quantities of gas are trapped within the body, due to the risk of gas retention, for example, in women with middle ear occlusion (BOC 1995, Marshall and Longnecker 1996, Twycross 1994). Nitrous oxide may also diffuse into air bubbles formed by intra-spinal analgesia, hindering the spread of local anaesthetic (Reynolds et al 1996).

Nitrous oxide may impair levels of consciousness. It should not be administered to women whose level of consciousness is already impaired.

Conclusion

Although it is not always effective, nitrous oxide combined with oxygen has relatively few side effects and these can be minimised if administration is supervised and monitored by the midwife. Rapid elimination from maternal and neonatal circulations is an added advantage (Olofsson & Irestedt 1998). In view of this, nitrous oxide remains a flexible and useful method of pain relief during labour.
**Implications for practice: Entonox ®**

Although the use of nitrous oxide is generally safe, careful supervision of the woman and her breathing pattern is important.

<table>
<thead>
<tr>
<th>Potential problem</th>
<th>Management and Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sedation</td>
<td>Supervise closely. Self administration.</td>
</tr>
<tr>
<td></td>
<td>Be alert for vomiting</td>
</tr>
<tr>
<td>Maternal and foetal hypoxia</td>
<td>Use premixed oxygen with nitrous oxide.</td>
</tr>
<tr>
<td></td>
<td>Ensure the cylinder is correctly stored and fully mixed.</td>
</tr>
<tr>
<td></td>
<td>Supervise - ensure slow, even inspirations</td>
</tr>
<tr>
<td></td>
<td>Use a pulse oximeter for example, if opioids are co-administered.</td>
</tr>
<tr>
<td></td>
<td>Avoid prolonged use</td>
</tr>
<tr>
<td></td>
<td>Monitor foetal heart rate intermittently</td>
</tr>
<tr>
<td></td>
<td>Be prepared to administer oxygen to the neonate</td>
</tr>
<tr>
<td>Dizziness, tetany</td>
<td>Prevent hyper-ventilation.</td>
</tr>
<tr>
<td></td>
<td>Discontinue should tingling in hands and feet occur. Specifically question the woman</td>
</tr>
<tr>
<td></td>
<td>about this.</td>
</tr>
<tr>
<td>Nausea</td>
<td>Supervise closely. Position to avoid aspiration.</td>
</tr>
</tbody>
</table>

**Potential problem**

**Management and Care**
<table>
<thead>
<tr>
<th>Condition</th>
<th>Precaution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hallucinations, dissociation</td>
<td>Warn recipients. Avoid over-use.</td>
</tr>
<tr>
<td>Vitamin B$_{12}$ deficiency</td>
<td>Limit maternal administration to 24 hours</td>
</tr>
<tr>
<td>Affects on reproduction</td>
<td>Monitor the concentration in the environment. Avoid excessively close staff contact with gas</td>
</tr>
<tr>
<td>Risk of fire</td>
<td>Avoid contact with cigarettes, greases and oils.</td>
</tr>
</tbody>
</table>
**OPIOIDS**

Opioid drugs, such as meperidine (pethidine), are used extensively in labour. The term "opioid" is used to describe any preparation acting on the body's opioid receptors, which normally respond to endorphins and enkephalins. Thus morphine, diamorphine, meperidine, meptazinol, codeine, buprenorphine (Temgesic), pentazocine (Fortal) and the "morphine antagonists", such as naloxone (Narcan®), are all opioids. In the absence of evidence favouring any particular opioid (Fairlie et al 1999), the opioid offered is often based on institutional preference (Brownridge 1991). This section considers the pharmacology of opioids. The distinctive features of meperidine, meptazinol and diamorphine are described below.

**USES OF OPIOIDS**

Opioids are used in labour, pre-operatively, intra-operatively, post-operatively and in intensive care for analgesia, sedation and reduction of anxiety. Opioids are able to reduce the hyperventilation induced by pain and maintain carbon dioxide at near normal concentrations (Clyburn and Rosen 1993). Various low-dose opioid preparations are sold as ‘over the counter’ preparations for controlling symptoms of cough or diarrhoea in all age groups.

**Analgesia**

Opioids provide greater pain relief in labour than either no treatment or injection of sterile water (Howell 1994). Nevertheless, mothers frequently report that pain relief in
labour from meperidine (pethidine) is inadequate (Ranta et al 1995). However, when opioids are discontinued, there is frequently a rebound increase in pain sensitivity. Opioids such as pethidine, morphine and the more powerful synthetic drugs, fentanyl and alfentanil, may also be administered epidurally or intrathecally and give rapid and effective analgesia (Herpoisheimer and Schretenthaler 1994). Although 6-30 hours of analgesia is provided by this route, the side effects may be troublesome, particularly urinary retention, sedation, nausea, itching, hypotension and respiratory arrest (Chrubasik et al 1992). Intraspinal* opioids are discussed at the end of this chapter.

* The term ‘intraspinal injection’ is used to refer to administration within the spinal column i.e. to encompass epidural, intrathecal (spinal) and combined spinal epidural administration (Wildsmith 1996).

**Anaesthesia and reduction of anxiety**

The benefits of opioids can be attributed to both their analgesic and anxiolytic actions. The release of adrenaline / epinephrine and noradrenaline / norepinephrine due to pain and anxiety decrease uterine blood flow. This is reversed by opioids, to the benefit of the foetus (Hollmen 1993).

**How the Body Handles Opioids**

Opioids are not given orally during labour, due to delays in absorption and metabolism. Intramuscular injection is the most convenient alternative. Opioids are metabolised in the liver and excreted via urine and bile. The metabolic pathways for each opioid differ.
Opioids are rapidly transferred across the placenta: changes are detected by foetal scalp electrodes within 7 minutes of intramuscular administration of meperidine (pethidine). The foetus and neonate excrete opioids more slowly than adults, due to the immaturity of their liver enzymes (chapter 1). In addition, due to the lower pH in the foetus, basic drugs, such as meperidine, are more likely to be ionised (glossary) in the foetus. Therefore, they may become ‘trapped’, unable to return to the maternal circulation.* At steady state, their concentration will always be higher in the foetal circulation than in the mother.

*Footnote. Drugs are only transferred across the placenta in their non-ionised state.

**Practice Points**

- If the foetus becomes acidotic, due to lack of oxygen, the side effects of opioids are magnified (Clyburn and Rosen 1993). Therefore, blood flow to the placenta and maternal oxygen saturation must be maintained at all times.

- The blood supply to the placenta is considerably reduced during uterine contractions. Therefore, transfer of drug to the foetus may be minimised by intra-muscular administration immediately before a contraction (Carson 1996).

Following a single intramuscular dose of meperidine (pethidine) to the mother, the foetus receives maximum exposure 2-3 hours later; therefore respiratory depression in the neonate is most likely in babies born at this time. If delivery occurs within 1 hour of meperidine administration, very little drug is transferred to the foetus. Should delivery
occur more than 6 hours after administration, much of the meperidine will have been transferred back to the mother, although the active metabolite normeperidine will remain in the neonatal tissues. This is gradually excreted over several days. During this time the neonate’s behaviour will be suboptimal (irritable and difficult to feed) (Crowell et al 1994). The amount of normeperidine transferred to the baby is greater the longer the time between delivery and pethidine administration (Crowell et al 1994).

Meperidine (pethidine) is metabolised to normeperidine, which is toxic in high concentrations. The half-life [glossary] of meperidine is 3 hours in the mother and 4-5 hours in the neonate. The half-life of normeperidine is 20 hours in the mother and 60 hours in the neonate. Therefore, this metabolite takes several days to clear from the neonate, during which time, side effects persist. With multiple doses, normeperidine may accumulate in the foetus/ neonate and cause respiratory depression and fits which are resistant to, or even exacerbated by, naloxone (Narcan ®) administration.

**Practice Points**

- *Each institution imposes a maximum dose of meperidine/ pethidine, which is never exceeded.* *(The BNF (2000) gives 400mg in 24 hours, which will be excessive for some women.)*

- *Extra help will be needed to ensure the infant suckles correctly over the first 3-5 days of life. An irritable or jittery baby is unable to suckle the whole areola. Unless corrected, the resulting tissue damage will be painful and may lead to infection.*
Meperidine/ pethidine passes into breast milk, which compounds early difficulties with feeding (Yerby 2000).

The dose of meperidine is subject to institutional preference and standing orders. Doses usually range from 50-100 mg. by subcutaneous or intramuscular injection (BNF 2000).

**Actions of opioids**

Opioids are chemically related to the body's endorphins and enkephalins, which are natural mood changers and analgesics, particularly in times of stress. Opioids act at many sites in the central nervous system including the spinal cord, the medulla, the midbrain and the cerebral cortex. (see fig. 1 The pain pathways) Several classes of opioid receptors exist and different opiate drugs act selectively at different receptors, to produce diverse responses. In some situations, the euphoriant or sedative effects of opioids predominate over their analgesic actions (Arner and Meyerson 1988, Olofsson et al 1996).

Opioids bind to the cell surface receptors for the endorphins and enkephalins, fitting-in like keys into a lock (see chapter 1). This binding triggers changes within the nerve or smooth muscle cells, usually inhibiting their activity and neurotransmitter release. In general, opioids (endogenous and pharmacological) depress the activity of target tissues and have a calming effect. They inhibit the hypothalamus and ‘damp-down’ the level of activity in the autonomic nervous system, partly by reducing the stress response attributable to noradrenaline (norepinephrine).
There are several classes of opioid receptor, some are assigned a Greek letter. Several classes of opioid receptor are of pharmacological importance: μ₁, (mu1); μ₂, (mu2 ); δ (delta); κ, (kappa); and peripheral opioid receptors. These are summarised in relation to common side effects in table 1.
<table>
<thead>
<tr>
<th>Table 1. Actions and Side Effects of opioids summarised.</th>
</tr>
</thead>
</table>

**Actions of opioid receptors**

κ (kappa) receptors  
analgesia, sedation and dysphoria

μ₁ (mu 1) receptors  
supraspinal analgesia, euphoria and addiction.

μ₂ (mu 2) receptors  
depression of vital centres: respiration
                        heart rate
                        orthostatic hypotension
                        thermoregulation
                        cough

affect smooth muscle of:

- uterus  prolonged labour
- urinary tract  retention of urine
- gut  constipation, ileus, gastric stasis blood
- vessels  hypotension
- eye  pupillary constriction

(not seen in meperidine/pethidine overdose)

δ (delta) receptors  
spinal and supraspinal analgesia

**Stimulation of**

Chemoreceptor trigger zone  
nausea and vomiting

Histamine release  
pruritus

vasodilation and hypotension

bronchospasm in asthmatics

**Neuroendocrine function**

**Inhibition of**

Substance P release  
spinal analgesia
**SIDE EFFECTS of OPIOIDS** *(See Implications for Practice)*

**Central Nervous System – Higher Functions**

Opioids act on more than one type of receptor in the cerebral cortex. While sedation is the usual result, central nervous system excitability, including hallucinations and convulsions, sometimes occurs.

**Depression and Obtunding of Central Nervous System (CNS)**

Opioids produce drowsiness, mental clouding and sometimes euphoria. These actions may be beneficial in some situations, for example in intensive care, but sedation is disadvantageous to both mother and baby in a normal labour. Opioids may provide sedation rather than analgesia (Olofsson et al 1996): following administration of opioids, a woman may fall asleep, only to be woken by the pain of contractions (Fairlie et al 1999). Central nervous system depression/obtunding (glossary) and sedation induced by opioids reduces the mother’s ability to co-operate with labour. Sedation may be profound if any degree of thyroid imbalance is present. (See chapter 18, thyroid disorders).

**Practice Point**

*A woman who has received opioids may be sedated, and less able to ‘push’ in the second stage, which will prolong labour.*

For *neonates*, exposure to meperidine (pethidine) reduces the muscle tone and depresses the CNS (Wagner 1993). This causes delay in the sucking and rooting responses (Nissen et al 1995). The establishment of breast feeding appears to be delayed by several hours.
if opioids are administered 1-5 hours before delivery (Crowell et al. 1994): several mothers in this study who had received meperidine discontinued breast feeding because the infant was not feeding well. If delivery is delayed by more than 8 hours after meperidine administration, there is less impact on feeding behaviour. In one study, infants who failed to suck had higher plasma concentrations of meperidine than those who started to feed, which suggests that failure to feed is a dose-dependent side effect (Nissen et al. 1997).

**Practice Point**

*Problems with breast feeding are more likely to arise if the dose of meperidine is 100mg, rather than 50 mg (Nissen et al. 1997).*

The foetal electroencephalogram is modified soon after the intramuscular administration of meperidine to the mother; this effect persists for the first 4 days of life, and corresponds to the neonate’s decreased level of arousal and muscle tone (Clyburn and Rosen 1993). Due to the long half-life (60 hours) of the metabolite (normeperidine), neonatal behaviour is depressed for approximately 3 days after the administration of meperidine (pethidine) during labour. During this time reflexes and thermoregulation are compromised and abnormal reflexes are more likely (Crowell et al. 1994).

**Practice Point**
The poor muscle tone of affected infants means that they are less likely to suckle on the whole areola, thus traumatising the nipple. It is better to supplement breast feeding, preferably by expressed milk in a cup, over the first 2-5 days than to abandon it entirely.

**Central Nervous System Excitability**

Opioids may induce euphoria, dysphoria, tremulousness, restlessness or delirium. Visual disturbances, hallucinations and nightmares may accompany opioid use. Normeperidine (a metabolite of meperidine) may cause neuro-behavioural abnormalities such as twitching and convulsions. Although respiratory depression produced by meperidine (pethidine) can be reversed by naloxone, any convulsions and respiratory depression caused by normeperidine are less likely to respond (Clyburn and Rosen 1993).

**Practice point**

The midwife should be aware that not all respiratory depression will respond to naloxone, particularly in infants where normeperidine may have accumulated, for example following repeated doses and long delays between administration and delivery.

**Central Nervous System – Brain Stem**

Opioids inhibit the activity of the vital centres in the brain stem. Therefore, midwives always pay close attention to the vital signs of the mother, foetus and neonate.

**Respiratory depression.**
Opioids act directly on the respiratory centre in the medulla to depress respiration, and also on the peripheral receptors to induce apnoea, in rare instances (Bowdle 1998). Opioids reduce the sensitivity of the respiratory centre to carbon dioxide, thus reducing the normal drive to respiration (Reisine and Paternak 1996). Therefore, respiration fails to increase to meet the high metabolic demands of labour. Rate, depth and regularity of respirations are decreased, reducing alveolar ventilation and oxygenation. This effect is intensified if the woman becomes so sedated that she falls asleep. If the circulation is adequate, respiratory depression is maximal within 90 minutes of intramuscular administration.*

* Footnote. If the peripheral circulation is ‘shut down’ as in shock or haemorrhage, the absorption and side effects of intramuscular drugs can be delayed.

Depression of the carbon dioxide respiratory drive means that the patient’s breathing depends on the hypoxic respiratory drive. Administration of a high concentration of oxygen to a patient (adult or neonate) whose respirations are depressed due to opioids can remove the remaining respiratory drive and precipitate a sudden respiratory arrest. This may be difficult to reverse, due to a sharp rise in carbon dioxide concentration (Reisine & Pasternak 1996).

Respiratory depression of the woman during labour may lead to:

- retention of carbon dioxide and respiratory acidosis, in mother and foetus.
- hypoxia in mother and foetus, which causes foetal heart rate decelerations.
Under these conditions, the foetus becomes acidotic, increasing his/her accumulation of meperidine and metabolites.

**Practice Points**

- *Maternal respirations must be carefully monitored for rate, depth and rhythm.*
- *A pulse oximeter offers a useful guide as to the degree of oxygen saturation in the mother.*
- *Foetal monitoring for signs of acidosis is important in prolonged labours.*

In the **neonate**, measurements with foetal scalp electrodes indicate that transcutaneous oxygen tensions (levels) fall to 37% of baseline values 7 minutes after the intramuscular administration of 50mg. meperidine (pethidine), but recover within 15 minutes (Clyburn and Rosen 1993). Depression of the central nervous system (see above) reduces the neonate’s reflexes, including the respiratory reflexes needed to cope with hypoxia and birth (Wagner 1993).

The resultant respiratory depression in the neonate is potentially lethal; premature infants are particularly at risk (Karch 1992). Rapid reversal with naloxone, an opioid antagonist (glossary) is mandatory. An overview of clinical trials found an association between opioid analgesia and low APGAR scores (Howell 1994).

**Practice point**
If opioids are administered, naloxone, oxygen and means of ventilation for the neonate must always be available.

**Bradycardia**

Opioids reduce the heart rate, by direct action on the cardiovascular centres in the medulla, by decreasing the activity of the sympathetic nervous system and by reducing anxiety. In labour, this may contribute to a fall in blood pressure and a reduction in placental perfusion. The subsequent depression of the foetal heart rate and loss of foetal heart baseline variability may be interpreted as foetal distress, triggering medical interventions.

Some foetal bradycardia on administration of analgesia is normal. This is attributed to the transient release of oxytocin (see below), which causes a brief tetanic contraction of the uterus (Eberle & Norris 1996). However, bradycardia lasting beyond 5-8 minutes may be a sign of metabolic stress (Arkoosh 1991).

**Practice point**

*Foetal heart monitoring should be undertaken soon after administration of opioids and interpreted cautiously. Intermittent monitoring is often the preferred option.*

**Hypotension**

Opioids act on the cardiovascular centres in the medulla, the blood vessels and the sympathetic nervous system to produce a fall in blood pressure. This is exaggerated on
standing or sitting up, partly due to inhibition of the baroreceptor reflex (Reisine & Pasternak 1996). Sudden standing may result in dizziness, loss of balance or falls. Bed rest, fluid depletion, alcohol or phenothiazines, such as prochlorperazine (Stemetil ®), will exacerbate the effects of opioids on blood pressure. Hypotension can also impair placental and renal perfusion. Any hypotension is likely to be exaggerated by the foetal head compressing the maternal aorta and vena cava if the mother adopts the supine position.

**Practice points**

- *The woman should not lie in a supine position.*
- *The woman will need assistance to get up slowly after administration of opioids.*
- *Opioids should be used with caution, if at all, in women with decreased blood volume, as the effects of hypovolaemic shock will be aggravated* (Reisine & Pasternak 1996).

**Depression of thermoregulation**

Opioids act on the hypothalamus to reduce the thermoregulatory set point. This has been recorded following meperidine (pethidine) administration during labour (Clyburn and Rosen 1993). It is hazardous for the neonate, whose thermoregulatory mechanisms rely on the sympathetic nervous system. The vasoconstrictor and shivering responses are depressed in all neonates, and this is accentuated by opioids.

**Practice point**
The neonate must be kept warm, preferably by the mother. However, the mother may be sedated following opioid administration, and she should be carefully observed to minimise any danger of 'over-lying'.

Cough

Opioids suppress the cough and sigh reflexes and depress the movement of respiratory cilia. This causes accumulation of the mucus secreted by the respiratory tract. Depression of the respiratory cilia is compounded by smoking. These factors increase the risks of pulmonary atelectasis (glossary) and chest infections (Govoni and Hayes 1990).

Actions on Smooth Muscle

Generally, opioids cause relaxation of smooth muscle, and contraction of sphincters.

Prolonged labour

Administration of intramuscular meperidine briefly stimulates the hypothalamus to release oxytocin, which causes a brief tetanic uterine contraction (Eberle & Norris 1996). However, this effect is superceded by reduced contractility of uterine smooth muscle, due to decreased release of oxytocin and the direct action of the μ2 opioid receptors. These actions are similar to those of endogenous opioids (Carson 1996). Although the literature in this area suffers from absence of human randomised controlled trials, animal and in vitro studies suggest that meperidine and morphine reduce both the uterine response to oxytocin and the oxytocin release from the posterior pituitary gland (Thompson and Hillier 1994). Uterine contractions may diminish following the
administration of meperidine (pethidine) (Baxi et al 1988), but this is disputed by some authorities (Reisine and Pasternak 1996).

A literature review (Thompson and Hillier 1994) indicated that the duration of both first and second stages of labour is directly related to the amount of meperidine (pethidine) administered during the first stage of labour.

**Retention of Urine and Dysuria**

Opioids reduce urine formation by increasing the secretion of antidiuretic hormone and reducing renal perfusion. They also inhibit the smooth muscle of the bladder. The voiding reflex is inhibited, while the tone of the internal urethral sphincter is increased. Combined with trauma to the urethra during labour, retention of urine is common following delivery.

**Practice points**

- **Urine output should be monitored during and after labour.**
- **A full bladder may impede contraction of the uterus post partum, increasing blood loss.**

**Gastrointestinal Tract**

The motility of the stomach, small intestine and colon are decreased. Opioids inhibit the propulsive, peristaltic actions of the gut, while increasing segmental, non-propulsive contractions, particularly in the pyloric region of the stomach, the first part of the duodenum and the colon. Gastric stasis may cause oesophageal reflux (heart burn),
nausea and vomiting. Opioids contribute to the constipation which commonly follows delivery. Opioids decrease gastro-intestinal secretions, causing a dry mouth. Spasm of the biliary tract, producing pain on the right side of the abdomen, is a rare side effect of opioids.

**Practice points**

- Painful abdominal cramps may follow administration of opioids.
- The woman must be positioned so that gastric contents do not enter the airway.

**Nausea and vomiting**

Gastric stasis and stimulation of the chemoreceptor trigger zone (in the medulla) combine to cause nausea, which is experienced by 30-60% of women receiving opioids. Ambulation and sudden movement stimulate the vestibular apparatus, and contribute to the nausea associated with opioids. Nausea and vomiting are less likely to occur if the patient remains resting. Pain, labour, fear and anxiety also induce gastric stasis, nausea and vomiting. When these physiological effects of labour are combined with the sedative actions of opioids, the dangers of gastric aspiration become very real.

**Practice points**

- A woman who has vomited following opioid administration should be warned that emesis is likely to recur on any subsequent administration of the same opioid.
- Vomiting can disrupt fluid and electrolyte balance, and increase the risk of thromboembolism. (see chapter 5, anti-emetics)
**Histamine Release**

Opioids stimulate release of histamine. This may cause pruritus or bronchospasm and contribute to hypotension.

**Pruritus**

Histamine release may cause flushing, itching, "nettle rash" and sweating, particularly in the upper part of the body. This is the most common side effect when opioids are given by the intrathecal route (Herpolsheimer and Schretenthaler 1994).

**Practice points**

- **Coolant gels may help relieve discomfort.**
- **Anti-histamine creams can be administered on medical advice, but they do not always abolish the itching.**
- **Naloxone may be effective in relieving symptoms** *(Reisine & Pasternak 1996).*

**Bronchospasm**

Histamine release causes bronchoconstriction and may occasionally precipitate an attack of asthma *(Beischer et al 1997).* Opioids are not administered during an asthma attack, as they may worsen symptoms.

**Neuroendocrine Actions**

Opioids act on the hypothalamus to alter hormone secretion. With short term administration, problems may, occasionally, arise.
• In women whose adrenal or thyroid function are disturbed, opioids may suppress the release of these hormones.

• Opioids act on the hypothalamus to enhance the secretion of antidiuretic hormone. Occasionally, this can cause water retention and hyponatraemia (glossary), which is a medical emergency. This is described in chapter 6.

**Practice point**

*Women should be advised to drink only moderate quantities of plain water. Fluid balance must be checked following delivery.*

**Dependence**

Some studies have linked the use of opioid analgesia in labour with an increased risk of opiate addiction in adult offspring in later life through a process of imprinting (Jacobson et al 1990). However, Clyburn and Rosen (1993) suggest this work should be interpreted cautiously, since there were more males in the study group than the control group, and males have a greater risk of drug addiction.

**CAUTIONS**

Opioids are used with caution, if at all, in the following circumstances:

• Reduced respiratory reserve: for example, in asthma, obesity, kyphosis (excessive spinal curvature), disease of muscles or nerves (e.g. disseminated sclerosis). Opioids
are contra-indicated if the partial pressure or concentration of carbon dioxide (pCO₂) is raised, as in severe respiratory disease.

- With increasing age or debility or malnutrition, lower doses are needed since standard doses will produce excessive side effects. For example, a forty year old may need half the analgesic dose required by a twenty year old (Twycross 1994).

- Pre-existing hypotension may be dangerously worsened, for example, following haemorrhage.

- Excessive sedation and coma may result from administration of opioids to women with hypothyroidism or Addison’s disease.

- Meperidine (pethidine) and propoxyphene are the opioids most likely to cause convulsions with repeated administration. This may be exacerbated by fluid retention following oxytocin administration.

- The CNS depressant effects of opioids will complicate any rise in intracranial pressure (for example, following a CVA or an eclamptic seizure), by worsening respiratory depression and obscuring vital signs. Opioid-induced respiratory depression causes carbon dioxide retention, which will exacerbate any rise in intracranial pressure and increase cerebral ischaemia and seizures.
- Reduced doses of opioids are needed if liver or kidney function is impaired, for example in pre-eclampsia.

- Possibility of paralytic ileus.

- Known allergy to opioids

**DRUG INTERACTIONS**

Opioids interact with many drugs, and this section offers only a guide.

- **Enhanced depression of CNS and vital centres.**
  Administration of more than one depressant will intensify any opioid-induced reduction in blood pressure, respiration and conscious levels. CNS depressants include: alcohol, anti-histamines, barbiturates, anaesthetics (nitrous oxide), benzodiazepines, metoclopramide, phenothiazines (e.g. prochlorperazine, Stemetil ®), tricyclic antidepressants, and other non-opioid sedatives, such as chloral hydrate. While phenothiazines have useful anti-emetic actions, they worsen postural hypotension, respiratory depression, sedation and bradycardia. Fentanyl plus diazepam or midazolam may cause hypotension and profound respiratory depression in adults and neonates (Stockley 1999).

**Case Report**

This case illustrates the dangers of combining sedative drugs.
A woman with severe pre-eclampsia was induced at 26 weeks gestation. She received intravenous hydralazine and chlormethiazole, plus 100mg. meperidine (pethidine) intramuscularly for analgesia. An hour later she was deeply sedated, and her airway was obstructed. The sedation was unrelieved and urine output was poor. She died later of adult respiratory distress syndrome, probably due to gastric aspiration while unconscious. (DOH 1991 p79)

Two potent sedative drugs were administered. Together, these drugs inhibited the vital reflexes. Aspiration of stomach contents is a risk in unconscious or heavily sedated patients. The dose of meperidine (pethidine) seems high for a woman known to have a reduced circulatory volume due to pre-eclampsia.

- **Selective Serotonin Uptake Inhibitors (SSRIs) or Monoamine oxidase inhibitors (MAOIs)** (including moclobemide and fluoxetine (Prozac ®)) and meperidine (pethidine), pentazocine, dextromethorphan or tramadol interact to produce hyperpyrexia, accompanied by either hypotension or hypertension, which can be fatal (Bowdle 1998). (The serotonin syndrome, chapter 16) *This drug combination must be avoided for 2 weeks after discontinuation of a MAOI.* This reaction is possible, but less well documented with other opioids (Drugs and Therapy Perspectives 1993).

- **Gastric emptying**

  The gastric stasis induced by opioids is reversed by metoclopramide (Maxalon), cisapride and domperidone.
• **Drugs suppressing gastric acid secretion**

Cimetidine inhibits liver enzymes, preventing the breakdown of other drugs. This may increase the concentration of meperidine (pethidine), methadone, fentanyl or morphine. Apnoea and confusion may result. Isolated reports exist of a similar reaction between morphine and ranitidine (Stockley 1999).

• **Increased doses needed**

Anticonvulsants (phenytoin, carbamazepine, phenobarbitone), rifampicin, oestrogens and tobacco all induce (speed up) liver enzymes. Therefore opioids (meperidine / pethidine and pentazocine) are more rapidly eliminated from the body, and more frequent dosing may be required to achieve pain relief (Stockley 1999).

• **Cyclizine co-administered with opioids can precipitate pulmonary oedema, but only in seriously ill patients (BNF 2000).**
### Implications for Practice: Opioids

<table>
<thead>
<tr>
<th>Potential problem</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal</td>
<td></td>
</tr>
<tr>
<td>Respiratory depression, leading to hypoxia</td>
<td>Respirations should be assessed prior to, during and after administration of opioids and if the respiration rate is below 12/min. or the breathing is unduly shallow, or irregular, the opioid should be withheld until further assessment. A pulse oximeter should be used to check oxygenation (Bem et al 1996). Administration of prochlorperazine will intensify these problems.</td>
</tr>
<tr>
<td>Respiratory arrest due to loss of carbon dioxide respiratory drive</td>
<td>Avoid administration of high dose oxygen to a patient whose respirations are depressed due to opioids.</td>
</tr>
<tr>
<td>Chest infection</td>
<td>The detrimental effects of reduced airway clearance can be mitigated by breathing exercises, positioning and turning. Avoid smoking until the opioid has been eliminated.</td>
</tr>
<tr>
<td>Potential problem</td>
<td>Management</td>
</tr>
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<td>----------------------</td>
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</tr>
<tr>
<td>Hypotension</td>
<td>Women should be advised to mobilise slowly and to report any dizziness, in order to reduce the likelihood of any falls. Monitor the lying and sitting BP and heart rate. This will also detect dehydration. Administration of prochlorperazine will intensify these problems. Fluid balance charts. Intravenous fluid available to correct hypovolaemia and hypotension.</td>
</tr>
<tr>
<td>Prolonged labour</td>
<td>Monitor uterine contractions. Advise women of this prior to labour.</td>
</tr>
<tr>
<td>Sedation</td>
<td>Monitor level of consciousness and drowsiness. Avoid other sedating drugs e.g. prochlorperazine. Avoid administration to women with a history of thyroid or adrenal imbalance. Encourage the mother not to allow sedation to interfere with appropriate ‘pushing’.</td>
</tr>
<tr>
<td>Potential problem</td>
<td>Management</td>
</tr>
<tr>
<td>----------------------------------------</td>
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</tr>
<tr>
<td>Aspiration of gastric contents</td>
<td>Prevent / minimise sedation and nausea. Adopt the recovery position should nausea &amp; vomiting occur</td>
</tr>
<tr>
<td>Reduced renal perfusion</td>
<td>Urine output should be monitored to exclude oliguria and retention of urine.</td>
</tr>
<tr>
<td>Retention of urine</td>
<td></td>
</tr>
<tr>
<td>Pruritus</td>
<td>Coolant gels, calamine or antihistamines should be available. For intraspinal administration, substitution of fentanyl may be helpful.</td>
</tr>
<tr>
<td>Scarring at injection site (meperidine)</td>
<td>Document site of injection. Do not re-use that site.</td>
</tr>
<tr>
<td>Neonatal</td>
<td></td>
</tr>
<tr>
<td>Respiratory depression</td>
<td>Close observation. Availability of naloxone, oxygen and ventilatory support. If naloxone is required, a second dose will usually be necessary.</td>
</tr>
<tr>
<td></td>
<td>If high doses of meperidine /pethidine have been administered, be aware that the infant may not respond to naloxone.</td>
</tr>
<tr>
<td></td>
<td>Monitor to prevent foetal acidosis.</td>
</tr>
<tr>
<td>Potential problem</td>
<td>Management</td>
</tr>
<tr>
<td>------------------------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Foetal bradycardia</td>
<td>Monitor foetal heart rate regularly. Recognise a prolonged, abnormal foetal bradycardia, and refer as appropriate.</td>
</tr>
<tr>
<td>Sedation and / or irritability</td>
<td>When an opioid analgesic has been administered during labour, babies should be left with their mothers and additional assistance given to establish breast feeding.</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>Ensure neonate is well wrapped and close to mother.</td>
</tr>
</tbody>
</table>

**Features of individual opioids**

Although opioids have many side effects in common, there are some important differences between individual agents. The main distinguishing features are listed below.

**Meperidine (Pethidine)**

- Meperidine given by subcutaneous or intramuscular injection causes local irritation and frequent repetition at one site may lead to severe fibrosis of muscle tissue. *It is recommended that no site is used twice during labour.*

- Meperidine is the opioid most likely to induce maternal tachycardia and myocardial depression; therefore it is contra-indicated in women with heart disease.
• Myoclonus and muscular rigidity, while potential side effects of all opioids, are most likely with meperidine (Cherny 1996). This rigidity may be reversed with naloxone (Bowdle 1998).

• Meperidine is more likely to cause nausea than either morphine or diamorphine (Olofsson et al 1996) or tramadol (Elbourne & Wiseman 2000). A woman who has experienced nausea with morphine may not feel sick with meperidine and vice versa.

• Meperidine has also been used as the sole agent for epidural analgesia since it has both local anaesthetic and opioid properties

**Meptazinol**

• Meptazinol (Meptid®) produces less respiratory depression, but more nausea, than either meperidine or morphine. It is used intrapartum and post-operatively in some centres, but an anti-emetic is often necessary.

• Pain relief has been found to be indistinguishable from meperidine (Sheikh & Tunstall 1986, Osler 1987, Elbourne & Wiseman 2000).

• Duration of action (2-7 hours) is shorter than morphine or meperidine. Unlike meperidine, meptazinol can be metabolised by the neonate (Bushnell and Justins 1993).
**Diamorphine (heroin)**

- Diamorphine is rapidly metabolised in the liver to 6-monacetylmorphine (6MAM) and then to morphine. Both diamorphine and 6MAM are highly lipid soluble (more so than morphine) and therefore readily cross the blood-brain barrier to achieve rapid symptom relief (Reisine and Pasternak 1996).

- Due to its high lipid solubility, enough diamorphine for 24 hours can be placed in a small volume patient controlled analgesia (PCA) device.

- Diamorphine is sometimes used in labour and post-operatively. It is reported to produce less nausea but more euphoria and CNS obtunding than equi-analgesic doses of morphine. This may be useful if death *in utero* has occurred.

- One study found higher Apgar scores (glossary) in neonates whose mothers had received diamorphine rather than meperidine (Fairlie et al 1999).

**Naloxone**

- Naloxone (Narcan®) is an opioid antagonist: it reverses many of the actions of other opioids. It may be administered subcutaneously, intramuscularly or intravenously to reverse the respiratory depression of opioids in neonates following maternal intrapartum analgesia.
- The half life of naloxone is $1.1 \pm 0.6$ hours; the duration of action is 1-4 hours (Reisine and Pasternak 1996). These values are much shorter than (approximately half) those of meperidine, meptazinol and morphine. Therefore, following administration of naloxone, close observation of the neonate is required to identify a recurrence of the initial respiratory depression, and *a second dose is usually required*.

- In adults, administration of naloxone is usually followed by a return of pain. Other side effects of naloxone include nausea, vomiting, tachycardia and ventricular fibrillation (BNF 2000).

**Conclusion**

Although only 50% of women feel that opioids offer adequate pain relief in labour, they are often preferable to no analgesia (Fairlie et al 1999). Intramuscular opioids provide greater pain relief than placebo. However, they may be providing sedation, rather than analgesia (Olofsson et al 1996, Reynolds & Crowhurst 1997). Professionals are more likely than mothers to consider pain relief to be adequate and tend to underestimate the level of pain experienced (Rajan 1993, Rajan 1994).

The adverse affects of opioids on the mother, the foetus and the neonate are significant and therefore their use should continue to be approached with caution, as summarised in ‘Implications for Practice’. Labour may be prolonged and breast-feeding more difficult.
to establish following the administration of intramuscular opioids. Meanwhile, intraspinal administration of opioids is becoming increasingly popular \textit{vi}. 
LOCAL ANAESTHETICS

Introduction

Local anaesthetics have been developed from cocaine, which was first used in dentistry and ophthalmology in the nineteenth century. Cocaine has been superseded by lignocaine (lidocaine), bupivacaine (Marcain ®), prilocaine and ropivacaine. Prilocaine is primarily used in topical preparations. This chapter focuses on bupivacaine and lignocaine / lidocaine. Ropivacaine is described on p. ??.

Uses of Local Anaesthetics

Local anaesthetics have an important role in providing short term pain relief. In midwifery, they may be administered by several routes:

- **Topical**, for example, for intravenous cannulation
- **Subcutaneous / intradermal** for suturing
- **Infiltration** around a single nerve, for example, a pudendal block
- **Epidural**, on the surface of the dura for labour or Caesarean section.
- **Spinal (intrathecal)**, into the cerebrospinal fluid of the sub-arachnoid (intrathecal) space for labour and Caesarean section. (see fig.2)
Local anaesthetics will be discussed first in relation to the drugs themselves, followed by a consideration of the routes of administration.

**HOW THE BODY HANDLES LOCAL ANAESTHETICS**

Regardless of their route of administration, local anaesthetics pass into the bloodstream, whence they are eliminated (Catterall and Mackie 1996).

Local anaesthetics pass from the woman to the foetus, where they may be responsible for side effects. As with meperidine (pethidine), placental transfer and ‘trapping’ is increased if the foetus becomes acidotic. Local anaesthetics are extensively bound to tissues and alpha 1-acid glycoprotein (a plasma protein) in the circulation of the woman and the foetus. Only the unbound (free) fraction of the drug is responsible for actions and side effects. The foetus / neonate is relatively deficient in plasma proteins to bind these drugs, therefore, the proportion of free drug is higher and side effects are more likely.

The elimination of local anaesthetics is important, because any failure to clear these drugs may result in toxicity. Local anaesthetics in the bloodstream are eliminated by metabolism in the liver of the woman, foetus or neonate and the metabolites are eventually excreted by the kidney. In view of this, local anaesthetics should be avoided in patients with liver problems as they may not be able to metabolise them effectively (BNF 2000).
**Lignocaine** (lidocaine) has been used for over fifty years. It is metabolised in the liver of the woman, foetus and neonate into active metabolites. Although the duration of action and the half life of lignocaine / lidocaine are relatively short (82 minutes in the woman and 95 minutes in the neonate), the metabolites continue to be excreted by the neonate for 36-48 hours after delivery, depending on the route of administration. These metabolites are responsible for some of the toxic effects of lignocaine (Kuhnert 1993). With repeated administration, there is a danger of accumulation (Carson 1996).

**Bupivacaine** (Marcain®) has a longer duration of action than lignocaine (2-3 hours as epidural, or 8 hours as nerve block) and because of this it is used extensively for epidural analgesia in labour. However, in the event of accidental overdose, the effects of bupivacaine will take longer to ‘wear off’. The half life of bupivacaine is 9 hours in the woman and 18 hours in the neonate. Bupivacaine, and its (relatively inert) metabolites, continue to be excreted by the neonate for 36 hours after birth. The continued presence of the drug and its metabolites may induce subtle neuro-behavioural changes in the neonate, which may not be clinically significant (Kuhnert 1993).

To reach their site of action (the sodium channels in the axon membrane vi), local anaesthetics must diffuse through surrounding tissues, the myelin sheath surrounding the axon and the cell membrane itself. Therefore, pain relief is not achieved for about 30 minutes, with bupivacaine, which is too slow for many emergency Caesarean sections (MCHRC 2000).
**ACTIONS of LOCAL ANAESTHETICS**

Communication in the nervous system and mechanical activity in muscle depend on the electrical excitability of the cell membranes of those tissues. Nerve impulses depend on the generation of action potentials in the cell membranes of axons of neurones. The main action of local anaesthetics is to reduce the ability of nerves to conduct action potentials and impulses.

At rest, the cell membranes of nerve and muscle are polarised (or charged). When an action potential is triggered, the nerve is depolarised (or discharged) by a rapid influx of sodium ions, followed by repolarisation (recharging), due to an efflux of potassium ions. The entire process takes about 1 millisecond. Local anaesthetics prevent the rapid influx of sodium ions, by blocking the fast sodium channels in the nerve cell membranes. This inhibits the formation of action potentials, preventing the transmission of impulses and signals along the axons and therefore blocking normal nerve function. The action of local anaesthetics is reversed when the drug passes into the bloodstream and is excreted.

The effect of a local anaesthetic on any axon depends on both the size and myelination of the axon (Catterall and Mackie 1996). Small diameter, unmyelinated axons which transmit pain sensation and impulses of the sympathetic nervous system are the most sensitive to local anaesthetics, while larger, myelinated axons responsible for movement and pressure/ touch sensation are relatively resistant. The interruption of sensory functions in a nerve by the action of a local anaesthetic progresses in a definite order: the sensation of pain is the first to disappear, followed by cold, warmth, touch and pressure.
This means that movement and coarse touch are often preserved during local anaesthesia. The interference with the functioning of the sympathetic nervous system (SNS) is responsible for many of the side effects of epidural anaesthesia, such as hypotension.

**SIDE EFFECTS of LOCAL ANAESTHETICS**

The potential side effects of local anaesthetics are the same, regardless of the route of administration. However, when normal doses are used topically and intradermally, problems are very rarely encountered. The midwife should be particularly alert for side effects when local anaesthetics are used *via* the epidural or spinal routes or if a local anaesthetic has been inadvertently injected into a vein. (See ‘Implications for Practice’)

The side effects of local anaesthetics are related to their actions, in particular their ability to inhibit conduction of impulses in excitable tissues. Local anaesthetics block the fast sodium ion channels of all the body’s conducting tissue, namely:

- Central Nervous System (CNS).
- Heart and Cardiovascular System
- Peripheral Nervous System
- Sympathetic Nervous System
- Smooth Muscle - uterus, bladder, gut
- Skeletal Muscle
CNS EXCITATION AND INHIBITION

In the CNS, the sodium ion channels of the inhibitory neurones are blocked more readily than those of the excitatory neurones. Therefore, the CNS responses to local anaesthetics pass through several stages from excitation through to inhibition and depression:

- ‘Ringing in the ears’, ‘Funny taste in the mouth’
- Confusion/Agitation, Blurred Vision, Shivering
- Restlessness, Euphoria, Chills
- Nausea
- Tremor
- Convulsions
- Respiratory Depression
- Coma & Death

In the event of accidental intravenous administration, the initial response, to local anaesthetics, is usually excitation, restlessness, tremor and even convulsions (Hughes 1992). This paradoxical excitation is followed by CNS depression, particularly respiratory depression. However, if the systemic administration of lignocaine / lidocaine or bupivacaine is rapid, the excitatory responses may not be seen. Instead, the woman may experience only CNS depression, and a sudden respiratory arrest.

Practice points

- It is important that the midwife is aware of these side effects. Failure to attribute the early signs of toxicity to excessive absorption of local anaesthetic could mean that:
symptoms may be allowed to progress to more profound stages of CNS depression

further doses of local anaesthetic could be administered, intensifying the problem (Hughes 1992).

- Nausea caused by local anaesthetics may be attributed to opioid administration or the physiological response to labour and treated with anti-emetics. However, nausea, disturbed mood, feelings of faintness or light-headedness may be due to hypotension, caused by local anaesthetics, and this possibility should be considered before further doses of local anaesthetic are administered (Brownridge 1991).

SYMPATHETIC BLOCKADE

Consequences of Sympathetic Blockade:

- Reduced maternal blood pressure
- Maternal and neonatal thermoregulation failure
- Loss of neonatal asphyxia reflexes

Local anaesthetics inhibit the functioning of the sympathetic nerves. These control the diameter of the blood vessels, and thus affect an important aspect of blood pressure regulation (the total peripheral resistance). With the activity of the sympathetic nerves impaired, blood vessels dilate, causing both a drop in blood pressure and an inability to vasoconstrict in response to a cold environment. The woman may complain of feeling cold, shiver uncontrollably or conversely, may develop a pyrexia. Likewise, the neonate will be vulnerable to the cold (Howell 1995a, Reynolds et al 1996, El-Refaey et al 2000).
**Practice point**

*Blankets should be available to provide optimum comfort for the woman in labour. The neonate should be maintained in a warm environment, preferably by contact with the mother.*

In association with the administration of epidural analgesia, pyrexia (>98°C or 100.4°F) was recorded in 16.6% (120 / 724) of healthy parturients (n = 1218). Their infants were more likely to convulse or to be hypotonic and require resuscitation (Lieberman et al 2000). These authors suggest that maternal intrapartum fever may induce an even higher temperature in the foetus (by 0.5-0.9°C); where the neonate is also suffering from an ischaemic insult, this degree of pyrexia may increase the extent of neurological damage.

At delivery, the neonate relies on his or her reflex response to asphyxia to take a first breath, and this reflex depends on the activity of the sympathetic nervous system. With the use of local anaesthetics, the neonate’s reflex responses to delivery may be suppressed, requiring careful assessment and possibly prompt action by the midwife.

**HYPOTENSION**

The fall in blood pressure, that may accompany the intraspinal use of local anaesthetics, is due to vasodilation plus simultaneous myocardial depression. However, the relief of pain and distress afforded by effective analgesia may be a contributory factor.
Local anaesthetics inhibit the sympathetic nervous system, which is responsible for keeping the arterioles constricted and the blood pressure and heart rate within normal limits. Therefore, they have the potential to compromise the cardiovascular system, causing hypotension, bradycardia and even cardiac arrest. Clinically significant maternal hypotension, defined as a fall of 20-30% in pre-anaesthetic systolic blood pressure, or a systolic blood pressure below 100 mmHg, occurs in 5-15% of deliveries with epidural anaesthesia and 5-82% of deliveries with spinal anaesthesia (Hollmen 1993, Shennan et al 1995).

The risk of hypotension is greater if the woman is dehydrated or hypovolaemic. Therefore, prior to the intraspinal administration of local anaesthetics, intravenous fluids are infused, for example, 20-25ml/kg crystalloid solution (Hollmen 1993) or 1 litre of compound lactate solution (Sheenan et al 1995). The infusion of fluids should maintain venous return and therefore cardiac output, thus countering any hypotension.

Case Report

A woman was given epidural analgesia 36 hours after a forceps delivery to control perineal pain, despite refusing an intravenous infusion. She was passing little urine, with evidence of dehydration; frusemide had no effect on the urine output. This indicates poor renal perfusion, due to hypotension. Her hands became numb, due to the effects of the local anaesthetics. There were no recordings of: blood pressure; respirations; level of block; pulse oximetry.
She received sedation when she became agitated. Restlessness may have been due to either hypoxia or the drugs administered. Hypoxia was diagnosed on the ECG. Only then was oxygen given. Hypotension developed, leading to cardiac arrest and death (DOH 1996 p 93).

This woman died of hypoxia, due to hypotension and poor ventilation. Hypotension was caused by the combination of epidural opiates and local anaesthetics administered without intravenous fluids. With better monitoring and the appropriate use of intravenous fluids, this woman would have lived.

However, rapid administration of crystalloid intravenous fluids (such as Ringer’s, saline or glucose) may induce a diuresis, and fail to prevent a drop in blood pressure (Richardson 2000).

**Practice Point**

Cardiac output and circulating volume are assessed by careful monitoring of urine output, which can act as a ‘early warning sign’. Oliguria (low urine output) indicates that renal autoregulation is occurring in an attempt to counteract impending or actual hypotension. It is essential that the midwife responds to any decline in maternal urine output.

Failure to monitor urine output in women receiving epidural anaesthesia is cited as a contributory factor in maternal deaths (DoH 1998).
Case Report

Three hours after the administration of epidural analgesia, an emergency Caesarean section was performed for foetal distress. 0.5% bupivacaine (2 x 10 ml.) was administered prior to section. Recovery and initial observations taken by the midwife were normal. However, forty minutes later, the woman was unrousable. Autopsy showed extensive haemorrhage into parametrial tissues. (DOH 1994 p91)

The physiological signs of haemorrhage were modified by the blockade of the sensory and sympathetic nervous systems. The inadequacy of vital sign recordings indicated to the assessors that post-operative care was substandard.

Local anaesthetic induced vasodilation may reduce the ability of blood vessels to constrict in response to haemorrhage. Therefore, even a moderate haemorrhage may cause hypotension and blood loss post-partum may be increased (Beischer et al 1997). However, for Caesarean section, blood loss is less than with general anaesthesia (Lertakyamanee et al 1999).

It is important that any maternal hypotension is recognised immediately, because the blood flow to the uterus, and hence foetal oxygenation, decline in direct relation to maternal blood pressure. By jeopardising the blood supply to the placenta, hypotension
causes foetal acidosis, and depress the neonate’s central nervous system (Roberts et al 1995).

Hypotension is compounded by aorto-caval compression by the baby’s head, particularly if the woman is supine or obese, or if the uterus is enlarged due to multiple pregnancy, diabetes or polyhydramnios (Hollmen 1993). To avoid compression of the vena cava, the uterus must be displaced laterally; a woman receiving local anaesthetics during labour should avoid the supine position, including reclining chairs, and the midwife should regularly ascertain the position of the uterus. A lateral position should be adopted, or alternatively, a 20 degree tilt achieved by using a ‘wedge’. Aorto-caval compression may be less if the woman is upright and ambulant (Al-Mufti et al 1997). If a woman [inadvertently] lies supine at term, the placental blood flow will decrease by 20-30%, without any change in maternal vital signs. If position is not corrected, the supine hypotension syndrome, leading to maternal collapse, may follow. This suggests that practitioners should consider performing vaginal examinations with the woman in a lateral position (Yerby 2000).

Case Report

A woman of 30 weeks gestation was given a spinal anaesthetic. She was premedicated with 15 mg papaveretum and given 400 ml. of Hartman’s solution, followed by 1ml of 0.5% of heavy bupivacaine. She noticed her legs becoming weak, which was attributed to bupivacaine and she was placed in a supine position with the table tilted laterally. Her blood pressure fell rapidly and she
was treated with fluids and ephedrine (2x 15 mg). Further measures taken were, the administration of oxygen, atropine, epinephrine (adrenaline) and a further 1,600 ml. of fluids were administered. Pulmonary oedema, and subsequently death from adult respiratory distress syndrome followed. (DOH 1994 p83)

It is likely that the hypotension was due to aorto-caval compression, because a small degree of lateral tilt would not prevent this. The interventions which led to this catastrophe followed attempts to correct the hypotension. Pulmonary oedema was caused by the combination of fluids and 2 vasoconstrictors (i.e. epinephrine (adrenaline) + ephedrine).

Aldrich et al (1995) found that when 14 healthy labouring women, receiving effective epidural analgesia, 0.25-0.5% bupivacaine, adopted the supine position for 10 minutes, an 18% fall in maternal lower limb digital artery pressure, and a, clinically significant, 8% fall in foetal cerebral oxygen delivery occurred. Hence, measuring the maternal blood pressure in the arm could allow significant hypotension at the level of the uterus to remain undetected. This suggests that the use of leg cuffs should be considered when intraspinal analgesia is used (Hollmen 1993).

If placental blood flow is already compromised, for example by pregnancy induced hypertension, the vulnerable foetus may not be able to withstand the extra stress of low maternal blood pressure. Maternal deaths have occurred when epidural analgesia has
been used alone to control hypertension in women with pre-eclampsia or eclampsia (DoH 1994). Thus the use of epidural analgesia in these women remains controversial (Hollmen 1993).

**Practice point**

*Particularly careful BP monitoring is needed on initial administration, during the first 30 minutes of spinal anaesthesia, and when ‘top-up’ doses are administered into the epidural space (Sheenan et al 1995).*

Hypotension is more likely with a spinal (intrathecal) than an epidural anaesthetic. ‘High risk’ situations include:

- within the first 30 minutes of administration
- when ‘top-up’ doses are administered
- aorto-caval compression (exacerbated in the supine position)
- hypovolaemia
- when anaesthesia reaches the level of the T₄ segment (nipple level)
- if there are pre-existing cardiac problems, such as heart block
- standing may induce postural hypotension

Clinically significant maternal hypotension, jeopardising the foetus, may not be manifest as maternal symptoms. If hypotension is not **corrected within 2 minutes**, foetal bradycardia, acidosis and depression will follow (Hughes 1992, Downing and Ramasubramanian 1993). Clinically, it may be difficult to attribute foetal heart rate
abnormalities to the direct action of the local anaesthetics or to maternal hypotension caused by drugs, although foetal acidosis during Caesarean section is a recognised complication of local anaesthetics (Steer 1995).

**Practice Points**

- **If a fall in the blood pressure should occur, the woman should be turned on her left side, her legs elevated (Trendelenburg position) if possible and intravenous fluids administered. Medical advice must be sought immediately. If the blood pressure does not improve within 2-3 minutes, oxygen and ephedrine may be given, vi (Davis 1992).**

- **Following epidural anaesthesia, the functions of the sympathetic nervous system and blood pressure control may return after the return of sensation. It is therefore important that blood pressure monitoring is continued during this period.**

Bupivacaine has more myocardial depressant action than lignocaine / lidocaine. This is important with both spinal and epidural administration. It is most severe if the parturient is acidotic or hypoxic. The cardiotoxicity threshold is lower in pregnancy. Cardiac arrests and maternal deaths have been reported, therefore, the use of the 0.75% solution is absolutely contra-indicated in obstetrics (BNF 2000). Bupivacaine is never used for intravenous anaesthesia since bupivacaine-induced cardiotoxicity is difficult to treat (Catterall and Mackie 1996). Accidental intravenous administration of bupivacaine during epidural anaesthesia in labour has produced cardiovascular collapse (Kuhnert 1993).
DEPRESSION OF SMOOTH MUSCLE

Uterine, gut and bladder contractions are depressed by local anaesthetics. Inhibition of the bladder usually produces retention of urine, but conversely urinary and faecal incontinence are possible (Karch 1992). Epidural analgesia is associated with an increased risk of post-partum urinary retention (Olofsson et al 1997). It is important not to underestimate the potential problems, short and long term, arising from repeated urinary catheterisation (Mander 1994).

Ephedrine

To correct hypotension, 3-6mg ephedrine may be administered by a slow intravenous injection, repeated every 3-4 minutes if necessary, up to 30mg (BNF 2000).

Ephedrine has the potential to constrict uterine vessels (it is an alpha agonist, see glossary), but this is minimised if the drug is given slowly or as an infusion. Although this is considered safe for a full-term healthy foetus, a high risk foetus, may not be able to tolerate this vasoconstriction (Hollmen 1993), therefore a lower dose (2.5mg) is preferable (Hughes 1992).

Several side effects associated with ephedrine, such as tachycardia and cardiac dysrhythmia, require monitoring. These are similar to the side effects of ritodrine (see chapter 7, tocolytics). Like epinephrine (adrenaline), ephedrine may interact with oxytocin to cause severe hypertension.
**Practice Point**

*Since bladder sensation may be absent or diminished, the woman should be encouraged to micturate every 2-3 hours.*


- the first and second stages of labour are more likely to be prolonged (The mean differences between epidural anaesthesia and parenteral opioids were 42 and 14 minutes (Halpern et al 1998)
- cervical dilatation is slower
- oxytocin is twice as likely to be used
- foetal malposition is more common
- Caesarean section for dystocia (glossary) is more likely
- instrumental deliveries are 2-4 times more common

**Local anaesthetics prolong labour** by:

- relaxing the pelvic floor muscles
- diminishing the “bearing down” reflexes
- decreasing expulsive efforts
- direct action on the uterine muscle, to reduce the muscle tone
• diminishing the pulsatile release of oxytocin from the posterior pituitary gland.

Although studies offer no consensus (Dewan and Cohen 1994, Fung 2000), in a large study (n=1250), the combined use of oxytocin, induction and epidural analgesia appeared to be additive in bringing about a higher rate of instrumental and operative deliveries (Carli et al 1993). In a cohort study involving 1561 nulliparous parturients, Traynor et al (2000) found that the risk of Caesarean section increased 3 fold with the use of combined spinal epidural analgesia and 4.7 fold with the use of continuous infusion epidurals. The risk of Cesarean section is increased if 2 or more bolus doses of bupivacaine are administered (Hess et al 2000) or if epidural analgesia is administered prior to either cervical dilatation > 5 cm (Thorpe et al 1993) or engagement of the foetal head (Traynor et al 2000).

Case Report

A woman had received an ineffective epidural in a previous pregnancy. She underwent a trial of labour with a breech presentation with effective epidural analgesia. However, when there was failure to progress in the second stage, it was decided to deliver the baby by Caesarean section. An additional 30 mls of 0.5% bupivacaine was administered over 30 minutes, but this did not provide adequate anaesthesia for Caesarean section. During the induction of general anaesthesia, a hypoxic episode occurred, which led to death 2 days later (DOH 1991 p 75)
Continuation of epidural analgesia into the second stage probably contributed to this woman’s failure to progress.

Some authors recommend that epidural analgesia is not continued into the second stage of labour, due to increased incidence of malrotation of the presenting part, necessitating assisted vaginal delivery (Howell and Chalmers 1992, Howell 1995a). This discontinuation of epidural analgesia increases pain, which may have adverse psychological and physiological consequences, including hyperventilation and alkalosis (see p.??).

**Practice Point**

*Women should be advised that although epidural analgesia is more likely to be effective than other methods of analgesia, its effects on the physiology of labour reduce the chances of a ‘normal’ vaginal delivery (Howell 1995a).*

Reduction in the muscle tone of the uterus may impair the contraction of the uterus after delivery, and increase the risk of haemorrhage (Campbell & Lees 2000).

**NEUROMUSCULAR BLOCKADE**

**Loss of sensation and motor control**

When administered by the intravenous, epidural or spinal routes, local anaesthetics affect the motor neurones as well as the sensory neurones. The recipient may feel weak and numb. Blockade of motor neurones of the lower spinal segments by epidural anaesthesia inhibits movement during labour. Paraesthesia or paralysis of the legs may occur, so that
the woman is unable to stand or walk. This is less evident with bupivacaine or ropivacaine than lignocaine (Catterall and Mackie 1996), and with 0.0625% or 0.125% rather than 0.25% bupivacaine (Harms et al 1999). Laxity of the pelvic floor muscles, due to the action of local anaesthetics, is the mechanism behind malrotation, malposition and shoulder dystocia (glossary) (Thorp et al 1993, Howell 1995a).

Some studies have linked bupivacaine with reduced neonatal muscle tone, suckling and reflex responses.

Loss of sensation prevents the woman from feeling aware of uterine contractions and the birth process, which may lead to dissatisfaction later (Brownridge 1991).

An intraspinal nerve block in childbirth is intended to anaesthetise the spinal nerves below the 12th thoracic segment (innervation of the uterus). If the local anaesthetic rises above the 10th thoracic segment, too many nerves controlling the intercostal muscles will be inhibited, causing breathing difficulties. At the 4th thoracic segment, sympathetic nerves supplying the heart muscle will be depressed.

**Practice Point**

_The level of skin sensation should be monitored regularly, and medical advice sought if necessary. Sensation at the level of the nipple represents the 4th thoracic segment and at the umbilicus the 10th thoracic segment, although some overlap exists (Tortora & Grabowski 2000)._
Respiratory failure

The intercostal muscles may be impaired by high spinal anaesthesia, causing over-reliance on the diaphragm. However, at term the diaphragm is ‘splinted’ by the uterus, and is less able to increase its movement to compensate for any inadequacies of the intercostal muscles. When these problems are compounded by the risk of medullary paralysis and the respiratory depression associated with spinal anaesthesia, there is a possibility of inadequate ventilation, and even arrest.

Practice Points

*It is important to monitor the rate and depth of respirations and check oxygenation by pulse oximetry if necessary.*

*Pulse oximetry may not detect mild or moderate ventilatory depression (Herman et al 1999).*

HYPERSENSITIVITY REACTIONS

Rare individuals are hypersensitive to local anaesthetics or their preservatives and some cross sensitivities occur. The clinical manifestations of hypersensitivity include:

- DERMATITIS
- ASTHMA
- ANAPHYLAXIS
- METHAEMOGLOBINAEMIA *
*Footnote. Both prilocaine, contained in EMLA ® cream, and lignocaine/ lidocaine may induce methaemoglobinemia in rare, genetically susceptible individuals. Methaemoglobin is an oxidised form of haemoglobin which is unable to transport oxygen and is normally converted back to haemoglobin by various enzymes. Genetic deficiencies of these enzymes can be magnified by certain drugs, with disastrous consequences. Methaemoglobinemia presents as cyanosis, accompanied by headache, weakness and breathlessness. Severe methaemoglobinemia is incompatible with life (Bunn 1991). Management of methaemoglobinemia involves an intravenous injection of methylthioninium chloride (methylene blue) 1% 1mg/kg. (BNF 2000).

**EFFECTS ON THE NEONATE**

Older studies have linked epidural anaesthesia with neonatal depression and neurobehavioural abnormalities at 24 hours post partum (Catterall & Mackie 1996). Epidural local anaesthetics may have subtle neurobehavioural effects on the neonate, which are undetectable at 18 months (Kuhnert 1993, Howell and Chalmers 1992). The auditory system of the neonate may be transiently impaired (Reynolds et al 1996). Halpern et al (1999) suggest that any neurobehavioural side effects are no impediment to breast feeding, providing effective support is offered.

The use of epidural analgesia increases the risk of neonatal hypoglycaemia, tachypnoea and a disturbance of lipid metabolism (Howell and Chalmers 1992). Foetal acidaemia, without obvious clinical sequelae, was more likely when regional, particularly spinal, rather than general anaesthesia was used for Caesarean section (Roberts et al 1995).
Nevertheless, neonates generally fare better with epidural analgesia than with either general anaesthesia or systemic opioids (Reynolds et al 1996). Neonates are less likely to have low APGAR scores at 5 minutes or to require naloxone after epidural analgesia than after intramuscular opioids (Halpern et al 1998).

<table>
<thead>
<tr>
<th>Box. Ropivacaine</th>
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<tbody>
<tr>
<td>This local anaesthetic has been developed to provide long-lasting local anaesthesia without the cardiotoxicity of bupivacaine, to which it is chemically related. While some authors consider these two agents to be equally effective (Muir et al 1997, Irestedt et al 1998), others have found that ropivacaine is less potent (Capogna et al 1999, Fisher et al 2000). Therefore, ropivacaine may provide a less intense motor blockade than bupivacaine, which could reduce the rate of instrumental deliveries (Cederholm 1997) and improve ambulation and micturition (Campbell et al 2000). In one study (n=60), ropivacaine was found to have fewer neurobehavioural effects on neonates (Stienstra et al 1995, Writer et al 1998). However, onset of action and termination of motor blockade following delivery may be slower than with bupivacaine (McCrae et al 1995).</td>
</tr>
</tbody>
</table>

**CAUTIONS and CONTRA-INDICATIONS (see box below)**

- Local anaesthetics should not be used in individuals where a previous allergy has occurred to any chemically related anaesthetic or other constituent of the preparation.
- Hypovolaemia must be corrected before intraspinal administration (BNF 2000).
• Administration of local anaesthetics is not advised if the woman has had a recent haemorrhage, as the cardiovascular responses to blood loss will be compromised (Beischer et al 1997).

• Local anaesthetics should be applied cautiously, if at all, to inflamed areas.
Cautions and Contra-indications for local anaesthetics

Local anaesthetics are used cautiously in:-

- heart block or impaired cardiac conduction
- hypovolaemia and other forms of shock
- maternal bradycardia
- porphyria
- epilepsy
- respiratory impairment
- liver or kidney disease
- hyperthyroidism
- family history of malignant hyperthermia
- myasthenia gravis
- lactation

Epidural anaesthesia is avoided in:-

- placenta praevia
- abruptio placenta
- haemorrhage or anticipated haemorrhage
- Bacteraemia
- coagulation disorders, including:
  - use of aspirin or heparin (see epidural haematoma below & chapter 8)
  - pre-eclampsia with bleeding abnormalities

Spinal (intrathecal) anaesthesia is avoided in:-

- inflammatory conditions of the spine
- meningitis
- lumbar TB
- spinal metastases
- septicaemia
**DRUG INTERACTIONS**

The unwanted effects of local anaesthetics may be enhanced by H₂ antagonists (cimetidine), anti-arrhythmics and other central nervous system depressants, including alcohol and prochlorperazine (Malseed et al 1995).

- Regular use of alcohol increases the risk of therapeutic failure (Stockley 1999).

- Beta blockers, cimetidine, and possibly ranitidine interfere with the hepatic clearance of bupivacaine. This increases the risk of toxicity (Kuhnert 1993).

- BENZODIAZEPINES may affect the clearance of local anaesthetics. Increased bupivacaine (but not lidcaine/ lignocaine) concentrations have been reported in patients taking diazepam (Stockley 1999).

- Tricyclic anti-depressants and phenothiazines (e.g. prochlorperazine) increase the risk of heart block, particularly if epinephrine / adrenaline is used.

- Calcium channel blockers (nifedipine, verapamil) enhance the cardiotoxicity of bupivacaine.
### Implications for practice. Local Anaesthetics.

<table>
<thead>
<tr>
<th><strong>Problem</strong></th>
<th><strong>Management</strong></th>
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<tbody>
<tr>
<td><strong>Topical applications (EMLA)</strong></td>
<td></td>
</tr>
<tr>
<td>Contact dermatitis</td>
<td>Coolants available</td>
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<tr>
<td></td>
<td>Wear gloves</td>
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<tr>
<td><strong>Epidural or Spinal Anaesthesia</strong></td>
<td></td>
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<tr>
<td><strong>Maternal</strong></td>
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<tr>
<td>Hypotension</td>
<td>Avoid supine position</td>
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<td></td>
<td>Prehydration with intravenous fluids</td>
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<td></td>
<td>Monitor BP, heart rate + rhythm, &amp; urine output</td>
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<td></td>
<td>Assess skin &amp; oxygen saturation with pulse oximeter</td>
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<td></td>
<td>Ensure vasopressor agents available e.g. ephedrine</td>
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<td></td>
<td>Check history &amp; ECG for heart block</td>
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<td></td>
<td>Check history for: liver disease, malignant hyperthermia</td>
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<tr>
<td></td>
<td>Ensure no signs of shock present</td>
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<td></td>
<td>Use of test dose</td>
</tr>
<tr>
<td>Loss of uterine contractility</td>
<td>Monitor.</td>
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<tr>
<td></td>
<td>Advise of possibility of prolonged second stage and increased incidence of instrumental deliveries</td>
</tr>
<tr>
<td>Urine retention / incontinence</td>
<td>Monitor output &amp; specific gravity</td>
</tr>
<tr>
<td></td>
<td>Catheterise if necessary</td>
</tr>
<tr>
<td>Risk of fits</td>
<td>Diazepam available</td>
</tr>
<tr>
<td>Loss of thermoregulation</td>
<td>Prevent shivering. Blankets should be available.</td>
</tr>
<tr>
<td></td>
<td>Monitor maternal temperature and pre-empt non-infectious fever / pyrexia.</td>
</tr>
<tr>
<td></td>
<td>Monitor infant for convulsions</td>
</tr>
<tr>
<td>Hypersensitivity</td>
<td>Be aware of cross-sensitivity between local anaesthetics</td>
</tr>
<tr>
<td>Methaemoglobinaemia</td>
<td>Recognise cyanosis. Have oxygen ready. Methylene blue antidote, if needed.</td>
</tr>
</tbody>
</table>
Implications for practice. Local Anaesthetics. (continued)

<table>
<thead>
<tr>
<th>Problem</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foetal / neonatal</td>
<td></td>
</tr>
<tr>
<td>Depression of foetal heart rate</td>
<td>Monitor. Liaise with medical staff.</td>
</tr>
<tr>
<td>Depression of neonatal respiratory &amp; suckling reflexes.</td>
<td>Prepare to assist neonate to establish respirations. Give extra assistance to initiate breast feeding</td>
</tr>
<tr>
<td>Spinal anaesthesia</td>
<td></td>
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<tr>
<td>Respiratory depression</td>
<td>Monitor rate &amp; depth of respirations regularly Ensure resuscitation equipment is available</td>
</tr>
</tbody>
</table>

**Routes of ADMINISTRATION OF LOCAL ANAESTHETICS**

**SURFACE ANAESTHESIA**

*EMLA* (eutectic mixture of local anaesthetics) is a mixture of lignocaine / lidocaine and prilocaine which may be applied to the skin surface to provide analgesia for venepuncture or cannulation. A thick layer under an occlusive dressing will provide analgesia if applied 1-5 hours before the procedure. Alternatively, amethocaine (tetracaine) gel may be similarly applied 30-45 minutes before venepuncture or cannulation. Application to mucous membranes, wounds or areas of atopic [glossary] dermatitis must be avoided (BNF 2000).

**SUBCUTANEOUS / INTRADERMAL INJECTION**

Local anaesthetics may be infiltrated directly into tissue, to varying depths, to anaesthetise relatively small areas. The addition of a vasoconstrictor (adrenaline/ epinephrine) approximately doubles the duration of anaesthesia and reduces the peak
concentration of local anaesthetic in plasma (Catterall and Mackie 1996). However, vasoconstrictors carry an inherent danger of ischaemic necrosis. Due to potential cardiotoxicity, the total dose of adrenaline / epinephrine is limited to 500 micrograms (BNF 2000).

When intradermal lignocaine / lidocaine is being administered to decrease the pain of perineal trauma or an episiotomy, accidental injection into the presenting part of the neonate may produce serious side effects: apnoea; loss of muscle tone; fixed dilated pupils.

NERVE BLOCK

A solution of local anaesthetic is injected into or around individual nerves or nerve plexuses. The onset of action is 3 minutes for lignocaine / lidocaine and 15 minutes for bupivacaine. The duration of actions are 2-3 hours & 5-7 hours respectively, affecting motor as well as sensory modalities. A pudendal block may be performed prior to short procedures, such as instrumental delivery, suturing or manual removal of placenta. This procedure may increase the administrator’s risk from transmission of blood borne infections (Hughes 1992).

INTRASPINAL* ANALGESIA

* The term intraspinal is used to refer to administration within the spinal column i.e. to encompass epidural, spinal and combined spinal epidural administration (Wildsmith 1996).
The problems encountered with intraspinal analgesia are those attributed to the route of administration, plus the side effects of the drugs themselves. Comparisons of intraspinal analgesic regimens on the progress of labour, neonatal outcome and long term sequelae await the results of larger studies (Drugs and Therapy Perspectives 1996).

Drugs administered intrathecally pass into the foetus to a limited extent; very low concentrations of opioids are found in the systemic circulation or cord blood following spinal opioid administration (Clyburn and Rosen 1993). Drugs administered epidurally are administered in much larger doses and absorbed into the systemic circulation via the epidural veins, making side effects more likely.

**EPIDURAL ANAESTHESIA**

This entails injection into the fat in the narrow space between the dura and the bony canal. (see figure 3) The drug diffuses through the dura, where it acts on the nerve roots. There is also an effect at the intervertebral foramina.

Sufficient local anaesthetic is injected to be absorbed into the circulation, via the epidural veins, in proportion to the total dose used. The local anaesthetic than passes into the foetus. Absorption is increased at delivery when the mother is spontaneously pushing and ‘top up’ injections are usually avoided at this time.

Following a test dose and initial administration, ongoing epidural analgesia may be by:
• bolus injection on request
• patient controlled infusion
• a constant infusion device
• scheduled bolus injections (Drugs and Therapy Perspectives 1996).

In most maternity units the anaesthetist will administer the initial bolus injection, with subsequent bolus doses given by midwives. Although scheduled bolus injections provide more effective analgesia, they call for more careful monitoring of the level of sensory blockade, and risk the administration of higher doses (Howell 1995b). Unfortunately, pre-set infusion devices fail to take account of individual difference either in analgesic requirements (Brownridge 1991), or the need for increasing concentrations as labour advances (Capogna et al 1998). In one small study (n=55), patient controlled administration of epidural analgesia resulted in less hypotension, possibly because the drugs were delivered more slowly (Al-Mufti et al 1997).

Addition of Adrenaline (epinephrine)

Adrenaline (epinephrine) may be added to epidural analgesia to increase the duration and intensity of analgesia, for example, with continuous epidural infusions (Clyburn and Rosen 1993, Norris et al 1994). It may act directly on the pain pathways to enhance analgesia. Bupivacaine is usually administered without adrenaline / epinephrine (plain), but adrenaline / epinephrine is added to lignocaine / lidocaine if perineal analgesia is required quickly (Brownridge 1991).
Adrenaline / epinephrine vasoconstricts the epidural venous plexus, thereby reducing the systemic absorption of local anaesthetic (Catterall and Mackie 1996). The addition of adrenaline / epinephrine to bupivacaine may increase the placental transfer of bupivacaine, due to changes in protein binding. Therefore, the addition of adrenaline / epinephrine reduces maternal, but not foetal exposure to local anaesthetic (Reynolds 1993b).

The side effects and interactions of adrenaline / epinephrine mitigate against its use:

- Adrenaline / epinephrine is a vasoconstrictor, and reduces placental blood flow. In women where placental blood flow is already compromised, for example by chronic hypertension or pregnancy-induced hypertension, adrenaline / epinephrine may further jeopardise foetal blood supply and cause foetal heart decelerations (Hollmen 1993). However, this is a secondary consideration in the emergency management of anaphylaxis, see chapter 1 p. ?? 20 Box.

- Adrenaline / epinephrine can precipitate cardiac dysrhythmias or alterations in maternal blood pressure, which can decrease placental perfusion.

- Adrenaline / epinephrine may prolong the first stage of labour (Dounas et al 1996).

- Adrenaline / epinephrine interacts dangerously with:
  - volatile general anaesthetic gases, causing dysrhythmias
  - oxytocin, causing hypertension
• beta blockers, causing hypertension (BNF 2000).

Case Report

A young primipara in normal labour received epidural analgesia containing adrenaline / epinephrine. When labour failed to progress, an oxytocin infusion was commenced. Over the next two hours, the woman became hypertensive, drowsy and comatose, and developed a hemiparesis. Following an emergency Caesarean section, the woman made a full, but gradual recovery in intensive care. This involved transfer to a tertiary centre for several weeks.

If administering ‘Bupivacaine with Adrenaline ®’ professionals need to consider the interactions of both components.

SPINAL / INTRATHecal ANAESTHESIA

This entails injection into the subarachnoid space, affecting the lower part of the spinal cord and the nerve roots, which affords rapid pain relief (see figure 3) (Sheenan et al 1995). Hypotension and headache occur more commonly with spinal than epidural analgesia (Reynolds et al 1996). Low spinal anaesthesia, combined with epidural anaesthesia, is currently preferred to general anaesthesia for most Caesarean sections (Marx and Rabin 1993, DoH 1996).

Combined spinal epidural (CSE) analgesia.

Opioids and local anaesthetics may be administered epidurally or intrathecally, often in combination. The combined spinal-epidural technique allows lower doses of both drugs
to be administered. When an opioid, usually fentanyl, is added to bupivacaine or ropivacaine, the dose of local anaesthetic is much less than with epidural administration. Some (not all) authors suggest that this may reduce the unpleasant motor blockade, paresis or paralysis of the lower body caused by the higher doses of local anaesthetics needed for epidurals, and permits ambulation during labour. Careful monitoring is required to avoid hypotensive episodes, which are potentially damaging to the foetus (Steer 1995, Shennan et al 1995).

Intrathecal opioids afford more rapid analgesia than epidural anaesthetics, for example, fentanyl is effective within 5 minutes, compared to 30 minutes for bupivacaine. The addition of local anaesthetics overcomes the short duration of action of intrathecal opioids. In a large study (n=1,000), the use of 0.125% bupivacaine with sufentanil was associated with reduced administration of oxytocin and fewer Caesarean sections when compared to 0.25% bupivacaine with adrenaline / epinephrine (Olofsson et al 1998).

However, CSE analgesia has some disadvantages when compared to traditional epidural analgesia: the incidence of hypotension and headaches are not improved by the addition of opioids (Norris et al 1994); the rates for Caesarean section are not improved (Traynor et al 2000); the common side effects of opioids, such as nausea, vomiting and itching, may still be troublesome; the potential for local problems, such as meningism, is increased. Also, the onset of analgesia is only shortened by 2 minutes when opioids are added to both epidural and intrathecal analgesia (Nickells et al 2000).
**Opioids Administered by Intraspinal Injection**

Advantages of intraspinal opioids over local anaesthetics include:

- no blockade of the sympathetic nervous system, but hypotension remains a problem
- no motor blockade, therefore, movement and ambulation are unaffected
- minimal effect on other sensory systems
- reversal of shivering induced by local anaesthetics (Reynolds et al 1996).

Some of the problems associated with intramuscular opioids are diminished, such as constipation. However, many of the opioid side effects remain (Kan and Hughes 1995):

- pruritus / itching, which is more troublesome at higher doses (Lyons et al 1997)
- nausea and vomiting
- respiratory depression or even arrest
- hypotension
- foetal heart rate changes
- sedation, slurred speech
- retention of urine


When opioids are administered epidurally or intrathecally, hypotension is likely to occur within 30 minutes of administration, particularly with meperidine (pethidine). This may be accompanied by severe foetal bradycardia (Richardson 2000). Following the administration of normal doses, maternal respiratory depression, apnoea and sedation may occur 30 minutes later or be delayed up to 16 hours, presumably due to the gradual

**Case Reports**

Epidural or intrathecal opioids may cause sudden, profound maternal respiratory depression.

**Case 1.** 1mg of morphine was administered intrathecally during labour. Apnoea occurred 7 hours later, after delivery. It was merely fortuitous that apnoea did not occur during labour.

**Case 2.** 100 micrograms of fentanyl were administered extradurally for Caesarean section. Profound respiratory depression occurred 100 minutes later.

These cases, cited by Clyburn and Rosen (1993) show the effects of delayed respiratory depression on the mother.

**Practice Points**

- It is important that vital signs continue to be monitored up to 16 hours after administration of intraspinal opioids (Hall 1996).

- If the spinal (intrathecal) anaesthetic has 'worn off', administration of other opioids, for example meperidine (pethidine) intramuscularly, may intensify respiratory depression (Arkoosh 1991).
Recurrence of *Herpes simplex* infections have been reported with spinal administration of opioids (Bowdle 1998).

**MORPHINE**

Intraspinal morphine induces pruritus and emesis in the majority of women (Richardson 2000).

*Practice Point*

*Anti-histamines do not always relieve this pruritus, but naloxone in low doses is often effective* (Bowdle 1998).

There are case reports of intrathecal morphine or diamorphine worsening pain, due to the unopposed action of a metabolite (morphine-3-glucuronide) in the CNS (Twycross 1994). Nalbuphine may be more effective than naloxone at reversing the side effects of epidural morphine in post-Caesarean patients.

Nausea and pruritus are less frequent with the more lipid-soluble opioids, such as fentanyl, alfentanil and sufentanil, which are superseding morphine in combined spinal epidurals (CSE) (Kan and Hughes 1995, Bem et al 1996). However, these drugs have the potential to cause respiratory depression in mother and foetus, in the absence of maternal sedation (Herman et al 1999).

**FENTANYL**

This lipid-soluble opioid can be administered by several routes: transdermal, transmucosal, intrathecal. Since it is 80 times more potent than morphine, relatively
small volumes are required. The rapid action of fentanyl (within 5 minutes) and longer
duration of action (80-90 minutes) offer a considerable advantage over morphine (Kan
and Hughes 1995). The lipophilic (glossary) properties of fentanyl make it more likely to
remain in the spinal cord and less likely to spread to the medulla, and cause respiratory
depression (Clyburn and Rosen 1993). There is less reliance on the kidneys for
elimination, making it more suitable in pre-eclampsia and for long term administration,
but fentanyl may accumulate in the occasional patient (Bem et al 1996). Fentanyl
administered via the epidural route passes into the foetus, and has the potential to
produce neonatal depression, which is not always detected by the APGAR score
(Reynolds 1993b). Passage of fentanyl into colostrum is very low (Dailland 1993).

Fentanyl may reduce the heart rate of mother and foetus, and even cause asystole if the
mother is intubated. Although reductions in blood pressure are usually minor, severe
hypotension has been reported. Increases in heart rate and blood pressure occur in a
minority of patients (Bowdle 1998). Fentanyl provokes less histamine release than
morphine, which gives the following advantages:

- reduced incidence of pruritus (66% incidence)
- less hypotension
- less risk of asthma attack.

Fentanyl requirements are increased in women regularly taking anti-convulsants.
The fentanyl analogues are relatively new drugs. Alfentanil and sufentanil are less likely to induce hypotension than fentanyl (Marshall and Longnecker 1996), but late hypotension has been reported with sufentanil (Gautier et al 1997). Their distinguishing features are outlined below.

**SUFENTANIL**

Sufentanil is more potent than fentanyl. Duration of action may vary from 30-300 minutes. Onset of analgesia is within 5 minutes of intrathecal administration (Kan and Hughes 1995, Harsten et al 1997). However, the rapid passage into the brain may increase the risks of opioids myoclonus or muscular rigidity (Bowdle 1998) or swallowing difficulties (Richardson 2000). Itching was reported by 44% of women receiving intrathecal sufentanil (Norris et al 1994). Sufentanil gives a longer duration of both analgesia and pruritus than fentanyl (Gaiser et al 1998). Placental transfer of sufentanil is lower than other opioids and neonates studied have not demonstrated any adverse effects following the epidural administration of 50 micrograms, although a dose of 80 micrograms has caused neonatal respiratory depression (Armand et al 1993).

**ALFENTANIL**

Alfentanil has shorter onset and duration of action than sufentanil, but is more likely to cause nausea (Scholz et al 1996, Bowdle 1998). Neonatal elimination of this drug is delayed (Clyburn and Rosen 1993) with cases of neonatal hypotonia being reported (Armand et al 1993).
The implications for practice associated with intraspinal opioids are considered in association with administration of CSE and intraspinal analgesia.

**ADMINISTRATION OF INTRASPINAL ANALGESIA**

The technical complexities of administration and the need for specialist skills and support counterbalance the advantages of intraspinal analgesia (Reynolds 1993a).

The use of ‘test doses’ is mandatory. It is suggested that the administration of large bolus doses of local anaesthetics “will sooner or later lead to a catastrophe” (Hughes 1992 p.R21).

Epidurals are more likely to fail if: the first dose fails; presentation is posterior; pain occurs during placement; the epidural is given for < 1 hour or > 6 hours (Le Coq et al 1998).

Common technical problems associated with intraspinal analgesia include:

- Failure to flex the spine
- Kinking of lines
- Accidental removal of lines
- Infection
- Systemic absorption
- Intravascular injection
- Dural puncture

### Complications of intraspinal administration

**Intravascular injection**

The prominent venous plexus in the epidural space makes inadvertent intravascular injection a potential hazard of epidural analgesia (Catterall and Mackie 1996). An accident of this type may cause cardiac toxicity and profound hypotension.

**Dural Puncture**

**Headache**, sometimes with tinnitus and photophobia, is the most common complaint following intraspinal anaesthesia. It is attributed to the puncture of the dura by the spinal needle or accidentally by the epidural needle (Reynolds et al 1996). This may cause a leak of CSF, reducing intracranial pressure; this take a few weeks to resolve (McKenry and Salerno 1995). Headache is more likely to follow spinal anaesthesia if large needles (> 25 gauge or without pencil point tips) are used or if the woman does not remain supine during the immediate postpartum period. In one series (n=924), 2.7% of parturients suffered unintended dural puncture. This was more likely when either the parturient was suffering severe labour pains, and therefore unable to maintain a constant position, or combined spinal-epidural analgesia was administered (Norris et al 1994).

Severe post-dural puncture headache, which is hindering mobilisation, may require an epidural ‘blood patch’ (Tay et al 1994, Wildsmith 1996). This is the epidural injection of 15-20 ml. of the patient’s own blood. If a blood patch is performed to treat a headache,
the epidural needle must be re-introduced; this prospect may deter some women from accepting the treatment. Prophylactic blood patch is the administration of 15 ml. blood after delivery, before removal of the epidural needle. This has been shown to reduce, but not eliminate, the need for a second procedure (Howell 1995c).

Both epidural and spinal anaesthesia are associated with headache and backache. Prolapsed intervertebral disc has been reported in association with epidural analgesia (Forster et al 1996). The relationship between new long-term backache and epidural analgesia during labour remains controversial. Studies suggest that 18% of women who receive epidural analgesia suffer long term neurological or orthopaedic problems, compared to 10% of those receiving other forms of analgesia (Howell and Chalmers 1992, Mander 1994). Whereas retrospective studies have indicated that this association exists (MacArthur et al 1990, Russell et al 1993), a prospective randomised study of 599 women found no association between new onset long term backache and either the use of epidural analgesia or the dose of bupivacaine administered. Previous backache was significantly associated with new onset long-term backache (Russell et al 1996, Butler & Fuller 1998). Attention to posture before, during and after labour may reduce long term backache (Reynolds 1993a).

**Epidural haematoma**

An epidural haematoma may form if insertion of the intra-spinal needle causes bleeding and bruising. This can compress vital structures e.g. in the spinal cord.
**Practice Point**

To reduce the risk of epidural haematoma, the woman should be examined for signs of bleeding (see chapter 8) and coagulation and platelet count should be checked before the procedure if:

- **HELP syndrome is even a remote possibility (Yerby 2000)**
- **anticoagulants have been administered**
- **low molecular weight heparin has been administered within the last 24 hours**
- **other haematological disorders are present.**

Spinal analgesia is hazardous if the woman has disseminated intravascular coagulation (Richardson 2000).

**Neurological deficit**

It is estimated that serious neurological complications arise in around 1 in 2530 women receiving epidural analgesia in childbirth (Holdcroft et al 1995). Neurological deficit may arise from either accidental damage to nerve roots during injection or chronic inflammatory reactions to impurities injected. There have been rare cases of incomplete recovery from the blockade of sensory, motor and sympathetic neurones. Septic and aseptic meningitis and reversible bilateral hearing loss have been reported (Karch 1992, McKenry and Salerno 1998, Reynolds et al 1996).

**Case Report**

This case illustrates the rare complication of septic meningitis.
A healthy 22 year-old primigravida received epidural analgesia with fentanyl. Following uncomplicated delivery, she was discharged 24 post-partum with a healthy infant. She returned 48 hours later, vomiting and febrile, but alert and complaining of headache. She rapidly deteriorated and developed neck rigidity. Despite treatment, she died 4 weeks later.

The skin is not sterilised prior to intra-spinal analgesia. Puncture of the skin and dura may allow entry of micro-organisms into the cerebro-spinal fluid, which in very rare cases, can bring about infection (Choy 2000).

**Practice Points**

- Vomiting, headache and fever alert practitioners to possible serious complications
- New long term headache requires urgent attention (Reynolds 1993a).
- To minimise the potential for error, all intraspinal drugs must be:
  - double-checked
  - freshly prepared
  - administered slowly
  - sterile
- Some intraspinal drug regimens are complex, and involve more detailed calculations than are normally performed in hospital practice. The possibility of error should be reduced if all intraspinal infusions are:
  - prepared in the pharmacy, under sterile conditions
• standardised

• prescribed on charts reserved for spinal infusions

• accompanied by charts detailing the clinical monitoring required (Cousins 1996).

• **Monitoring must include:**

  • *Maintaining maternal non-supine position*

  • *BP, HR every 5 minutes for first 30 minutes + every 15 minutes until at least 2 hours post-partum and hourly for 16 hours if opioids are administered.*

  • *Maternal respirations*

  • *The height of sensory block*

  • *The height of motor block, until complete recovery*

  • *Continuous foetal heart monitoring*

  • *Pulse oximetry if needed*


**Use of intravenous fluids.**

During intraspinal analgesia, fluids are infused to maintain maternal blood pressure and to prevent a fall in placental blood flow, with subsequent foetal distress (Hofmeyr 1995).

The administration of intraspinal analgesia requires skilled and experienced personnel. When life threatening incidents have occurred, they have usually been associated with lapses in standards of administration and management (Brownridge 1991, DoH 1996,
Maternal death has also occurred from circulatory overload during induced labour (DoH 1996 p.26), which indicates the importance of careful monitoring.

**Practice points**

- **To ensure safety, protocols for management of complications (however rare) must be in place, and experienced personnel must be available. The necessary equipment, including facilities for resuscitation, and ‘rescue drugs’, such as ephedrine, must be in place and checked daily (Brownridge 1991, Drugs and Therapy perspectives 1996).**

- **In view of the risk of complications, all women receiving intraspinal analgesia must have intravenous access established.**

**Conclusion: Intraspinal Analgesia**


Although epidural anaesthesia with local anaesthetics is the most effective available method for relieving the pain of labour (Armand et al 1993), the benefits of epidural
anaesthesia are tempered not only by side effects, but also by increases in: the duration of
labour; the need for oxytocin augmentation; the incidence of malrotation; the incidence
of instrumental deliveries and Caesarean sections. The problems associated with
instrumental deliveries, such as vaginal lacerations, should be considered when
(1993) suggest that epidural anaesthesia may be responsible for the current ‘epidemic’ of
instrumental deliveries and Caesarean sections in primagravidae. The rising rates of
Caesarean section may be attributed to many factors, including fear of the complications
of instrumental delivery (Drife 1996).

Interpretation of the studies in this area can be confusing, because: variables such as
posture and fluid management are not always mentioned; individual differences exist
between patients; some studies do not compare equivalent groups of parturients; dytocia
may cause painful and protracted labour, and may therefore be the cause, not the effect,
of epidural administration (Hess et al 2000). Possibly, the women with the highest risks
of prolonged labour and complications will require the most invasive analgesic regimens,
which complicates any assessment of the risks of side effects (Traynor et al 2000).
Considering the widespread use of intraspinal analgesia during labour, and the potential
for adverse reactions, the absence of large randomised controlled trials is surprising and
should be rectified.

**Conclusion: Pain Relief in Labour**

All pharmacological methods of pain relief have side effects which may adversely affect
the mother, the foetus, the neonate or the progress of labour. The midwife should discuss
with the woman all the options available, while taking into account her medical and obstetric history (Findley and Chamberlain 1999). The information given should include the relevant side effects. Non-disclosure of serious risks is not acceptable to women (Pattee et al 1997).

There may be advantages in selecting analgesia which permits ambulation and mobility during labour, as this, by itself, may shorten labour and reduce the need for analgesia (de Jong et al 1997, Al-Mufti et al 1997, Larimore & Cline 2000). Mobility is obviously hindered by sedation or motor blockade of the legs. Psychologists suggest that perception of ‘loss of control’ in labour may be linked to poor adjustment post-partum (Czarnocka and Slade 2000).

Dissatisfaction with childbirth may be linked to the experience of pain (Waldenstrom 1999). However, it is not always necessary to achieve complete analgesia during normal childbirth. Many women will be satisfied if the pain is made ‘tolerable’. While this reduces the amount of drug administered, the greater risk of analgesic failure requires closer supervision and more frequent dosage adjustments.

The current regional variations in pharmacotherapy indicate the need for practice guidelines (Williams et al 1998). In the majority of cases, the midwife will be administering these drugs on her own responsibility, either as initial or subsequent doses. It is essential that the midwife makes a careful assessment of the woman, the condition of the foetus and the parameters of the labour, to ascertain whether it is clinically
appropriate to administer any drug before doing so. Knowledge of the potential side effects of the drug administered will empower the midwife to monitor for adverse reactions and to take timely remedial action.

**Further reading**

