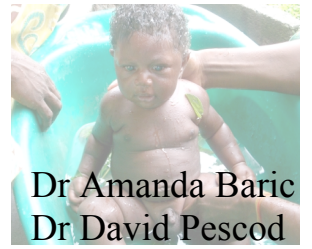


Obstetric Anaesthesia



July 2006

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www.developinganaesthesia.org

Welcome to www.developinganaesthesia.org. This web site has been created to promote the advancement of anaesthetic practice and to empower anaesthetists in countries with limited resources. The site also hopes to foster the growth of an online community of anaesthetists throughout the world.

A web-based resource has significant advantages. The information provided can remain current and be tailored to the requirements of the community. Hard copy texts may be expensive, difficult to access and inappropriate to the delivering of anaesthesia outside of tertiary institutions. The majority of journals have similar limitations.

DevelopingAnaesthesia.org is a free, up to date resource, specifically designed to address these problems.

The authors envisage the web site will have five principle functions, though the dynamic nature of web publishing will allow the evolution of the site as directed by the anaesthesia community.

- **1. Continuing education**
DevelopingAnaesthesia.org will provide an anaesthetic educational resource for anaesthetists. The site contains a textbook, articles, case studies and links. with time the site will contain power point and video presentations.
- **2. Anaesthetic training**
DevelopingAnaesthesia.org will provide an anaesthetic educational resource for anaesthetic trainees. The site will contain lecture notes for physiology, pharmacology, equipment, monitoring and statistics.
- **3. Teach the teacher**
DevelopingAnaesthesia.org will provide a resource to aid anaesthetists in educational methods.
- **4. Peer-reviewed publication**
DevelopingAnaesthesia.org will provide a venue for peer-reviewed publication online at no cost to authors or readers. All submitted material (case studies, articles, audits etc) is welcomed and encouraged.
- **5. Discussion forums**
DevelopingAnaesthesia.org has an open forum for discussion, exchange of ideas/experience and seeking advice. A panel of anaesthetists with experience in delivering anaesthesia and teaching in developing countries will moderate the forum but colleges in similar countries may provide the most relevant advice.

Success and the growth of www.developinganaesthesia.org will depend on feedback from the anaesthetic community it serves. Please have a look at the site and register as a user, there is no cost. Registration allows you to participate in forum discussions, submit your own articles and comments and in doing so help foster community growth.

VENOUS GAS EMBOLISM

Venous gas embolism may occur as a consequence of aviation, scuba diving, trauma and surgery. Fortunately venous gas embolism is rare during laparoscopy (estimated 0.0014-0.6%). Unfortunately the associated mortality is high (estimated 28%).

Numerous medical procedures can result in venous gas embolism including air through a central venous line, air through a peripheral line (especially via a pressurized infusion device), insufflating carbon dioxide into veins, pulmonary barotrauma secondary to ventilation, air into veins during craniotomy, laser surgery to the trachea, air via a dialysis circuit or cardiopulmonary bypass circuit and air into myometrial veins during pregnancy or delivery. Venous gas embolism may occur if the operative site is 5 cm or higher above the right atrium or gas is forced under pressure.

The clinical outcome of venous gas embolism depends on the volume, rate of entry and type of gas.

Small bubbles may pass through the right heart into the pulmonary vasculature causing obstruction, a rise in pulmonary arterial pressure and right heart strain. The increase resistance to right ventricular outflow causes diminished pulmonary venous return and therefore diminished left ventricular venous return, resulting in diminished cardiac output which may be sufficient to cause cardiovascular collapse.

Alterations to pulmonary flow will cause significant ventilation/perfusion mismatch leading to hypoxia and hypercarbia. Tachyarrhythmias often develop.

Insufflation of carbon dioxide to create a pneumoperitoneum is likely to cause large bubbles that will coalesce in the vena cava and right heart. The bubbles compress with contractions and cannot be expelled. This “air lock” can cause severe decrease in venous return, cardiac output and cardiovascular collapse.

If right atrial pressure exceeds that in the left atrium gas may pass from right to left atrium via a patent foramen ovale causing a paradoxical arterial gas embolism. (A probe patent foramen ovale is detectable in 30% of the population at post mortem). It is also possible that if the pulmonary circulation is overwhelmed by intravascular gas it may fail to filter out all the gas and some bubbles may pass into the pulmonary veins and on to the arterial system. Animal studies suggest that a bolus of 20 ml of gas injected into the venous system can cause arterial emboli in the absence of cardiac defects. Tommasino et al [1], report cases of cerebral arterial air embolism after venous air embolism in the absence of intracardiac defects.

The lethal volume of venous air has been estimated from studies in dogs as 375 ml. The lethal dose for carbon dioxide has been estimated as 1,750 ml. The difference is because of the high solubility of carbon dioxide, the buffering capacity of blood for carbon dioxide and the rapid excretion of carbon dioxide through the lungs.

In the conscious patient, venous gas emboli may cause chest pain, coughing, dyspnoea and ultimately cardiovascular collapse.

The most sensitive method of detecting venous gas embolism is using transoesophageal echocardiography (TOE) and can detect as little as 0.02 ml/kg of air administered as a bolus. It is however expensive, invasive and requires education to interpret but also allows detection of paradoxical embolism. Doppler ultrasonography may detect as little as 0.5 ml/kg venous gas embolism.

The pulmonary artery catheter is the next most sensitive monitor.

End tidal CO₂ monitoring can provide early diagnosis of gas embolism and give an indication of the size. Theoretically end tidal CO₂ monitoring may show a biphasic response with a transient increase in end tidal CO₂ secondary to increased excretion before the decrease due to decreased exchange at the pulmonary capillary bed and/or decreased cardiac output. (Only venous gas emboli rates of less than 0.3 ml/kg/min in dogs demonstrate an increase in end tidal CO₂). End tidal CO₂ monitoring may detect as little as 1.5 ml/kg.

2 ml/kg of venous air embolism will cause tachycardia, hypotension, raised central venous pressure, a millwheel murmur and ECG changes of right ventricular strain [2].

A precordial stethoscope is an insensitive way to detect venous gas embolism (1.5-4.0 ml/kg).

The anaesthetist must be aware of surgery that has an increased risk of venous gas embolism and prepare monitoring and be especially vigilant during the creation of a pneumoperitoneum. Insufflation rates must be limited to 1 litre/minute. Even at this rate, a lethal dose of carbon dioxide can be administered in less than 2 minutes. Poor preparation and/or distraction during this critical time may be fatal.

If a venous gas embolism is suspected the anaesthetist must immediately prevent further entry of gas, deflate the pneumoperitoneum, hyperventilate with 100% oxygen (discontinue nitrous oxide) and be prepared to support the circulation with inotrope drugs and cardiopulmonary resuscitation.

There are recommendations to place the patient in Durant's position (left lateral decubitus with head down position) in an attempt to raise the gas to the apex of the right ventricle away from the right ventricle outflow as well as inserting a central venous catheter to aspirate the entrained air however this may be of limited benefit and time will be better spent with aggressive resuscitation.

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CAESAREAN SECTION: SPINAL ANAESTHESIA & HYPOTENSION

Hypotension is the most common adverse event when spinal anaesthesia is used for caesarean section. The onset is usually rapid. Principle causes include a decrease in venous return, vasodilatation, decrease in cardiac output and blood loss. The quoted incidence varies depending on the definition and technique but has been estimated to be as high as 80%. Most studies define hypotension as a mean systolic pressure of 70-80% of baseline or an absolute systolic pressure of less than 90-100 mmHg. Hypotension has adverse effects on the mother (nausea, vomiting, dizziness, unconsciousness, aspiration) and the foetus (contributes to foetal acidosis [1] and hypoxia).

Uterine blood flow (UBF) is determined by maternal mean arterial pressure (MAP) minus uterine venous pressure (UVP) divided by uterine vascular resistance (UVR).
$$UBF = (MAP - UVP) / UVR$$

Uterine venous pressure is fairly constant at around 10 mmHg. Uterine vascular resistance is variable and is affected by the tension in the myometrium and by vasoconstriction of the uterine, ovarian, arcuate and radial arteries. The mature placenta is a passive, low pressure, high conductance organ with a limited ability to vasoconstrict, and without autoregulation. Hence, the maintenance of an adequate uteroplacental perfusion pressure is highly dependent on maintaining an adequate maternal blood pressure.

Traditional anaesthetic teaching based on animal experiments, promoted non-pharmacological methods of preventing and treating hypotension and discouraged the use of alpha-adrenergic agonists. Classically a combination of crystalloid preload and left uterine displacement has been advocated but more recent studies challenge these recommendations.

Various techniques (pharmacological and non-pharmacological) have been employed including leg elevation, graduated compression stockings, colloids and vasopressors with varying success. Historically alpha-adrenergic agonists were thought to cause significant increase in uterine vascular resistance and ephedrine was the preferred agent to maintain maternal mean arterial pressure because of its beta-adrenergic effects. In 1974, Ralston and Shinder administered ephedrine, metaraminol and methoxamine to sheep, without regional anaesthesia, until the blood pressure was increased by 50% over baseline. The uterine blood flow was unchanged with the ephedrine group but decreased by 45% and 62% with the alpha agonists.

Recent studies have showed that the use of potent vasopressors is associated with less neonatal acidosis and better control of maternal blood pressure compared with ephedrine [2] [3]. Though numerous studies have consistently reported improved foetal acid-base status with alpha agonist treated groups, the difference between ephedrine and alpha agonist groups have not been clinically significant.

Most non-pharmacological methods remain beneficial. The optimal use of alpha-adrenergic agonists (choice of drug, prophylactic or treatment, infusion or bolus) needs further evaluation.

Uterine displacement and intravenous fluid preloading.

Avoidance of aortocaval compression is an essential element of obstetric anaesthesia.

The use of intravenous preloading is less clear. Volume preloading is recommended to prevent maternal hypotension and a reduction in uteroplacental blood flow, although positive effects of volume preloading on maternal cardiac output and arterial pressure are debatable. All patients undergoing any anaesthesia must have intravenous access. All patients should be in optimal physiological condition and it is sensible to correct dehydration caused by fasting prior to caesarean section however the efficacy of aggressive fluid loading has been questioned. Usually 1-2 litres of intravenous fluid is administered 15-20 minutes before the spinal block with the aim of filling capacitance vessels and limiting hypotension when venodilatation occurs. However volume preloading is not without risk, particularly volume overload and pulmonary oedema. The mother at full term has reduced plasma oncotic pressure, an increased plasma volume and volume loading will be augmented by uterine contraction and block regression.

Even large volumes of crystalloid have minimal effect on the incidence of hypotension [7] [8] perhaps due to rapid redistribution, although there may be a reduction in the severity of hypotension and the vasopressor requirements. Husaini SW et al compared 1 litre of Ringer's solution preload, administered over 10 minutes, before spinal anaesthesia against no preload. Both groups received a prophylactic infusion of ephedrine. There was no statistical difference in ephedrine requirements or the incidence of hypotension between the two groups. There was also no difference in APGAR score, umbilical arterial and venous pH and Neonatal Adaptive Capacity Scores. Ngan Kee et al similarly concluded that when a metaraminol infusion (starting rate 0.25 mg/min) is used to maintain arterial pressure during spinal anaesthesia for caesarean delivery, crystalloid bolus (20 ml/kg) is not essential provided sufficient vasopressor is given in the immediate post-spinal period [16].

Debate continues over the value of preloading volume, including the rate [4] and amount [5]. Dyer et al investigated the timing of preloading and suggest that rapid crystalloid administration (20 ml/kg) after (coload), rather than 20 minutes before (preload) spinal anaesthesia may be advantageous in terms of managing blood pressure prior to delivery (significantly more patients in the coload group did not require vasopressors pre-delivery). However there was no difference in neonatal outcomes, total number of ephedrine doses or total ephedrine dose [9]. Colloids may be more effective than crystalloids [10] and control [11]. Colloid preload improved haemodynamic stability compared to no preload but did not affect neonatal outcome when arterial pressure was maintained by a metaraminol infusion. Colloids are less available, more expensive, more prone to cause fluid overload and may cause allergic reactions.

Anaesthetic technique.

Reducing the dose of local anaesthesia will reduce the severity and incidence of hypotension but at the risk of increasing the incidence of failed spinal. Hypotension can be anticipated and effectively treated. Failed spinal anaesthesia is not acceptable.

The anaesthetist must determine the local anaesthetic recipe that guarantees success with the lowest incidence of hypotension for their patient population. The addition of 15-20 micrograms of fentanyl allows the dose of 0.5% bupivacaine (hyperbaric or plain) to be reliably reduced to 2.0-2.5 ml.

A combined spinal epidural is an elegant technique that allows a lower spinal dose to be topped up with the epidural if required. However, it requires more equipment and greater skill.

Vasopressors.

Vasopressors may be given before hypotension occurs (prophylactic) or to treat hypotension (reactive). They may be given as a bolus or as an infusion. Vasopressors are more effective than crystalloid preloading.

Ephedrine.

Traditionally ephedrine has been recommended and alpha-adrenergic agonists avoided however this advice is based on animal studies. Although ephedrine is commonly used as the agent of choice due to its presumed favourable effects on maternal circulation and uterine arteries, its overall efficacy is poor. A quantitative systematic review concluded that prophylactic ephedrine is more effective than control for preventing hypotension during spinal anaesthesia for elective caesarean delivery but a clinically relevant positive effect on neonatal outcome was not observed [14].

Studies have shown that increasing prophylactic doses of ephedrine (up to 30 mg IV) will reduce hypotension but will also increase the incidence of reactive hypertension and decrease umbilical pH. The reason for the foetal acidosis is uncertain but may be related to placental transfer of ephedrine and the effect of beta stimulation on the foetus. A dose response meta-analysis of prophylactic intravenous ephedrine, by Lee et al [12], demonstrated a significant direct dose response relationship for ephedrine and preventing hypotension. Increasing the dose of ephedrine will reduce the risk of hypotension however they also demonstrated the risk of reactive maternal hypertension was also directly related to the dose as was the risk of umbilical acidosis. The authors concluded that 12 mg was the largest dose of prophylactic ephedrine for preventing hypotension where a small benefit outweighed the risk of reactive hypertension. At this dose the number needed to treat (NNT) was 8.8 and the number needed to harm (NNH) was 9.4. At doses less than 12 mg there was only a small decrease in the risk of hypotension and with 30 mg the rate of harm to benefit was 2:1. The authors concluded that prophylactic ephedrine could not be recommended. Maternal hypertension and tachycardia and unfavourable reductions in uteroplacental perfusion and neonatal acid-base status have been described with a prophylactic bolus dose greater than 15 mg [13].

The number needed to treat is a measure to assess the consequences of treatment. It is derived in this case from the difference in incidence of maternal hypotension between the control group and the treated group. This difference is known as the absolute risk reduction (ARR). The reciprocal of the ARR (1/ARR) is the NNT and expresses the number of patients who need to be treated to prevent the complication occurring once. Infusions of ephedrine may provide better blood pressure control than a bolus, however they also tend to use a greater total dose and therefore may cause more foetal acidosis.

Alpha-adrenergic agonists.

Both metaraminol [3] [15] [16] and phenylephrine [17] [18] have been studied. There is evidence that the alpha-adrenergic agonists metaraminol and phenylephrine are safe and are associated with better foetal acid base status. If infusions of phenylephrine or metaraminol are used, umbilical cord blood gases are significantly better compared with ephedrine but decreases in maternal heart rate are more common. The bradycardia is usually a baroreceptor-mediated event and resolves on stopping the infusion. Occasionally atropine may be required.

A study suggested that prophylactic metaraminol (1mg IV given 2 minutes after intrathecal injection of local anaesthetic) delayed the onset of maternal hypotension, lessened ephedrine requirements and was associated with better umbilical vein acid-base status.

As with ephedrine, infusions appear to be superior to intermittent boluses. A prophylactic infusion of phenylephrine 100 micrograms/minute commenced immediately after spinal anaesthesia decreased the incidence, frequency and magnitude of hypotension with equivalent neonatal outcome compared with a control group receiving IV bolus phenylephrine [17].

A recent study suggests that the optimal rate of phenylephrine infusion may be to aim for normal baseline maternal systolic arterial pressure (SAP). (Phenylephrine 100 micrograms/min for 2 minutes then continue infusion at 100 micrograms/min each minute if the blood pressure was equal to or less than baseline SAP).

By using a combination of crystalloid coload and phenylephrine infusion 100 micrograms/minute titrated against blood pressure, Kee WD et al had only 1 of 53 patients with hypotension. Rapid crystalloid infusion was given by fully opening the clamp of the infusion administration set at the start of intrathecal injection and continuing the infusion to a maximum of 2 litres until uterine incision. Patients received 2 ml hyperbaric 0.5% bupivacaine with 15 micrograms of fentanyl [19]. The authors concluded that this was the first technique to be described that is effective for preventing hypotension during spinal anaesthesia for caesarean delivery. High dose phenylephrine infusions require strict blood pressure monitoring. Despite patients in this trial having one minutely non-invasive blood pressure monitoring, 47% in each group had one or more transient episodes of reactive hypertension often associated with bradycardia.

Other trials have evaluated mixed phenylephrine and ephedrine infusions. By using a combination of the two vasopressors it was hoped that the total amount of each could be reduced and therefore side effects lessened.

Conclusion.

A significant number of patients who have spinal anaesthesia for caesarean section will experience hypotension, which may have adverse effects for mother and newborn. Prophylactic measures are useful. Avoiding aortocaval compression and correcting dehydration will assist in reducing the incidence and severity however the anaesthetist should not be reluctant to use an adrenergic agonist. Moderate co-loading seems appropriate. Ephedrine is associated with foetal acidosis, maternal tachycardia and reactive hypertension with increasing doses. Alpha agonists may decrease maternal heart rate. Prophylactic bolus ephedrine is not supported by current data. Prophylactic infusions of ephedrine, phenylephrine, metaraminol and mixtures of phenylephrine and ephedrine have been described. Infusions may be more efficient techniques, however requires expensive equipment and vigilance. Intermittent boluses provide identical neonatal outcome despite more frequent episodes of hypotension.

Many techniques have been investigated and all are better than control groups at reducing the frequency and severity of hypotension however, possibly with the exception of co-loading plus phenylephrine infusions, none will eliminate hypotension.

Importantly all studies demonstrated excellent neonatal outcome despite episodes of hypotension, if those episodes were effectively treated. Hypotensive parturients who do not respond to conservative measures such as correction of the volume status and lateral uterine displacement will require vasopressors to maintain adequate uteroplacental blood flow. As long as the hypotensive episode is only transient, small incremental bolus injections of ephedrine or an alpha agonist is adequate for treatment of maternal hypotension and both agents can effectively be used without worsening foetal well-being.

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? CORRECT DOSE FOR SPINAL CAESAREAN SECTION

Spinal anaesthesia provides a rapid reliable anaesthetic technique for caesarean section that may provide greater safety than general anaesthesia with less cost.

Any anaesthetic technique must produce adequate surgical anaesthesia of adequate duration and minimal maternal and neonatal side effects.

The principle side effects of spinal anaesthesia for caesarean section are a reduction in maternal and uteroplacental blood flow/pressure, maternal pain (up to 10.9%) [1] and conversion to general anaesthesia (1.7 to 2.9%) [2]. Reducing the dose of intrathecal local anaesthetic will improve cardiovascular stability but may not provide adequate surgical anaesthesia.

The addition of various opioids may allow a reduction of the local anaesthetic dose.

Newer local anaesthetics (ropivacaine and levobupivacaine) have reduced cardiotoxicity and more specific sensory effects than motor but these advantages may not be clinically significant with single shot spinal anaesthesia.

The anaesthetist needs to decide what local anaesthetic to use, what dose and what additive to use.

Choice of local anaesthetic:

Some preparations of local anaesthetics contain additives such as preservatives and are not suitable for intrathecal administration.

The duration of action of lignocaine may be too short to guarantee adequate surgical time and lignocaine has a higher incidence of transient radicular irritation [3].

Kyokong and others suggested that 2.2 ml of 0.5 per cent hyperbaric bupivacaine plus 0.2 mg of morphine can be used interchangeably with 1.2ml of 5 per cent hyperbaric lignocaine plus 0.1 mg of adrenaline and 0.2 mg of morphine for elective spinal caesarean section without significant differences in the incidence of hypotension [4].

Tetracaine has a slower onset and may have excessive duration of action.

There are numerous studies comparing bupivacaine, ropivacaine and levobupivacaine. A recent study [5] investigated if intrathecal sufentanil 2.5 microgram plus ropivacaine 12 mg or levobupivacaine 8 mg provided anaesthesia and postoperative analgesia of similar quality to sufentanil 2.5 microgram plus bupivacaine 8 mg for caesarean section. Bupivacaine combined with sufentanil provided a significantly superior success rate than an equal dose of levobupivacaine (97 vs. 80%). Other studies confirm that a larger dose of ropivacaine is required to be equally effective as bupivacaine (hyperbaric 0.5% ropivacaine 18 mg vs. hyperbaric 0.5% bupivacaine 12 mg [6] and ropivacaine 0.5% 20 mg plus 0.1 mg morphine vs. bupivacaine 0.5% 15 mg plus 0.1 mg morphine [7]).

Subsequently, hyperbaric levobupivacaine for Caesarean section has been found to be 38% less potent than hyperbaric bupivacaine [8].

Bupivacaine also provides faster onset and a longer duration of analgesia and motor block than both ropivacaine and levobupivacaine. 18 mg of 0.5% hyperbaric ropivacaine produces sensory block of 165 +/- 20.2 minutes and motor block of 113.7 +/- 18.6 minutes compared to 188 +/- 28.2 minutes and 158 +/- 31.2 minutes respectively for 12 mg of 0.5% hyperbaric bupivacaine [6]. The shorter duration of motor block is considered by some authors to be an advantage.

Dose of local anaesthetic agent:

There are many recommended combinations of local anaesthetic/opioid for caesarean section spinal anaesthesia. Unless the anaesthetist uses an exceptionally large dose of local anaesthetic, total spinal is a rare complication (1:10,000).

Importantly in many studies, though recording sensory block to T6, patients still have a significant incidence of visceral pain when using lower doses, especially when opioids are not added.

Reducing the dose of local anaesthetic will reduce the incidence of decreased maternal and uteroplacental blood flow/pressure but this will be at the risk of maternal pain and conversion to GA. Reduced maternal and uteroplacental blood flow/pressure can be predicted, monitored and treated.

Bupivacaine:

Common hyperbaric bupivacaine doses range between 7.5 mg and 15 mg (1.5 ml to 3 ml of 0.5%) however 71% of mothers who received less than 10mg of hyperbaric bupivacaine alone complained of inadequate analgesia [9]. In a study comparing 12 mg of hyperbaric bupivacaine and 18 mg of hyperbaric ropivacaine, none of the mothers receiving 12 mg of hyperbaric bupivacaine required supplemental analgesia [6]. Another study which aimed to reduce the dose of intrathecal bupivacaine by the addition of fentanyl found that bupivacaine alone at doses less than 12.5 mg could not abolish visceral pain [10].

The ED95 providing effective spinal block of women undergoing elective caesarean section has been calculated at 0.06 mg hyperbaric bupivacaine/cm height [16].

The addition of an opioid will allow the safe reduction of the local anaesthetic dose with equal success and less severe side effects. Ultra low doses such as 5 mg of bupivacaine with 25 micrograms of fentanyl have been reported to be adequate [11] but the maintenance of cardiovascular stability is straightforward and surgical anaesthesia should not be compromised due to unrealistic concerns about cardiovascular instability.

If the anaesthetist wishes to achieve maximal cardiovascular stability a combined spinal-epidural (CSE) anaesthesia technique is often employed, since this allows for epidural supplementation should analgesia for low dose spinal be inadequate.

Two studies [7], [12] have used 15 mg of bupivacaine plus 0.15 mg of morphine with no reports of pain though one study [7] reported 33% incidence of hypotension requiring treatment with ephedrine to prevent the mean arterial pressure falling below 20% of baseline. This may be an unacceptable incidence of hypotension given that other studies using lower doses have not required supplemental analgesia.

Carvalho [13] calculated that the ED95 for bupivacaine with 10 micrograms of fentanyl and 0.2 mg of morphine to be 13.0 mg. A study with 12.5 mg of heavy bupivacaine and 15 micrograms of fentanyl similarly had no incidence of maternal discomfort however in the comparison without fentanyl 7/20 had discomfort [17].

11 mg of hyperbaric bupivacaine plus 20 micrograms of fentanyl produced the same sensory block as 6.5 mg but 10% of patients in the 6.5 mg dose group required conversion to general anaesthesia [15].

An important clinical investigation [18] advising against the use of doses of intrathecal hyperbaric bupivacaine less than the ED95, unless as part of a CSE technique found the

dose-response relationship for intrathecal hyperbaric bupivacaine co-administered with intrathecal fentanyl and morphine to have an ED50 of 7.6 mg and an ED95 of 11.2 mg for bupivacaine. Similarly 11mg of hyperbaric bupivacaine plus 0.2mg of morphine required no conversions to general anaesthesia or supplemental analgesia [4].

Bogra [10] reported no visceral pain with 8 mg of hyperbaric bupivacaine and 12.5 micrograms of fentanyl.

The author commonly uses hyperbaric bupivacaine 11 mg plus 15 micrograms of fentanyl.

Ropivacaine:

A dose finding study [14] for spinal ropivacaine for caesarean section found the ED90 to be 26.8 mg. In a study comparing 25 mg of ropivacaine and 25 mg hyperbaric ropivacaine none of the hyperbaric group needed extra analgesia compared to 5 in the other group [19].

20 mg of ropivacaine plus 0.1 mg of morphine produced satisfactory analgesia but 33% had significant hypotension [7]. Reducing the dose to 18 mg of hyperbaric ropivacaine but without opioid resulted in 10% requiring supplemental analgesia [6].

The addition of 0.15 mg of morphine [12] or 10 micrograms of fentanyl to 15 mg of hyperbaric ropivacaine produced good surgical anaesthesia in all cases. 15 mg of hyperbaric ropivacaine plus opioid would seem a reasonable intrathecal dose for caesarean section.

Choice of opioid:

The choice of intrathecal opioid depends on availability, side effects, and effectiveness at reducing local anaesthetic requirement and duration of action post operatively. The common side effects of intrathecal local opioids are dose dependent [20] and include nausea and vomiting, pruritus, sedation and urinary retention. Mothers may find some of these side effects less desirable and more difficult to treat than post operative pain that can be successfully managed with multi-modal analgesics. The life threatening side effects are early and late respiratory depression, especially in situations where respiratory and/or clinical monitoring resources are limited.

Intrathecal morphine (maximum dose up to 0.1 mg) can prolong the median time to the first request for postoperative analgesia to 27 hours however with a dose of 0.1 mg 43% of mothers complain of pruritus, 10% of nausea and 12% of vomiting [20]. Increasing the dose of morphine does not have an increased analgesic effect [21] though the incidence of side-effects do increase. Delayed respiratory depression is a rare but life threatening possibility.

Fentanyl (suggested dose of 20 micrograms) can prolong the median time to first analgesic dose to 4 hours. Increasing the dose of fentanyl may increase the effective time but also increase the incidence of pruritus.

Sufentanil (2.5 micrograms to 5 micrograms) has a shorter duration of action. Both show dose dependent side effects but are significantly less than intrathecal morphine.

Pethidine (1 mg/kg) can be used as the sole agent for spinal anaesthesia caesarean section but the effective surgical time is short (approximately 1 hour) and hypotension is very common (32 to 50%) [22]. Of 28 parturients who received 1 mg/kg subarachnoid pethidine [24]; two cases required general anaesthesia before incision and the duration of sensory anaesthesia was too short in four cases. 36% had a decrease in arterial blood pressure > 30 mmHg. No respiratory depression was documented in mothers and newborns. In contrast a study using 1 mg/kg spinal pethidine was successful in 50 full-term pregnant women [25] and another study using 50 mg pethidine mixed with 10% dextrose 0.5 ml successful in 182 cases [26]. The mean duration of postoperative analgesia was six hours.

0.2 mg of spinal pethidine is effective in reducing the incidence and intensity of shivering associated with spinal anaesthesia after caesarean section [23].

If intrathecal opioids are available they should be combined with the local anaesthetic to reduce the severity of side effects by reducing the dose of local anaesthetic. In choosing an opioid and dosage the anaesthetist must be aware that side effects are dose dependent and though rare, early and delayed respiratory depression is life threatening. Morphine provides prolonged postoperative analgesia but other multi-modal oral/per rectum techniques are probably equally effective and inherently safer. Intrathecal fentanyl (10 micrograms to 25 micrograms) may provide the best combination of minimal side effects, effective reduction in bupivacaine dose and duration of action.

The dose of intrathecal local anaesthetic should not be reduced to ensure cardiovascular stability at the risk of inadequate surgical anaesthesia. Cardiovascular stability can be easily maintained with careful monitoring, correct positioning, and adequate rehydration with preferably colloids and early intervention with alpha agonists.

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SPINAL ANAESTHESIA FOR CAESAREAN SECTION FOLLOWING INADEQUATE LABOUR EPIDURAL ANALGESIA.

Epidural analgesia provides safe, effective pain management during labour and may be used should operative delivery be required. On occasions a labour epidural may prove inadequate for surgery. The indications to persist with a regional technique are compelling, however the management of intrathecal anaesthesia for emergency caesarean section in the presence of an epidural block that is inadequate remains a clinical challenge. Case reports of high blocks [1], [2], [3], [4], [5], [6] & [7] necessitating the rapid conversion to general anaesthesia which has the potential for significant morbidity and mortality have been published as well as retrospective cohort analyses. The largest of these studies, by Frust et al., compared the incidence of unexpectedly high blocks from spinal anaesthesia (0.02%, 1/643) with that in the smaller group in whom spinal anaesthesia was administered after epidural failure (11%, 3/27).

Some anaesthetists [6], [4] have suggested that spinal anaesthesia is contraindicated upon ongoing epidural analgesia or following a failed epidural. Other authors recommend reducing the dose of spinal local anaesthetic by an arbitrary 20-30% however there are also studies that have demonstrated no high blocks (0/61) with normal intrathecal doses, provided that high standards of vigilance and careful positioning are observed [8] and there is an implicit risk of inadequate operative analgesia if intrathecal doses are unnecessarily reduced. Dadarkar et [9] al., who managed 115 inadequate epidurals with a reduced spinal dose of local anaesthetic, median 9.38 mg (7.5-11.3 mg) of 0.75% hyperbaric bupivacaine and fentanyl 15 micrograms had three patients who required intravenous supplementation of analgesia. Dadarkar et al., successfully provided spinal anaesthesia following inadequate epidural anaesthesia by avoiding epidural boluses in the 30 minutes preceding spinal injection, reducing the spinal dose (7.5-11.3 mg of 0.75% hyperbaric bupivacaine) and delaying supine positioning following spinal injection. Following subarachnoid injection the patient was left sitting for at least 2 minutes to limit cephalad spread. Stoneham et al., also stressed the importance of positioning [11].

Most case reports of high spinal anaesthesia after inadequate epidural analgesia have occurred with epidurals that have been had a bolus (15 to 60 minutes time from last epidural bolus to spinal) however Gupta [6] describes 3 cases of high spinal following the administration of spinal anaesthesia upon an ongoing epidural infusion. Spinal hyperbaric bupivacaine doses ranged from 8 [1]- 15 mg. The time to first signs of a high spinal ranged from 30 seconds to 10 minutes but commonly occurred between 2 and 5 minutes.

There are several of potential mechanisms for unexpectedly high blocks. There may be leakage of epidural anaesthetic through the dural hole made by the spinal or sub-clinical anaesthesia at higher dermatomal levels being revealed by spinal anaesthesia. Alternatively the volume of the dural sac may be compressed by the presence of adjacent epidural fluid, causing the spinal anaesthetic to spread higher than normal. Takiguchi et al., [10] demonstrated that injection 10 ml of saline through an epidural catheter at the L2-3 or L 3-4 interspace 10 minutes after spinal anaesthesia in surgical patients produced

levels of analgesia significantly higher than in the control group. Takiguchi et al. also showed myelographically in two volunteers that a 10 ml epidural injection of normal saline resulted in the upper level of intrathecal contrast medium rising from L3 to L1 and from L2 to T12. They also showed the diameter of the subarachnoid space diminished 25%.

Available data, although limited and contradictory, suggests the possibility of unpredictably high or total spinal anaesthesia.

Maternal morbidity and mortality is greater with general anaesthesia than regional for caesarean section. Usually it is important to continue to use a pre-existing epidural or replace it with another regional technique if operative delivery is required.

If a labour epidural is providing good analgesia it should be used (+/- bolus) for operative delivery. Attempting to establish surgical anaesthesia with a dysfunctional epidural may require large epidural volumes and still provide incomplete anaesthesia. These epidurals are best managed by replacement epidural or spinal anaesthesia.

The anaesthetist must be aware that high or total spinal may be a possible outcome regardless of the epidural and spinal technique/timing however avoiding larger spinal doses, frequent testing of block height and careful positioning will lessen the risk. Combined spinal epidural anaesthesia would appear to be a sensible alternative allowing the anaesthetist to use a smaller intrathecal dose while still having the flexibility of augmenting the block epidurally if required.

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SEPSIS

Sepsis is a leading cause of death of patients in ICU. Maternal infection in labour is associated with increased perinatal morbidity. Physiological changes of pregnancy may predispose the parturient to certain infections. Mechanical and hormonal (progesterone) factors cause urinary tract dilation resulting in urinary stasis and potential urinary tract infections. Pregnancy-induced changes in the composition of bile may increase the incidence of cholelithiasis. The function of the immune system is depressed which may predispose to infection. Gram-negative bacteria are the most frequently isolated bacteria in septic obstetric patients. Despite infectious obstetric conditions such as chorioamnionitis (up to 10%), pyelonephritis (estimated 1%) and puerperal infections being relatively common; bacteraemia is uncommon (estimated 10%) and septic shock is rare. However, sepsis is still one of the five leading causes of pregnancy related death worldwide. The WHO estimates the maternal mortality ratio as high as 1,000 per 100,000 live births, (mainly concentrated in African countries) but less than 20 per 100,000 live births in developed countries (1).

The treating doctors must be aware of the physiological effects of pregnancy, which will significantly affect the pathophysiology of sepsis, and be aware of foetal vulnerability.

The normal cardiovascular changes of pregnancy are peripheral vasodilation, increase in heart rate and increased cardiac output. Maternal arterial blood pressure is predominantly maintained by increased cardiac contractility. Sepsis will potentiate the peripheral vasodilation and, importantly, may cause sepsis-induced myocardial dysfunction that may rapidly progress to cardiovascular collapse.

Plasma colloid-osmotic pressure is reduced in pregnancy. This may exaggerate sepsis induced increased permeability of pulmonary microvasculature and subsequent development of pulmonary oedema and decreased lung compliance.

Renal hypoperfusion in association with sepsis results in a significant incidence of acute tubular necrosis.

Despite the altered physiology of pregnancy, septic shock may have reduced mortality in pregnant patients compared to the non-obstetric population. Factors implicated include the lack of associated underlying serious medical disorders, younger patient and focused sites of underlying infection (pelvis and genitourinary tract).

There is a lack of evidence to validate the extrapolation of some sepsis treatment modalities from other non-pregnant patient populations and data from severity scoring systems (e.g. APACHE) should be cautiously interpreted.

Definitions:

Bacteraemia is the presence of viable bacteria in the blood. It may be transient and of no clinical significance, and its presence alone is not sufficient to diagnose sepsis.

Infection is a microbial phenomenon characterised by an inflammatory response to the presence of microorganisms or the invasion of normally sterile host tissue by those organisms.

SIRS is a widespread inflammatory response to a variety of severe clinical insults. It is defined by the presence of two or more of the following: temperature above 38C or below 36C; respiratory rate greater than 20/minute or PaCO₂ less than 32 mmHg; heart rate greater than 90 beats/minute; white blood cell count more than 12,000/mm³, less than 4,000/mm³, or more than 10% immature (band) forms.

Sepsis is the clinical manifestation of SIRS, which results from a documented infection.

Severe sepsis is sepsis associated with organ failure.

Septic shock is sepsis with hypotension unresponsive to adequate intravenous fluid resuscitation.

The severity of sepsis is determined by many factors including the strength of the host inflammatory response (polymorphism in immune effector molecules and receptors), virulence of the organism and coexisting clinical conditions.

Cells of the innate immune system recognise microorganisms and initiate responses through pattern recognition receptors called toll-like receptors (TLR). Invading microorganisms and their toxins interact with monocytes and tissue macrophages to generate a cascade of inflammatory responses characterised by the production of inflammatory cytokines such as TNF- α , interleukins 1 and 6 (Il-1, Il6), and stimulation of coagulation pathways. Pro-inflammatory cytokines cause the release of proteases, and disruption of the clotting cascade and fibrinolytic system. TNF- α may be the principal inflammatory mediator of the pathophysiology of sepsis. TNF causes the release of tissue factor (the first step in the extrinsic coagulation pathway) by a direct effect on endothelial cells. It also down regulates thrombomodulin endothelial expression resulting in decreased protein C activity. (Activated protein C and its cofactor protein S inhibit factor Va and V111a, thereby providing a negative feedback for the coagulation cascade).

[Cytokines are small protein molecules that regulate communication among immune system cells and between immune cells and those of other tissue types. Cytokines act by binding to their cell-specific receptor. They are said to be pleiotropic, meaning that the same cytokine can have different effects on a cell depending on the state of the cell. Cytokines also often regulate the expression of other cytokines].

Sepsis had been considered as an uncontrolled inflammatory response however the failure of numerous trials of anti-inflammatory agents (including corticosteroids, anti-endotoxin antibodies, tumour necrosis factor antagonists, and interleukin1 receptor antagonists) to improve outcome (survival) has challenged the concept of sepsis as simply a pro-

inflammatory event. The theory that death from sepsis was due to an excessive inflammatory response was based on animal studies that used large doses of endotoxins or bacteria with consequently very high levels of circulating cytokines. These animal studies do not seem to reflect the usual clinical picture in humans. Though cytokines maybe considered harmful they may also have beneficial effects.

In some animal and clinical trials (2,3,4) immunotherapy against tumour necrosis factor alpha (TNF- α) and interleukin-1 receptors have worsened survival. A meta-analysis of clinical trials of high doses of anti-inflammatory agents showed that they were generally harmful but a small subgroup (approximately 10%) benefited (6). Patients with rheumatoid arthritis who were treated with TNF antagonists had septic and infectious complications (5).

One reason for the failure of anti-inflammatory strategies in patients with sepsis may be that the syndrome changes over time. Initially an intense inflammatory response may predominate but as sepsis persists, there may be a shift towards an anti-inflammatory immunosuppressive state. Patients with sepsis develop features of immunosuppression including a predisposition to nosocomial infections and an inability to clear infections. Patients with sepsis have been successfully treated with the interferon- γ .

Potential mechanisms of immune suppression in patients with sepsis include a shift from an inflammatory to an anti-inflammatory response with T cells, T cell anergy and death of immune cells.

CD4 T cells are activated by stimulation through macrophages or dendritic cells. Activated CD4 T cells may secrete either inflammatory cytokines (type 1 helper T cell [Th1]) or cytokines with anti-inflammatory properties (type 2 helper T cell [Th2]). Macrophages and dendritic cells are activated by the ingestion of bacteria and by stimulation through Th1. Th2 suppress macrophage activation. The factors that determine whether CD4 T cells have Th1 or Th2 responses are unknown.

T cells are anergic when they fail to proliferate or secrete cytokines in response to their specific antigens. Sepsis may induce anergy.

At autopsy, patients who have died from sepsis show markedly decreased levels of B cells, CD4 T cells and follicular dendritic cells.

The individual's immunological response (hyperimmune/hypo-immune) will be determined by many factors including the virulence of the organism, the size of the inoculum, the patient's co-existing condition, age and polymorphisms in genes for cytokines. Identified gene alterations include polymorphisms in TNF receptors, interleukin 1 receptors and TLRs. The initial response is hyperimmune but will progress to hypo-inflammatory with time. The time course of change will vary between patients.

Measurement of circulating concentrations of inflammatory mediators may prove to be useful in evaluating the stage of sepsis and tailor the timing of antiinflammatory treatment. Anti-inflammatory agents may worsen outcome during the hypo-immune phase when strategies to enhance immune function may be more appropriate (7).

Clinical trials of treatments for sepsis are difficult because of the heterogeneity of patients.

Sepsis during pregnancy is uncommon yet potentially fatal. Advances in the understanding of the pathophysiology of sepsis have presented new treatment modalities. Nevertheless early detection and diagnosis; aggressive resuscitation and antibiotics/source control remain the principles of management. The most common avoidable error from autopsy studies is a failure to diagnose and appropriately treat infections with antibiotics or surgical drainage (9) (10).

Diagnostic and therapeutic guidelines should predominantly follow current recommendations for non-pregnant patients. The 2004 Surviving Sepsis Campaign guidelines for the management of severe sepsis and septic shock (8) detail the consensus of 44 critical care and infectious disease experts representing 11 international organisations. They emphasise that “*the speed and appropriateness of therapy in the initial hours after the syndrome develops are likely to influence outcome*”.

Their recommendations (Initial resuscitation, diagnosis, antibiotic therapy, source control, vasopressors, inotropic therapy, steroids, activated protein C, blood product administration, mechanical ventilation, sedation/analgesia/neuromuscular blockade, glucose control, renal replacement, bicarbonate therapy, deep vein thrombosis prophylaxis, stress ulcer prophylaxis, limitation of support and paediatric considerations) are graded:

- A. supported by at least 2 level I investigations
- B. supported by 1 level I investigation
- C. supported by level II investigations only
- D. supported by at least 1 level III investigation
- E. supported by level IV and V evidences

Grading of evidence:

- I. large randomised trials (low risk α & β error)
- II. small randomised trials (mod - high) risk α & β error
- III. non-randomised contemporaneous controls
- IV. non-randomised, historical controls and expert opinion
- V. case series, uncontrolled studies, and expert opinion

The following is a summary of the recommendations for Surviving Sepsis Campaign guidelines (8).

Initial Resuscitation: should begin as soon as the septic syndrome is recognised and should not be delayed until admission to ICU. During the first 6 hours. Resuscitation should aim for:

- Central venous pressure (CVP) 8-12 mmHg (12-15 mmHg in ventilated patients)
- Mean arterial pressure (MAP) > 65 mmHg
- Urine output > 0.5 ml/kg per hour
- Central venous or mixed venous oxygen > 70% (Grade B)

The authors note that “although the cause of tachycardia in septic patients may be multifactorial, a decrease in elevated pulse with fluid resuscitation is often a useful marker of improving intravascular filling”.

The protocol in the cited study, Rivers et al, (11) consisted of initial fluid resuscitation (CVP 8-12 mmHg), then packed red blood cells (haematocrit at least 30%) and then dobutamine (up to a maximum of 20 µg/kg/min) to achieve the targeted SvO₂ of 70% or greater. Rivers et al were able to show a significant improvement in mortality when haemodynamic optimisation was provided within the first few hours of presentation. This emphasis on early diagnosis and rapid intervention has previously been shown to improve outcomes in trauma patients and inspired the concept of the “golden hour”.

Diagnosis: At least 2 blood cultures and cultures from other sites such as urine, cerebrospinal fluid, wounds, sputum etc should be obtained before antibiotic therapy is initiated.

(Grade D)

Diagnostic studies (e.g. CXR, ultrasound, CT) should be performed as soon as possible to identify a source of infection that may be drained.

(Grade E)

Antibiotic therapy: Observational studies suggest a significant reduction in mortality when antibiotics are administered within 4 hours of hospital presentation. The Surviving Sepsis Campaign recommends antibiotics should be started within the first hour, after appropriate cultures have been obtained.

(Grade E)

The empiric choice on initial antibiotics should include one or more drug with broad enough cover to be active against all likely pathogens and which will penetrate to the likely source of sepsis. The likely pathogen depends on many factors including susceptibility patterns in the community and hospital, patient’s history and underlying disease. Patients with severe sepsis warrant initial broad-spectrum antibiotic therapy. The antibiotics should be reassessed after 48 – 72 hours and on the basis of microbiological results and clinical data. Excessive use of broad-spectrum antibiotics may enhance the development of antibiotic resistant organisms and superinfections (e.g. candida species, clostridium difficile).

Generally, once a causative organism has been identified, there is no evidence that combination therapy is more effective than a single antibiotic though some experts prefer combination therapy for patients with pseudomonas infections.

(Grade E)

Given the polymicrobial nature of many infections in obstetric patients, initial broad-spectrum therapy is acceptable. Most cases of chorioamnionitis are caused by anaerobes and genital mycoplasmas, with less than 25% caused by Escherichia coli and group B streptococci. During pregnancy, antibiotic selection should consider the safety to the

foetus, especially during the first trimester. The safety of beta-lactams and aminoglycosides is well accepted. Tetracyclines and chloramphenicol should be avoided.

Source control: Once resuscitation is complete and antibiotic therapy has been initiated, appropriate investigations (eg ultrasound, CT scan) should be performed to identify a correctable (eg drainage, excision, debridement) source of infection. Timely intervention should maximize survival. The selection of optimal source control methods must weigh the benefits and risks of the specific intervention. Intravascular access devices are a potential source of sepsis and clinicians should consider removal and replacement to be a priority.
(Grade E)

Fluid therapy: The degree of intravascular volume deficit in patients with sepsis varies and fluid therapy may best be administered by a series of fluid challenges (500-1000 ml crystalloid or 300-500 ml colloids over 30 minutes) under close monitoring and repeated based on response (CVP, urine output, pulse rate) and tolerance (pulmonary oedema). There is no evidence to support one type of fluid over another in the septic population. Finfer S, Bellomo et al (13) compared 4% albumin with normal saline in the treatment of 6997 heterogeneous critically ill patients and found no significant difference in mortality although a subgroup analysis of patients with severe sepsis suggested a trend for a mortality benefit.

Vasopressors: may be required transiently to sustain life in the face of life threatening hypotension and/or if fluid challenges fail to restore adequate blood pressure and organ perfusion.
(Grade E)

Either norepinephrine (2-20 µg/min) or dopamine(5-20 µg/min) is the first choice of vasopressor to treat hypotension due septic shock. Possible disadvantages of epinephrine include tachycardia and deleterious effects on the splanchnic circulation.
(Grade D)

Low dose dopamine should not be used for renal protection as part of the treatment of severe sepsis.
(Grade B)

Vasopressin (0.01-0.04 unit/min) may be considered in patients with shock refractory to other vasopressors. Though vasopressin levels are initially high in sepsis, levels fall to normal (a relative deficiency in the presence of hypotension) in the majority of patients between 24 to 48 hours.
(Grade E)

Inotropic support: Sepsis may be accompanied by myocardial suppression in 10-15% of patients.

Steroids: In the absence of shock, corticosteroids should not be administered for the treatment of sepsis unless the patient requires stress dose replacement due to a prior history of steroid therapy or adrenal dysfunction (Grade E).

Many septic patients have relative adrenal insufficiency; the mechanism of which is incompletely understood but probably involves an inadequate release or response to adrenocorticotropin and peripheral steroid receptor resistance.

Intravenous corticosteroids (eg hydrocortisone 200-300 mg/day in 3 or 4 divided doses for 7 days) can be recommended in patients with septic shock who, despite fluid replacement, require vasopressors therapy to maintain blood pressure.

(Grade C)

Recombinant activated protein C (rhAPC): is an anti-inflammatory agent that may be effective in the treatment of sepsis. The inflammatory response in severe sepsis is intimately associated with procoagulant activity. Inhibition of thrombin by activated protein C decreases inflammation by inhibiting platelet activation, neutrophil recruitment, and mast cell degranulation. Activated protein C also has direct anti-inflammatory properties including blocking the production of cytokines by monocytes. Currently activated protein C is only approved for patients with severe sepsis, at high risk of death and no absolute contraindication related to bleeding risk.

(Grade B)

Blood product administration: The Transfusion Requirements in Critical Care (TRICC) trial suggests that a haemoglobin of 7 – 9 g/dl is adequate for most critically ill patients.

Fresh frozen plasma should be reserved for patients with a documented deficiency of coagulation and the presence of active bleeding or prior to surgical or invasive procedures. (Grade E). Platelets should be administered when platelet counts are less than 5,000/mm³, may be considered when counts are 5,000-30,000/mm³ and there is a significant risk of bleeding. Counts at least greater than 50,000/mm³ are required for surgery. (Grade E)

The randomised controlled trial of high dose antithrombin 3 by Warren, Eid, Singer et al (12) did not demonstrate any beneficial effect on 28 day all-cause mortality in adults with severe sepsis and septic shock.

Glucose control: Van den Berghe et al conducted a large single centre trial of postoperative surgical patients. They demonstrated that maintaining the blood glucose level at 80 to 110 mg/dl (4.4 to 6.1 mmol/l) resulted in lower morbidity and mortality. However intensive insulin therapy requires frequent monitoring and may risk hypoglycaemia. Post hoc data analysis revealed that although best results were obtained when blood glucose was maintained between 80 and 100 mg/dl, even maintaining blood glucose less than 150 mg/dl (8.3 mmol/l) improved outcomes.

The mechanism by which glucose control improves outcome in sepsis is uncertain. Hyperglycaemia impairs the phagocytic function of neutrophils and insulin prevents apoptotic cell death from numerous stimuli.

(Grade D)

Bicarbonate therapy: is not recommended for treating hypoperfusion induced lactic acidaemia pH > 7.15 and has not been evaluated at lower pH.
(Grade C)

Deep vein thrombosis prophylaxis: should be administered to patients with severe sepsis (either low dose unfractionated heparin or low molecular weight heparin). Mechanical devices (eg graduated stockings, intermittent compression devices) are recommended for septic patients with contraindications to heparin.
(Grade A)

Stress ulcer prophylaxis: should be given to all patients with severe sepsis. H2 receptor inhibitors are the preferred agents.

Sepsis is an infrequent yet important cause of death in pregnancy. There has been significant advancement in our concept of sepsis beyond sepsis representing an uncontrolled inflammatory response. Within the last 5 years, advances in the treatment of severe sepsis and septic shock have provided new therapies that have demonstrated a mortality benefit. There are other potential treatments, including interleukin-12, antibodies against complement activation product C5a and strategies to block apoptosis of lymphocytes that are under investigation.

The most valuable current treatment modalities are the rapid recognition of sepsis and the aggressive early management with resuscitation, diagnosis, antibiotic therapy, source control, fluids and vasopressor therapy.

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PLACENTA PRAEVIA AND ANAESTHESIA.

The placenta normally implants in the upper uterine segment. Placenta praevia refers to a placenta that overlies or encroaches the internal os of the cervix. It is unclear why some placentas implant in the lower uterine segment rather than the fundus.

Traditionally there are four grades of placenta praevia:

- *Complete* where the placenta completely covers the internal os.
- *Partial* where the placenta partially covers the internal os.
- *Marginal* where the placenta just reaches the internal os and
- *Low lying* where the placenta extends into the lower uterine segment.

Most (approximately 90%) low lying placentae, identified early in pregnancy, will “migrate” away from the internal os and out of the lower uterine segment.

Although the obstetric management of placenta praevia is established with expectant management until foetal lung maturity is assured, followed by aggressively moving to delivery, the mode of anaesthesia for caesarean section for placenta praevia is controversial. In the past, suspected placenta praevia was managed with vaginal examination and immediate caesarean section if placenta praevia was confirmed. It was erroneously believed that the first antenatal haemorrhage would lead to maternal death. In 1954 MacAfee (1) showed that when there was no interference, this rarely occurred and that the high perinatal mortality was due to prematurity. Women with suspected placenta praevia (bleeding in the second half of pregnancy) should have ultrasound diagnosis. Steroids should be administered in women between 24 and 34 weeks gestation to promote foetal lung maturation. The cautious use of tocolytics in women with placenta praevia who are having contractions, when both mother and foetus are stable appears reasonable (3, 4). Because prematurity is the main cause of perinatal mortality and morbidity, even moderate – severe haemorrhage may be managed with aggressive resuscitation/blood transfusion rather than delivery if the foetus is immature.

Placenta praevia has an estimated incidence of 4.8 per 1000 deliveries in the United States 0.03% are fatal. (2) The risk factors for placenta praevia include a history of termination of pregnancy, uterine surgery, smoking, increasing maternal age, multiparity and previous caesarean section. The relative risk of placenta praevia after one previous caesarean section is 4.5 (95% CI 3.6-5.5) rising to 44.9 (95% CI 13.5-149.5) after 4 prior caesarean sections (8). As the rate of caesarean section increases so will the incidence of placenta praevia.

With increasing gestational age, there is an increased risk of significant bleeding. Contractions and cervical effacement and dilatation in the third trimester may cause separation of the placenta and haemorrhage. This bleeding may stimulate further uterine contractions, causing further placental separation and greater haemorrhage. Preferably delivery should be performed as an elective procedure rather than as an emergency therefore it may be reasonable to aim to deliver at 36-37 weeks of gestation, after confirmation of foetal lung maturity or at 38 weeks without confirmation (5).

When the placenta completely or partly overlies the internal os, delivery is by caesarean section. The mode of delivery is controversial when the placenta lies in close proximity to the os. Some small retrospective unblinded studies and case series suggest that if the lower edge of the placenta is more than 2 cm from the internal os (demonstrated by transvaginal or translabial ultrasound), then patients may safely have a vaginal delivery (5).

The advancements in ultrasound diagnosis, effective tocolytics and safe blood transfusions have improved delayed delivery safety however placenta praevia still has significant associated morbidity and mortality. The relative risk of antepartum haemorrhage is 9.81 (95% CI 8.92-10.79), need for hysterectomy 33.26 (95% CI 18.19-60.89), post partum haemorrhage 2.48 (95% 1.55-3.98) and blood transfusion 10.05 (95% 7.45-13.55) (7).

Traditionally anaesthetists believed that general anaesthesia was mandatory for caesarean section for placenta praevia however, there is increasing evidence challenging this view. A survey of U.K anaesthetists, published in 2000, found that 60% used regional anaesthesia for placenta praevia (6). Some anaesthetists assert that regional anaesthesia can be used for all cases of placenta praevia including those at risk of placenta accreta and intraoperative emergency hysterectomy.

General anaesthesia had been preferred because of the fear of significant blood loss, possible prolonged surgery, possible suboptimal operating conditions and the stress of managing massive haemorrhage in a conscious patient.

Arcario et al (10) published a retrospective review of 180 patients in 1988 and felt that regional anaesthesia was not contra-indicated and further, that regional anaesthesia may decrease estimated blood loss at surgery for simple placenta accreta. Retrospective studies by Parekh et al (6) (514 cases) and Frederiksen et al (9) (350 cases) both concluded that regional anaesthesia was associated with reduced estimated blood loss and regional and general anaesthesia did not differ in the incidence of intra-operative and anaesthesia complications.

The prospective randomised trial of 25 patients with complete placenta praevia by Hong et al (11) concluded “epidural anaesthesia is superior to general anaesthesia in elective cesarean section for grade complete placenta previa with regard to maternal hemodynamics and blood loss”.

Regional anaesthesia should not be established in the presence of uncorrected hypovolaemia, however the fear that sympathetic blockade will make it difficult or impossible to control mean arterial pressure should severe haemorrhage occur may be unfounded. Conversely sympathetic activation may maintain arterial pressure despite massive blood loss, predisposing the anaesthetist to under-resuscitation. Seven of the women in Parekh’s retrospective study had an estimated blood loss of >35-40% of their estimated blood volume. Of these only two had a spinal anaesthetic but each lost an estimated 3000 and 6000 ml of blood.

The duration of surgery may not be reliably predicted with complicated placenta praevia. An anterior position, placenta accreta and hysterectomy may prolong surgery beyond the effective duration of spinal anaesthesia. In two prospective studies of anaesthesia for caesarean hysterectomy (12, 13) 24 of 60 and 7 of 28 cases initially commenced under regional anaesthesia required conversion to general anaesthesia. Potentially prolonged surgical time can be managed with epidural or combined spinal-epidural anaesthesia.

Regardless of the anaesthetic technique chosen, it is clear that placenta praevia can pose severe danger. In particular, massive haemorrhage, placenta accreta and cesarean hysterectomy. Though recent articles demonstrate that regional anaesthesia is not contraindicated and may, in fact, decrease the estimated blood loss, the anaesthetist must be comfortable with their chosen anaesthetic technique. In Frederiksen's (9) retrospective study the average blood loss caesarean delivery was 1176 +/- 727 ml compared to 4060 +/- 2440 ml for caesarean hysterectomy.

Placenta accreta refers to a placenta that is abnormally adherent to the uterus. Placenta increta invades the myometrium, and placenta percreta invades through the myometrium and serosa, sometimes into adjacent organs, such as the bladder. The incidence of placenta accreta is increasing, primarily as a consequence of the increasing caesarean delivery rate. It is estimated that the risk of having placenta accreta in women with placenta praevia increases from 24% with one previous caesarean section to 67% in women with 3 or more prior caesareans.

It is generally accepted that significant placenta accreta should be managed by elective caesarean hysterectomy and no attempt should be made to detach the placenta, though focal placenta accreta may not require as aggressive treatment. Balloon catheter occlusion and embolisation of pelvic vessels can potentially reduce blood loss. Management without hysterectomy has been described but there is insufficient data to recommend this approach routinely. It generally involves leaving the placenta in situ and adjunctive procedures including embolisation, methotrexate, resection of the affected uterine segment and oversewing of the placental bed.

Spinal and epidural anaesthesia for routine caesarean section is superior to general anaesthesia and may be the preferred choice of mothers. Traditionally mothers have been denied the option of regional anaesthesia in the presence of placenta praevia. Retrospective series and small prospective trials now conclude that regional anaesthesia is not contraindicated. However managing massive haemorrhage in a conscious patient may be too stressful for the anaesthetist. Crises are perceived as of sudden onset and rapid development, but usually result from series of underlying events. The anaesthetist and obstetrician must be aware of the potential catastrophic complications of placenta praevia and placenta accreta. The correct choice of anaesthesia where the potential for catastrophic complications is high will depend on the experience and support for the anaesthetist and while general anaesthesia remains the standard technique in the high risk cases there is some evidence that suggests opinions may be changing.

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POST-DURAL PUNCTURE HEADACHE.

In 1898 Karl August Bier probably gave the first spinal anaesthetic, injecting 10-15 mg of cocaine to seven patients, himself and his assistant. Bier, his assistant and four of the patients all described symptoms of a post-dural puncture headache (PDPH).

Incidence:

There is considerable variability in the incidence of PDPH, which is affected by many factors including age, gender, needle size and needle type. A prospective audit of 100 parturients who experienced accidental dural puncture with a Tuohy needle from Australia had a PDPH rate of 81% [6]. The diagnosis of dural puncture was delayed until presentation of headache in 27% of these cases. A similar incidence of PDPH has been found by other investigators [8], [9], [12] but Choi et al performed a meta-analysis of obstetrical studies and reported that the pooled risk for accidental dural puncture (ADP) for all epidural needles was 1.5%. Once dural puncture occurred, the risk of PDPH was only 52.1%. The risk of PDPH varied amongst spinal needles and ranged from 1.5% to 11.2% [5].

Recent measurements of dural thickness have demonstrated that the posterior dura varies in thickness within the individual and between individuals [10]. Dural puncture in a thick area may be less likely to lead to a CSF leak. This in part may explain the unpredictable consequences of a dural puncture.

Diagnosis:

A typical PDPH is described as being throbbing and frontal or occipital. Vertex, temporal and nuchal headache is less commonly reported. The headache is almost always exacerbated in the upright position and relieved by the horizontal position. Absence of a postural component should always lead to consideration of an alternative cause.

90% of PDPH occur within 3 days [1], 65% within 24 hours. The immediate onset of headache is rare [2] and other causes must be considered. Rarely PDPH develops between 5 and 14 days after the procedure. 80% will resolve within 1 week and most by 6 weeks. In a small percentage of cases, symptoms may persist for weeks or even months [4].

PDPH may have associated symptoms of nausea, vomiting, vertigo, dizziness, hearing loss, tinnitus, cranial nerve palsy, cortical blindness and diplopia.

Treatment of PDPH must always be preceded by careful history and examination to exclude other causes of headache. The differential diagnosis of PDPH includes pre-eclamptic toxemia, migraine, tension headache, paranasal sinusitis, intracranial haematoma, intracranial tumours, cerebral venous haematoma, pneumocephalus [7] and meningitis. Stein et al estimated that 39% of mothers have headache after childbirth unrelated to dural puncture [3].

The intracranial hypotension caused by dural puncture can lead to intracranial haemorrhage through tearing of dural veins. Paranasal sinusitis usually follows an upper respiratory tract infection, with tenderness to pressure over the frontal, ethmoidal or maxillary sinuses. Central vein thrombosis occurs in 1:3000 to 1:6000 deliveries. Cerebral vein thrombosis presents with headache associated with neurological symptoms

such as focal, multifocal or generalized seizures, coma, hemiparesis or bilateral papilloedema.

Pathophysiology:

About 500 ml of CSF is produced each day, mainly by the choroid plexus. The total CSF volume in an adult is about 150 ml, with 50% in the cranium. The normal CSF pressure in the lumbar region when supine is between 5 and 15 cmH₂O and over 40 cmH₂O when erect. Perforation of the dura will result in CSF leakage. The rate of CSF loss through the dural perforation (0.084-4.5 ml/sec) [11] may be greater than the rate of CSF production (0.35 ml/minute) especially with larger needles/holes. Excessive loss of CSF leads to intracranial hypotension.

Two mechanisms have been proposed for the cause of the headache. Intracranial hypotension may cause downward displacement of the brainstem and traction on pain sensitive intracranial structures and/or loss of CSF produces a compensatory adenosine mediated intracranial venodilation (Munro-Kellie doctrine). The venodilatation is then responsible for the headache. CT scan and MRI may show abnormal, intense, dural venous sinus enhancement, indicating a compensatory venous expansion [13].

Treatment:

Treatment of PDPH requires careful consideration of the benefits and risks. Most PDPH will resolve within one week however PDPH can be debilitating requiring the mother to remain supine. Maternal expectations and demands are high after delivery. Mothers expect to feel well and to care for their new baby and the cause of the headache is iatrogenic. It is important that risk of accidental dural puncture is discussed with the mother before an epidural and that the expected time course, therapeutic options and risks are discussed if a PDPH occurs.

Simple symptomatic treatment, rehydration, non-steroidal anti-inflammatory drugs, opioids, antiemetics and remaining in a comfortable posture may be sufficient treatment for less severe headache.

Both the prone position and abdominal binders have been advocated. Both will increase intraabdominal pressure, which is transmitted to the epidural space and relieves the headache but both are uncomfortable and seldom recommended.

Therapeutic treatment aims to restore CSF volume, seal the dural puncture and prevent cerebral vasodilatation. Several drugs have been tested including DDAVP, sumatriptan and caffeine, however there is a lack of large randomised, controlled trials to support their use. Caffeine produces cerebral vasoconstriction. Peak blood levels after oral administration occur at 30 minutes. The recommended dose is 500 mg oral or i.v. once or twice a day. (One cup of coffee contains 50–100 mg of caffeine and soft drinks contain 35-50 mg). Sumatriptan is a 5-HT receptor agonist that promotes cerebral vasoconstriction and is used for the treatment of migranous headaches.

In 1960 Gormley observed that bloody accidental spinal taps were less often complicated by PDPH [14]. He thought that epidural bleeding might lead to clot formation over the dural hole, preventing leakage of CSF and successfully treated PDPH patients with an epidural blood patch (EDBP). Many observational studies have reported success rates for

EDBP between 70% and 90% [15], [16], [17], [18], [19] if carried out more than 24 hours after dural puncture. If an epidural blood patch fails, repeating the blood patch has a similar success rate. However a Cochrane database systematic review recommended that further adequately powered, randomised trials are required before reliable conclusions can be drawn about the role of epidural blood patching in the prevention and treatment of post-dural puncture headache [20].

EDBP is contraindicated if the patient is febrile, has infection at the site of the epidural, coagulopathy or refuses. Of course performing another epidural carries the same risk of further accidental dural puncture and exacerbation of the headache. With the patient in the lateral position, the epidural space is located with a Tuohy needle at the level of dural puncture or one space lower. 20-30 ml of blood is drawn aseptically from the patient. (There has been a case report of an infected blood patch complicating regional analgesia for labour [21].) The autologous blood is slowly injected into the epidural space. If the patient complains of lancinating pain of dermatomal origin the procedure must be stopped. Approximately 35% of patients treated with an EDBP may report back pain that usually resolves within 48 hours. Neck pain, leg pain, paraesthesia, radiculitis, fever and temporary cranial nerve palsies have all been reported following EDBP.

Magnetic resonance imaging studies have reported the degree of spread of the epidural blood patch. [22]. Blood spreads both caudally and cephalad. The blood also spreads circumferentially and the thecal space is compressed for 3 hours by the epidural blood patch. This compression and presumed increase in intracranial pressure may explain the rapid relief of headache in some patients.

There have been case reports of ineffective epidurals after a blood patch however a large retrospective study showed a 96% success rate for repeat epidural analgesia [23].

Prophylactic epidural blood patch has been advocated but the effectiveness is not established. A double blind comparison of prophylactic EDBP compared to a sham procedure showed no decrease in the incidence of PDPH between the two groups [24]. Other studies have suggested that a prophylactic epidural blood patch, administered shortly after delivery before the epidural catheter is removed, may decrease the incidence of PDPH or the need for therapeutic EDBP [25], [26], [27].

Alternative invasive therapeutic options include epidural saline, epidural dextran and a subarachnoid catheter.

Because autologous blood for an epidural blood patch presents an infective risk and immediate relief of headache may be due to compression of the thecal sac, anaesthetists have investigated the effectiveness of bolus and infusions of epidural saline and dextran 40. Whilst there are case studies describing success, trials comparing epidural saline and epidural blood patches fail to demonstrate long-term efficacy [28]. The pressure rise with epidural saline is transient, lasting only 10 minutes and there is no evidence that saline accelerates the closure of a dural hole. The theoretical argument for dextran 40 is that the higher molecular weight and viscosity will slow its removal however there is no evidence that dextran is superior to saline.

Long-term subarachnoid catheters in animal and human studies cause an inflammatory response that will promote closure of a dural hole [29], however these catheters were left in for several days to weeks. The placement of a subarachnoid catheter after accidental dural puncture can provide excellent labour analgesia however it must be managed with

great care to prevent inadvertent administration of an epidural dose of local anaesthetic and subsequent total spinal.

Epidural analgesia provides excellent labour analgesia however the incidence of accidental dural puncture is 1.5% with 51% developing a post dural puncture headache. Mild to moderate PDPH may best be treated conservatively as the natural history is for resolution within a week. Mothers expect to be well and to care for the newborn. A headache that is debilitating may be best treated with an epidural blood patch after 24 hours with the expectation that 70 to 90% will be successful however epidural blood patch is not without risk. A repeat epidural blood patch has similar efficacy.

There are other serious causes of headache in the parturient and all patients with an unusual presentation or who fail to respond to treatment must be further investigated.

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ANAESTHESIA FOR LAPAROSCOPIC SURGERY.

During laparoscopic surgery the patient is positioned so as to produce gravitational displacement of the abdominal viscera away from the surgical site and a pneumoperitoneum is created to improve visual and physical access. The choice of insufflation gas, pneumoperitoneum and patient position induce complex pathophysiological changes that complicate anaesthetic management.

The anaesthetist must prepare preoperatively to limit and respond to these pathophysiological changes with appropriate monitoring and a high index of suspicion for complications such as gas embolism, extraperitoneal insufflation and surgical emphysema, pneumothorax and pneumomediastinum.

Patients who do not respond to routine treatment should have the pneumoperitoneum released and be returned to a supine position.

Choice of insufflation gas.

The most commonly (universal) gas used for creating pneumoperitoneum is carbon dioxide (CO₂). Other gases used include nitrous oxide (N₂O), helium (He), air, nitrogen (N₂) and argon (Ar).

Initially the pneumoperitoneum was created with room air and oxygen however both gases support combustion (oxygen may cause an intra-abdominal explosion), and both gases have the potential for severe venous gas embolism because both are poorly soluble in blood.

N₂O was used during the 1970s and 1980s. Its principle advantages are its anaesthetic properties, which may make it more suitable for procedures performed under local or regional anaesthesia. CO₂ may be less suitable local or regional anaesthesia as carbonic acid is produced when CO₂ dissolves. Carbonic acid may produce peritoneal irritation and be partly responsible for abdominal and shoulder tip pain.

N₂O also has no effect on acid base status and high plasma solubility (Ostwald solubility coefficient 0.47) however it does not suppress combustion and there are case reports of intraoperative explosions.

Helium, argon and nitrogen are less available, more expensive and dissolve slowly in the case of gas emboli. Helium also has high thermal conductivity. Argon may decrease hepatic blood flow.

The properties of an ideal laparoscopic insufflation gas include being readily available, inexpensive, suppresses combustion, highly soluble in plasma, physiologically inert and chemically stable. CO₂ possess many of these characteristics. The main advantages for CO₂ are that it will suppress combustion and its high solubility (Ostwald solubility coefficient 0.49) in the event of venous emboli. The capacity for CO₂ carriage in blood is

high (bicarbonate buffering and in combination with haemoglobin and plasma proteins) adding a further margin of safety in the event of gas embolism. Animal studies comparing the haemodynamic effects of CO₂ emboli to Ar, He or air emboli found CO₂ to be safer because of its greater solubility in blood.

The lethal venous gas embolism dose of CO₂ has been estimated to be 5 times that of air (1). From case studies, the lethal venous gas embolism dose of air has been estimated as 200 ml.

Absorption of CO₂ during pneumoperitoneum will result in some degree of hypercarbia and acidaemia. The principle cause of the hypercarbia is absorption of CO₂ from the peritoneal cavity that will depend on the diffusibility of CO₂, and the size and perfusion of the absorption area. There may be a minor component secondary to impaired ventilation/perfusion due to mechanical factors resulting from increased intra-abdominal pressure (IAP). After peritoneal absorption, CO₂ is transported to the lungs where it is eliminated by ventilation. In most healthy people the rise in PaCO₂ and fall in pH is not clinically significant. Severe hypercarbia is rare, except in patients with reduced cardiopulmonary function.

The IAP has a dual effect on the development of hypercarbia. Increasing IAP will increase CO₂ absorption and also decrease CO₂ elimination by reducing pulmonary function (including decreased vital capacity, decreased functional residual capacity, decreased pulmonary compliance and increased airway pressure).

With intermittent positive ventilation (IPPV) the PaCO₂ progressively increases over 15 to 30 minutes then remains relatively constant. Any significant change in PaCO₂ after reaching this plateau phase will have a significant cause (e.g. CO₂ subcutaneous emphysema, capnothorax, CO₂ embolism). Principally a balance between the IAP of CO₂ and the set minute ventilation will determine the degree of hypercapnia. Increasing the minute ventilation by 15-20 percent is necessary to maintain normocarbina in patients with normal physiological function.

The PaCO₂ is usually unaltered under local or regional anaesthesia because of a compensatory rise in the respiratory rate.

Hypercarbia and acidosis can cause haemodynamic changes by direct action on the cardiovascular system and indirectly by stimulation of the sympathetic nervous system. Haemodynamic changes occur only when PaCO₂ is increased by 30 percent. CO₂ and acidosis causes systemic vasodilatation, sensitises the myocardium to the arrhythmogenic effects of catecholamines and decreases myocardial contractility. Sympathetic stimulation results in tachycardia and vasoconstriction.

Pneumoperitoneum/Raised intraabdominal pressure (IAP).

The pneumoperitoneum produces an increased IAP, CO₂ absorption, hypothermia and endocrine/neurohumoral response.

Increased IAP will influence the cardiovascular system, respiratory system, gastrointestinal system, mesenteric circulation, hepatoportal circulation, renal function, and, intracranial and intraocular pressure.

Most of these are not clinically significant if appropriate anaesthetic care is provided however pneumoperitoneum is undesirable in patients with increased intracranial pressure, hypovolaemia, some cardiac disease and ventricular peritoneal shunts.

Cardiovascular system: An increase in IAP is the most important factor contributing to cardiovascular instability during laparoscopy. Other factors include the patient position (especially Trendelenburg and reverse Trendelenburg), hypercapnia, pre-existing disease and the patient's effective intravascular volume, and vagal stimulation.

The haemodynamic changes depend directly on intraabdominal pressure. Insufflation pressures should be strictly limited in patients with reduced cardiorespiratory reserve.

Usually a biphasic change in cardiac output (CO) is observed. With IAP less than 5-10 mmHg venous return (VR) is increased and CO improves. With greater IAP, there is progressive reduction in both VR and CO and increases in mean arterial pressure (MAP), systemic vascular resistance (SVR) and pulmonary vascular resistance (PVR) and decreased cardiac index (CI). Joris et al (2) observed an increase in MAP (35%), increased SVR (65%), increased PVR (90%) and decreased CI (20%).

VR and CO are reduced with increasing IAP due to subdiaphragmatic narrowing of the lower vena cava that reduces return of blood to the right atrium. The drop in right atrial pressure is proportional to the IAP. The increase in SVR may also reduce CO.

A rise in IAP will raise intrathoracic pressure and hence increase PVR.

The increase in SVR may in part be explained by the splanchnic vascular compression but the persistence of increased SVR after release of the pneumoperitoneum suggests a humoral factor. A rise in both antidiuretic hormone and noradrenaline has been found that parallels the increase in SVR and MAP.

These cardiovascular changes are usually not significant in healthy patients with good anaesthetic care however the anaesthetist must evaluate the consequences in patients with decreased cardiovascular reserve. An increase in SVR and myocardial oxygen requirements may precipitate acute coronary events in patients with significant ischaemic heart disease. Patients with untreated congestive cardiac failure would expect to suffer significant morbidity and possibly mortality with reduction in VR and increases in PVR and SVR. There are case reports of cardiovascular collapse occurring in hypovolaemic patients during laparoscopy especially with a head up tilt position. Most patients will benefit from judicious volume loading and untreated hypovolaemia is a contraindication to laparoscopic surgery.

For patients with significant cardiovascular disease, the postoperative benefits of laparoscopic surgery must be weighed against peri-operative risk. Advanced haemodynamic monitoring is required for ASA III and IV patients.

The anaesthetist should be prepared for the pharmacological treatment of hypertension, hypotension and arrhythmias. IAP must be increased slowly with the patient in the supine position and maintained at the lowest feasible level. Extreme positioning of the patient should be avoided.

The insufflation of gas into the peritoneal cavity can provoke arrhythmias. Rapid stretching of the peritoneum can induce vagal-mediated arrhythmias. Most arrhythmias are transient and respond to a reduction in IAP and 100% oxygen. Profound vagal reflex can cause asystole.

It is important that the anaesthetist is aware that the haemodynamic changes of laparoscopy are directly related to the peak IAP and speed of insufflation. IAP should be increased slowly and maintained as low as possible. The haemodynamic changes will also reach their maximum during insufflation, so are generally independent of the duration of surgery. Even short procedures will have maximal haemodynamic consequences.

Respiratory system: The increase in IAP will cause cephalad displacement of the diaphragm resulting in reduced lung volumes (vital capacity, functional residual capacity), decreased pulmonary compliance (30%) and increased airway resistance. Changes in pulmonary blood flow and ventilation will result in adverse changes in pulmonary ventilation perfusion matching (hypoxia and hypercarbia). With intermittent positive pressure ventilation, larger tidal volumes (10-12 ml/kg) will prevent progressive alveolar atelectasis and ventilation with positive end-expiratory pressure (PEEP) will significantly improve gas exchange. However both will also generate higher airway pressure that may be significant given that airway resistance is increased by raised IAP. Cardiac output is decreased with raised IAP and PEEP will cause an additional reduction. The increase in IAP will also cause cephalad displacement of the carina that may result in inadvertent endobronchial intubation despite the endotracheal tube (ETT) being correctly positioned at the start of surgery. Lobato et al (3) found that the average distance from the tip of the ETT to carina reduced from 2.1+/-0.8 cm to 0.7+/-1.4 cm after insufflation. Endobronchial intubation occurred in 8 of their 30 patients. An unusual increase in airway pressure associated with a decrease in oxygenation should alert the anaesthetist to the possibility of endobronchial intubation.

Complications involving the respiratory system include hypoxaemia, hypercarbia endobronchial intubation, venous gas embolism, pneumothorax, pneumopericardium and subcutaneous emphysema.

Subcutaneous emphysema, due to extraperitoneal insufflation, generally does not have clinical consequences however it may be associated with a pneumothorax or pneumomediastinum.

Gas may pass through aortic and oesophageal hiatuses or through congenital defects in the diaphragm to cause pneumomediastinum, pneumothorax (capnothorax) or pneumopericardium. It is also possible, but less likely, that a pneumothorax could occur during laparoscopy due to the higher airway pressures and rupture of alveoli.

The onset of hypoxia, hypercarbia, increased peak airway pressure and haemodynamic changes should alert the anaesthetist to the possibility of a pneumothorax.

A pneumothorax caused by passage of CO₂ into the pleural cavity may not require an intercostal catheter, since carbon dioxide will be rapidly reabsorbed at the end of surgery (30 – 60 minutes). Unless there is significant cardiac or respiratory compromise the

patient usually responds to stopping CO₂ insufflation, stopping N₂O and ventilation with 100% oxygen.

Gastrointestinal system: The risk of aspiration due to gastric regurgitation may be increased as a consequence of raised IAP.

Hepatoportal/Renal function: An IAP greater than 12 mmHg will reduce hepatic, portal and renal blood flow (and urine output).

Renal function is also affected by elevations in antidiuretic hormone, increased renin angiotensin activity and reduced cardiac output. Changes in renal function are transient and usually resolve within 2 hours postoperatively however prolonged renal hypoperfusion can result in acute tubular necrosis. An IAP greater than 15 mmHg in animal studies decreased cortical renal flow by 28%, medullary renal flow by 31% and glomerular filtration rate by 18-31% (4).

An IAP greater than 20 mmHg will reduce portal venous blood flow by 60% resulting in transient liver dysfunction.

Intracranial pressure/Intraocular pressure: Both ICP and IOP are increased due to intraabdominal vascular compression and impaired drainage of the lumbar venous plexus. Raised PaCO₂ will also cause cerebral vasodilation and increased cerebral blood flow.

Temperature: Though patients do not have heat loss from open body cavities during laparoscopy, the dry cold gases flowing over peritoneal surfaces can cause significant heat loss (up to 0.3C decrease in core temperature per 50L volume flow of CO₂).

Thromboembolism: Both raised IAP and reverse Trendelenburg position will reduce venous flow from the lower extremities increasing the chances of thromboembolism.

Positioning.

During laparoscopic surgery, the patient's position is changed in order to displace intraabdominal organs by gravity away from the operative area.

The Trendelenburg position increases VR, the right atrial pressure (RAP), CVP and CO. The reverse Trendelenburg position will decrease VR, RAP and CO. This position will exacerbate the decrease in VR caused by a pneumoperitoneum.

Anaesthetic techniques.

The anaesthetist must consider the physiological changes caused by laparoscopy and the health of the patient, especially their cardiorespiratory reserve. The anaesthetist must remember that a laparoscopy may need to be converted to a laparotomy.

Usually a relaxant general anaesthetic, with endotracheal intubation and intermittent positive pressure ventilation (IPPV) is the preferred choice of anaesthesia. This technique provides airway protection against aspiration, allows adjustment of minute ventilation to avoid severe hypercarbia, and provides good muscle relaxation and optimal operative conditions. Preloading with 5-10 ml/kg intravenous fluid may attenuate haemodynamic changes during pneumoperitoneum.

Mask ventilation, prior to intubation, may cause inadvertent inflation of the stomach that should be aspirated, through a nasogastric tube, before creating a pneumoperitoneum. Similarly the bladder should be emptied before pelvic laparoscopic procedures.

End tidal PCO₂ should be constant before insufflation with CO₂. Changes in end tidal CO₂ will then alert the anaesthetist to possible complications of insufflation rather than alterations in ventilation.

Insufflation should proceed slowly (1 – 1.5 l/min) to the minimal required IAP. IAP should not exceed 20 mm Hg. A sudden change in end tidal PCO₂ should alert the anaesthetist to the possibility of venous gas embolism. Venous gas embolism requires immediate management to avoid death.

The patient's position should be altered slowly, after establishing the pneumoperitoneum and extreme positions avoided. The position of the ETT should be checked after insufflation and positioning.

Patients may be positioned in Trendelenburg, reverse Trendelenburg and lithotomy positions with or without lateral tilt for different laparoscopic surgery. Special care should be taken to avoid nerve compression or over stretching. Heat loss may be considerable due to insufflation of cold gas. The patient's temperature should be monitored, all peritoneal irrigation fluid warmed and the patient may require active heating with a forced air warming device or a heated mattress. Patients are at increased risk of thromboembolism and should be given prophylactic subcutaneous heparin.

The pneumoperitoneum should be emptied as completely as possible at the end of surgery to reduce postoperative pain.

General anaesthesia with spontaneous ventilation has been successfully used for short duration, lower abdominal laparoscopy in carefully selected patients. It avoids the risks associated with muscle relaxation and intubation however provides inferior operating conditions, does not protect against aspiration and is unable to control hypercarbia.

Relaxant general anaesthesia with intermittent positive pressure ventilation has been successfully achieved through both classic and proseal laryngeal masks. However both the patient and procedure needs to be carefully selected. Laryngeal masks do not protect the airway from aspiration of gastric contents and the decrease in thoraco-pulmonary compliance during laparoscopy may result in airway pressures exceeding 20 cmH₂O.

Local and regional (epidural/spinal) anaesthesia has also been successfully used for laparoscopy. However there are potential disadvantages with local and regional anaesthesia. Deeb et al (5) used the technique of peritoneal irrigation with 100 ml of 0.5% lignocaine plus heavy sedation for laparoscopic tubal ligation. (Nitrous oxide has been suggested as an alternative insufflation gas for diagnostic laparoscopy under local anaesthesia because CO₂ insufflation will cause peritoneal irritation as CO₂ dissolves to form carbonic acid).

Regional anaesthesia needs to achieve a sensory level of T4 to minimise pain due to peritoneal irritation and manipulation of intraabdominal organs. This will result in significant sympathetic blockade that will exaggerate the decrease in VR and CO produced by the pneumoperitoneum. It is essential that patients be well-filled, intraabdominal pressure maintained at a minimal level and patient's position altered slowly. Theoretically the intercostal muscle paralysis of a T4 regional block may potentiate the respiratory dysfunction caused by a pneumoperitoneum.

Since shoulder tip pain is due to referred pain from diaphragmatic irritation, mediated by the phrenic nerve (C 3,4 and 5), it is difficult to provide complete analgesia by a regional technique.

As sedation is usually also required with regional anaesthesia for laparoscopic surgery, the combination of all factors will create a definite risk of hypercapnia and hypoxia.

Monitoring.

Standard monitoring during laparoscopy should include precordial stethoscope (endobronchial intubation, millwheel murmur), electrocardiography (arrhythmias), SaO₂ (late sign of complications), intraabdominal pressure (mandatory, excessive pressure should trigger an alarm), temperature, blood pressure, airway pressure and end tidal CO₂. Usually end tidal PCO₂ is 2 to 6 mmHg lower than PaCO₂. During IPPV the end tidal PCO₂ to PaCO₂ gradient may increase to 10 to 15 mmHg. With laparoscopic surgery the end tidal PCO₂ to PaCO₂ gradient is very variable (increased, decreased, no change and negative).

Higher risk patients, in whom the postoperative benefits of laparoscopy are deemed to outweigh the intraoperative risks, may require more advanced monitoring. Intra-arterial blood pressure monitoring provides beat-to-beat blood pressures. CVP traditionally guides optimal right heart filling however CVP readings will be altered by changes in body position and raised intrathoracic pressure. Swan Ganz catheter results will also be affected by position and intrathoracic pressure and similarly require careful interpretation. An increase in pulmonary arterial pressure is an early sign of gas embolism and theoretically, with the occurrence of a gas embolism, bubbles may be aspirated from the right heart.

Trans-oesophageal echocardiography enables early detection of gas embolism, assessment of the adequacy of venous return and competence of left ventricular function. Precordial doppler ultrasound is almost as sensitive as trans-oesophageal echocardiography in detecting gas embolism.

End tidal CO₂ (PetCO₂) will alert the anaesthetist to several significant complications. A rapid rise of a few mmHg for a few minutes followed by a return to normal may be a sign of a minimal CO₂ gas embolism. A rapid drop in PetCO₂ may be a sign of a massive gas embolism. The drop in PetCO₂ is usually proportional to the volume of CO₂ embolism. (Other causes of cardiovascular collapse during laparoscopy include severe vagal bradycardia/asystole, hypercarbic induced arrhythmias and tension pneumothorax). A

gradual and persistent rise in PetCO₂ may be an indication of extra-peritoneal diffusion of CO₂.

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EPIDURAL TEST DOSE.

Epidural catheters may be accidentally placed either intravascularly (1 to 10%) or intrathecally (as high as 2%). Usually routine aspiration of the catheter will identify misplacement however aspiration can be rarely falsely negative. Using multi-orifice, 20-gauge epidural catheters, Norris et al (1) identified 60 intravenously placed catheters by aspiration from 1,029 epidural catheters inserted in labouring women. Two other catheters may have been intravenously placed despite negative aspiration. Richardson, Lee and Wissler (2) report 5 cases of unintentional subarachnoid placement of the epidural catheter after negative aspiration for cerebrospinal fluid in 1,962 obstetric epidurals administered over a 17-month period.

Because the consequences of incorrect placement are severe, the anaesthetist must confirm the location of the epidural catheter. An article examining anaesthesia-related deaths during obstetric delivery in the United States (3), 1979-1990, concluded that about one fourth (33) of the 129 deaths were associated with problems during regional anaesthesia. 70% occurred with epidural anaesthesia. These deaths usually resulted from local anaesthetic toxicity or an inadvertent high block.

Though rare, aspiration can be falsely negative and the anaesthetist should reduce the risk of misplacement by a combination of epidural test dose, fractionation of epidural local anaesthetic injection and clinical judgment (ease of epidural placement, monitoring for objective and subjective signs/symptoms of misplacement and observing a fluid meniscus). Aspiration with a single-orifice catheter will reveal the presence of blood in 34% to 81% of cases. This is increased to 99.5% with a multi-orifice catheter.

A test dose should allow for the detection of an intravenous or subarachnoid catheter within an appropriate short time span, without increasing the risk to mother or foetus and with appropriate sensitivity (the chance that a positive result is truly positive) and specificity (the chance that a negative result is truly absent). It should be applicable to all clinical situations and ideally require only easily accessible monitoring and minimal cooperation from the patient.

Increased risk to mother or foetus includes excessive local anaesthetic (that would cause significant hypotension, high block, decreased uteroplacental blood flow), excessive adrenaline/epinephrine (that would cause decreased uteroplacental blood flow, exacerbate preeclampsia, coronary vascular disease or stenotic valvular disease) and neurotoxicity.

A survey of 500 members of the Obstetric Anaesthetists' Association of the United Kingdom in 1999-2000 (4) showed no consensus about the nature of a test dose in obstetric anaesthesia. Doses (20 mg bupivacaine and 90 mg lignocaine), that risk a high or total spinal block if accidentally given spinally, were used and epinephrine, aspiration testing and cardiovascular monitoring was uncommon. 90% of respondents gave a test dose for an epidural for labour, 93% gave a test dose for an epidural for elective caesarean section and only 37% used a test dose for an epidural top-up for emergency caesarean section.

With an epidural top-up for emergency caesarean section there are other factors that will influence the anaesthetist. A top-up will be given through a catheter whose position has already been confirmed during labour. However delayed migration of catheters has been reported. Though unclear, several mechanisms have been suggested including catheter migration, multi-compartment block (5) or arachnoid rupture after subdural block (6). If an emergency caesarean section is performed because of immediate threat to the life of the mother or foetus there may be insufficient time for slow incremental top-ups and the anaesthetist will need to balance the minimal risk of high or a total spinal and intravenous toxicity against the potential for foetal harm.

In 1981 Moore and Batra recommended an epidural test dose of 3 ml of either 1.5% lignocaine or 0.5% bupivacaine for non-pregnant patients (7). Prince and McGregor recommended that this dose should be reduced because of the decreased epidural requirements in pregnancy and that lignocaine be used instead of bupivacaine because of its faster onset (8).

An ideal test dose needs to correctly detect both intrathecal and intravenous misplacement.

Using a local anaesthetic alone may not be suitable to safely detect both. Intravenous ropivacaine 25 mg and levobupivacaine 25 mg in non-pregnant patients produced central nervous system (CNS) symptoms in only 52% and 57% respectively compared to 87% of patients receiving lignocaine 100 mg (10). Similarly only 50% of patients who received lignocaine 0.5 mg/kg reported CNS symptoms compared to 95% who received 1 mg/kg (11). The onset of CNS symptoms occurred at an average of 43 +/- 14 seconds after intravenous lignocaine. 73% of patients reported tinnitus, followed by dizziness in 47% and metallic taste in 40%.

The low response rate suggests that plain ropivacaine and levobupivacaine (25 mg) are unsuitable for intravenous test doses during regional anaesthesia. Plain lignocaine 100 mg has better sensitivity however is also unsuitable with epidurals as this dose is highly likely to produce a very high block or total spinal. Mulroy MF et al (17) found that 10 unpremedicated patients universally recognised the intravenous injection of 25 mg of bupivacaine but this dose would also be unacceptably large if inadvertently given intrathecally.

The ability of epinephrine (adrenaline) to identify intravascular misplacement has been extensively investigated. In Moore and Batra's original study (7) of 175 non-pregnant patients, 15 micrograms of adrenaline increased heart rate from 79 +/- 14 to 111 +/- 15 beats per minute within 23 seconds.

In 1987, Leighton and Norris found only a 50% sensitivity to adrenaline by using an increase in heart rate > 25 beats per minute over the base line.

By using a baseline to peak criterion of only greater than 10 beats/minute Colonna identified all intravascular injections with epinephrine (15 and 10 micrograms). There was a sensitivity of 100% in obstetric patients (13). All injections were given during uterine diastole and maternal heart rate was monitored with pulse oximetry. In a later prospective study of 209 unmedicated labouring patients Colonna and Nagaraj

determined the sensitivity of epinephrine to be 100% with a specificity of 96% (18). In this study if aspiration of the epidural catheter was negative a test dose of lignocaine 45 mg and epinephrine 15 micrograms was administered during uterine diastole. A sudden increase in maternal heart rate of 10 beats/minute occurred within 1 minute after injection, with a fast acceleratory phase of more than 1 beat/minute. (Colonna-Romano et al (16) determined a difference in the acceleratory phase of epinephrine and contraction associated maternal tachycardia with on-line analysis that may further improve accuracy in high tech obstetric units). All patients with a positive epinephrine test dose received 5 ml of lignocaine as a second test dose. The presence of tinnitus and/or metallic taste was defined as a positive test result.

Maternal heart rate is variable during labour, increasing by more than 20 beats/minute with uterine contractions. In pregnant women, reduced sensitivity to epinephrine has been proven. The anaesthetist must time the test dose carefully. Epinephrine produces a transient response (onset within 2 minutes and duration less than 5 minutes) that requires careful monitoring to detect. It should not be administered during uterine contractions. Though the literature supports the use of epinephrine it may need to be used with caution in some cases and always in combination with clinical judgment. Epinephrine (15 micrograms) is very unlikely to be harmful to a normal foetus or a foetus with compromised uteroplacental perfusion though the anaesthetist may wish to evaluate the risk benefit for mothers with preeclampsia, severe coronary vascular disease, stenotic valvular lesions, significant tachycardia, cocaine intoxication, patients taking beta-blockers and high uterine contraction frequency.

The use of epinephrine as a test dose for intravascular placement of an epidural catheter is not clear. Epinephrine test doses are 100% sensitive if a criterion of an increase greater than 10 beats/minute is used, however there are significant constraints and implications that must be considered.

Currently the test requires the exclusion of certain patients, monitoring capable of detecting rapid transient changes in heart rate and avoidance of injection during contraction. Aspiration through multi-orifice catheters is effective in 99.6% of cases so that the prevalence of undiagnosed intravenous catheters will be very low. In the Colonna-Romano study the specificity and positive predictive value for epinephrine was 96% and 63% respectively. Therefore some epidural catheters were withdrawn unnecessarily. Repositioning of an epidural catheter is not without risk.

The anaesthetist must also consider the potential effect of the dose of local anaesthetic if it is accidentally given intravenously. If the anaesthetist plans to administer a dose of local anaesthetic that would be toxic if given intravenously they must be certain of the catheter position. However, changes in the practice of obstetric epidural anaesthesia with multi-orifice catheters and the slow perfusion of low concentrations of local anaesthetics may justify abandoning a test dose with adrenaline if the aspiration test is conclusively negative. If aspiration is equivocal the anaesthetist should proceed with an epinephrine test dose or reposition the catheter. If an epidural block fails to be established the anaesthetist should be alert to the possibility of catheter misplacement and exclude an intravenous catheter before injecting boluses of higher concentrations of local anaesthetic.

Non-local anaesthetic test doses have also been suggested to detect intravascular epidural catheter misplacement. Subjective symptoms (drowsiness, euphoria) may accurately (sensitivity 92.4% and specificity 92%) distinguish intravenous from epidural fentanyl (100 micrograms) in labouring patients (9). The plasma peak of intravenous fentanyl is immediate and occurs 5 to 10 minutes after epidural injection.

Air (1 ml) has been evaluated for detecting intravenously located single-orifice epidural catheters using a Doppler foetal heart rate monitor placed over the precordium (12). The results suggested that air maybe a suitable indicator of intravenous epidural catheter location. However when repeated with multi-orifice catheters it only detected 82% of intravenous catheters.

Intravenous ephedrine 15 mg will produce a temporary increase of systolic blood pressure > 10 mmHg (20) however the necessity of close arterial pressure monitoring and the physiological variability of maternal blood pressure makes it less than ideal.

Inadvertent intrathecal placement of an epidural catheter may be detected after a local anaesthetic test dose by somatic motor function, sympathetic block (blood pressure, warm feet) and sensory change (block level, contraction pain). The local anaesthetic test dose should have a clinically practical onset time, clinically apparent effect but be safe (minimal risk of high or total spinal block). It must not be neurotoxic.

Daoud, Collis et al (14) evaluated S1 motor block to determine a safe reliable test dose for epidural analgesia. Using sequential analysis in mothers booked for elective caesarean section they calculated the ED 97.5 for bupivacaine to be 9.7 mg with 19.4 micrograms of fentanyl. They evaluated the S1 motor block after 10 minutes. Similarly Prince et al concluded that the only definite sign of intrathecal placement following a 7.5 mg of bupivacaine was an inability to straight leg raise after 10 minutes. Though extremely unlikely to produce a high block the 10 minute delay for assessing a bupivacaine test dose may not always be clinically practical. The survey of UK obstetric practice (4) found that the majority of anaesthetists looked for signs and symptoms at 5 minutes.

Lignocaine affords reliable detection within a short period.

Poblete B et al compared the efficacy of three test doses (60 mg lignocaine 2%, 7.5 mg bupivacaine 0.25% and 15 mg bupivacaine 0.5%) to detect epidural misplacement in orthopaedic patients (15). All patients who received 60 mg lignocaine intrathecally had motor block > or equal to 1 on the Bromage scale (inability to raise leg) after 6 minutes while none of the patients receiving the same test dose epidurally did so. The other test doses and signs/symptoms (sensory level > T12 and subjective variables) were not reliable. Colonna-Romano compared the effects of the intrathecal injection of an epidural test dose of 45 mg lignocaine with epinephrine against 3 ml normal saline. He concluded that a motor block four minutes after the injection had a sensitivity of 100% and specificity of 93%.

A subarachnoid injection of 3 ml of 1.5% lignocaine into the lumbar area will produce sensory anaesthesia affecting the S2 dermatome in 1.5 minutes before spreading to T9 (19) but will also produce sensory changes in L2 after 3 minutes if injected epidurally. These onset times may not allow accurate clinical assessment.

An epidural test dose with lignocaine and assessing lower limb muscle power may be the optimal test for inadvertent intrathecal catheter placement.

An epidural test dose for accidental intrathecal placement is performed to avoid the serious consequences of high or total spinal block. The management of epidurals for labour has changed since the 1980s with the addition of opioids and the use of very low concentrations. In some clinical situations the total epidural local anaesthetic dose (e.g. 8 ml of 1.25% bupivacaine) may be less than the dose that would be expected to cause a high block and even less than some recommended test doses. In this clinical situation the single epidural dose may be considered as a “test dose”.

Systemic toxicity and high or total spinal are rare but possible even if aspiration is negative, therefore appropriate test doses, fractionated injections, adequate monitoring, and resuscitation equipment are essential to safe anaesthetic practice.

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ANAESTHESIA FOR CAESAREAN SECTION IN THE SEVERELY PRE-ECLAMPTIC PATIENT.

Caesarean section is often indicated in severe pre-eclampsia because of sudden deterioration in maternal and/or foetal wellbeing. The selection of an anaesthetic technique for a severely pre-eclamptic patient requiring caesarean section is controversial. If sufficient time was available and there were no contraindications (e.g. coagulopathy) the traditional preferred anaesthetic technique of many anaesthetists was lumbar epidural.

The risk of general anaesthesia is significantly increased in the obstetric population. The incidence of failed intubation (1) is approximately eight times higher (1 in 280) than non-obstetrical patients (1 in 2330). The risks are further increased with severe pre-eclampsia. The upper airway and laryngeal oedema of normal pregnancy can be exaggerated to the point of airway obstruction. The anaesthetist must be prepared for (1) increased upper airway oedema with the increased risk of difficult/failed endotracheal intubation, (2) marked hypertensive response to anaesthetic/surgical stimuli and (3) the interaction of drugs to treat pre-eclampsia with general anaesthesia.

Spinal anaesthesia may be a better and more cost-effective technique than epidural block, especially if anaesthetic resources are limited. The rapid onset of spinal anaesthesia may be beneficial in patients who require immediate caesarean section. The quality of anaesthesia can be superior and spinal anaesthesia requires less equipment and training.

Both spinal and epidural anaesthesia are contraindicated when the patient has a significant coagulopathy or thrombocytopenia. Pre-eclampsia can reduce both the quantity and quality of platelets. These patients may also have hepatic dysfunction and be treated with aspirin or thrombo-embolic prophylaxis. Although there are no studies to support the idea, intuitively it would seem safer to choose spinal anaesthesia with a small-gauge needle rather than the larger epidural needle in patients with potential or actual mild platelet impairment.

Spinal anaesthesia for caesarean section in patients with severe pre-eclampsia is controversial because of associated cardiovascular pathophysiological changes. Concerns included prophylactic crystalloid administration, the potential for increased use of ephedrine and the potential for sudden and marked maternal haemodynamic instability.

Severely pre-eclamptic patients are at increased risk of developing pulmonary oedema if excessive intravenous fluid is administered. Traditional aggressive preloading before spinal anaesthesia could theoretically precipitate pulmonary oedema however, spinal induced hypotension is less frequent and less severe in severely pre-eclamptic patients and prophylactic crystalloid administration for the prevention of hypotension after spinal anaesthesia has been challenged.

Intravenous pressor agents have been thought to be hazardous to severely preeclamptic patients, who may be more sensitive to them (6) however this has not been confirmed and

ephedrine requirements may be reduced during spinal anaesthesia for caesarean section in pre-eclampsia (2).

Severe pre-eclampsia reduces plasma volume. This was thought to increase the risk for precipitous hypotension; decreased cardiac output and associated placental hypoperfusion in response to regional anaesthesia induced sympathectomy. Recent studies challenge this traditional view.

Several retrospective and prospective studies have demonstrated that, in comparison with healthy term parturients, patients with severe pre-eclampsia but who are haemodynamically stable, had a less frequent incidence of spinal hypotension, which was less severe and required less ephedrine (2) (3) (4).

Significant maternal hypotension was believed to be more likely with spinal compared to epidural anaesthesia, (epidural anaesthesia allows the gradual development of a sympathectomy), however studies have not confirmed this. A retrospective study of 103 non-labouring, severely pre-eclamptic patients showed that changes in the lowest mean blood pressure were similar after epidural or spinal anaesthesia. Intraoperative ephedrine use was similar but intraoperative crystalloid administration was greater in the spinal group (1780+/-838 ml) than the epidural group (1359+/-674 ml). Neonatal Apgars scores were also similar (5). Another retrospective study (7) with limited numbers of 41 cases concluded that spinal anaesthesia in severe pre-eclamptic patients has no significant differences in maternal blood pressure or neonatal Apgar scores compared to epidural anaesthesia and may be a safe alternative. The volume of intravenous fluid infused was similar.

The prospective, randomised study by Visalyaputra S et al (8) compared the haemodynamic effects of spinal and epidural anaesthesia for caesarean section in 100 severely pre-eclamptic patients. They found that there was a statistically significant difference in mean arterial pressure. The incidence of hypotension was more frequent in the spinal group and the use of ephedrine was greater, however the duration of significant hypotension was short in both groups and hypotension was easily treated in all patients. Neonatal Apgar scores and umbilical arterial gas analysis was similar in both groups.

Low-dose combined spinal-epidural anaesthesia (CSE) has also been compared with conventional epidural anaesthesia in a prospective trial (9), concluding that CSE is a safe alternative to epidural anaesthesia in severe pre-eclamptic patients.

It appears that spinal anaesthesia may be used with the same haemodynamic safety as epidural anaesthesia for caesarean section in haemodynamically stable severely pre-eclamptic women and offers some additional benefits with regard to rapidity, simplicity, and cost. Each case needs careful evaluation. For example, placental abruption, which is frequently associated with hypertensive diseases of pregnancy, would further reduce plasma volume such that spinal anaesthesia would be contraindicated.

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AMNIOTIC FLUID EMBOLISM

Amniotic fluid embolism is a rare catastrophic syndrome that occurs during pregnancy or in the immediate post partum period. Its incidence is quoted as between 1 in 8,000 to 1 in 80,000 pregnancies in the United States with maternal mortality rates as high as 86% (with 50% dying within the first hour). The discrepancy with respect to the incidence and mortality may be due to the variability of presentation and lack of a definitive diagnostic test. Recent studies have improved the understanding of amniotic fluid embolism, enhancing the definition, diagnosis and management.

Neonatal survival is reported at 70%.

Amniotic fluid embolism was first described in 1926 by Meyer (1) but was not recognised as a syndrome until the publication of an autopsy series of eight women who died of sudden shock during labour by Steiner and Lushbaugh in 1941 (2). The labours of these women were described as being violent, powerful and hard and they found foetal cellular material and/or meconium in the pulmonary circulation at autopsy. They postulated that hyperstimulation created a point of entry for amniotic fluid to enter the maternal circulation resulting in pulmonary embolism and a severe systemic reaction.

More recent research has questioned their conclusions that the symptoms of amniotic fluid embolism are purely an embolic event. The pathogenesis of amniotic fluid embolism syndrome is unclear. Morgan (3) found hyperstimulation in only 28% of 272 case reports of amniotic fluid embolism and only 22% used oxytocin. Clarke et al (4) analysed the national registry (46 cases, 1983-1993). Hyperstimulation was noted in only 2 cases, oxytocin was used in 50% of cases, 67% had a male foetus and 41% had a history of drug allergy or atopy. The overall mortality was 61% with only 15% of survivors neurologically intact. Previously Clark reported from animal and human studies that foetal elements were not always found in the maternal circulation of women who developed amniotic fluid embolism and that foetal material was often found in the circulation of women who did not develop amniotic fluid embolism syndrome. They speculated that amniotic fluid embolism syndrome might result from exposure to foetal material, rather than an embolic event (dependent on the amount of amniotic fluid), that initiates a syndrome similar to anaphylactic or septic shock in a susceptible mother. Clark suggested that the term "amniotic fluid embolism" be discarded in favour of "anaphylactoid syndrome of pregnancy".

Amniotic fluid typically contains lanugo, scalp hairs, skin cells, prostaglandins arachidonic metabolites and zinc coproporphyrin.

The diagnosis of amniotic fluid embolism remains a diagnosis of exclusion in parturients who develop sudden cardiovascular collapse, acute left ventricular failure, disseminated intravascular coagulation (DIC) and neurological impairment (hypoxia, hypotension with shock, uncontrolled bleeding and altered mental state). These symptoms occur in 80 to 100% of cases. The altered mental state is thought to be due to hypoxia and impaired oxygen delivery to the brain. It is unproven that amniotic fluid embolism has a direct effect on the central nervous system by either vascular obstruction or other mechanisms. Other common presenting signs and symptoms include seizures, confusion, agitation

cough, cyanosis, foetal bradycardia, fever, nausea and vomiting and headache. Seizure activity is present in 50% of patients.

There are case reports of amniotic fluid embolism presenting with severe haemorrhage and DIC as the first sign and others of a less severe presentation with early signs of respiratory failure and DIC but no progression.

Classically symptoms occur during labour and delivery or in the immediate postpartum period however rarely cases have been reported with a delayed onset of 48 hours. Amniotic fluid embolism has also been described after amniocentesis, removal of the placenta and first and second trimester abortion. There is inconsistent support for risk factors such as hyperstimulation, uterine tetany, use of oxytocin, multiparity, increased maternal age, increased gestational age and caesarean section. There is no evidence that survivors of amniotic fluid embolism are at increased risk with subsequent pregnancy.

The differential diagnosis of amniotic fluid embolism includes pulmonary embolism, air embolism, haemorrhage, aspiration of gastric contents, anaphylaxis, myocardial infarction, eclampsia, and transfusion reactions.

There are no specific laboratory tests to diagnose amniotic fluid embolism. Aspiration of foetal material from a pulmonary arterial catheter is unreliable. Some researchers have found elevated tryptase levels, suggesting an association with anaphylaxis however other investigators have found normal tryptase levels but low complement levels. Other methods described include foetal antigen (sialyl Tn) and maternal zinc coproporphyrin levels however these test have not been validated and diagnosis remains clinical.

Patients with suspected amniotic fluid embolism need urgent arterial blood gas analysis, electrolytes, haemoglobin and platelet count, and coagulation profile. Chest X-ray may reveal evidence of cardiogenic and non-cardiogenic pulmonary oedema. An ECG may reveal ischaemia and infarction.

Animal and human data suggest that there may be a biphasic pathophysiology in the development of the amniotic fluid embolism. Moore et al (5) suggest, "The clinical presentation of amniotic fluid embolism is complex and has various clinical manifestations that may or may not be present depending on the patient". They further suggest that "the clinical course seems to have phases that are likely temporally related to pathophysiological changes. When amniotic fluid embolism is severe, obstructive and cardiogenic shock appears to be dominant during the early phase, whereas the later phase seems to be marked by cardiogenic, distributive, and at times, haemorrhagic shock".

Initial hypotension, hypoxia and shock may result from acute right heart failure from embolisation of amniotic fluid. Haemodynamic data from animal studies show an early acute rise in right heart pressures, pulmonary hypertension and systemic hypotension.

Arachidonic acid metabolites have been implicated in the humoral mediated pathogenesis of sepsis and anaphylaxis. Echocardiography and pulmonary artery catheter data in women with amniotic fluid embolism is consistent with a second humoral induced acute left ventricular failure and cardiogenic shock. Left heart failure, coagulopathy and

cardiovascular instability may represent the second pathophysiological phase of the syndrome.

Hypoxia is present in 93% of patients and may be severe in both early and later phases though perhaps due to different aetiology. The initial hypoxia may be due to severe ventilation perfusion mismatch secondary to pulmonary embolism and/or cardiogenic pulmonary oedema. Though cardiogenic pulmonary oedema may continue to contribute to hypoxia, up to 70% of patients who survive the initial few hours develop non-cardiogenic pulmonary oedema.

Similarly hypotension may have several aetiologies whose importance varies with time. Cardiogenic shock and perhaps obstructive shock are likely to predominate early with an increasing contribution from distributive shock and at times haemorrhagic shock.

DIC occurs in up to 83% of patients. Amniotic fluid contains mediators, including thromboplastin, which may initiate the clotting cascade or DIC may develop later from the systemic inflammatory response.

There are no prophylactic measures to prevent amniotic fluid embolism and no reliable predictive risk factors. The management of amniotic fluid embolism is supportive. The initial focus is on rapid and aggressive cardiopulmonary stabilisation/resuscitation. (100% oxygen, large bore intravenous access and aggressive fluid resuscitation, vasopressor treatment for refractory hypotension, preparation for CPR and treatment of arrhythmias). The anaesthetist must be aware of the rapidity of onset and potential severity of amniotic fluid embolism. The time from collapse to death has been reported as 1-7 hours. 50% of patients will have seizures and require anticonvulsants. Early airway management with endotracheal intubation may be warranted for airway protection and will optimise oxygenation.

Pulmonary artery catheters or central venous catheters may help manage fluid resuscitation but their insertion must not delay the appropriate treatment. Transthoracic and oesophageal echocardiography can guide fluid management.

DIC with haemorrhage is best managed by repeated specific laboratory investigations and treated with specific blood products. DIC and uterine atony associated with amniotic fluid embolism may necessitate hysterectomy.

Amniotic fluid embolism prior to delivery of the foetus significantly complicates management. The goal of treatment must be the restoration/maintenance of normal maternal respiratory and cardiovascular performance. Vasopressors must not be delayed because of fear of uterine hypoperfusion. The uterus must be displaced for effective CPR. To prevent maternal and foetal mortality a perimortem caesarean section must be initiated within minutes.

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LABOUR ANALGESIA

Labour pain is frequently described as the most severe pain that a woman will experience during her lifetime. The pain of first stage of labour is due to cervical dilatation and effacement and uterine contraction. It is visceral pain, which means it is poorly localised and is mediated by the spinal segments from the tenth thoracic to the first lumbar segment. It is referred to the lower abdomen, lower back and anterior part of the thighs. The second stage of labour is somatic, which means that it is better localised. The pain is due to the stretching of the perineum and is mediated by the sacral segments two, three and four.

Pain in labour induces a stress response in the mother as well as significant respiratory and cardiovascular changes. When she is in labour, painful contractions increase minute ventilation by as much as 300%, which leads to hypocarbia and alkalaemia. In between contractions, the patient may hypoventilate, which can result in maternal and fetal hypoxia. Cardiac output is increased by 40% at term due to increased stroke volume and heart rate. Contractions in labour will further increase the cardiac output and there is a peak increase in cardiac output in the immediate post partum period.

Non-pharmacological methods of pain relief require patient preparation and antenatal education. Almost all non-pharmacological methods can facilitate more successful coping with labour pain, which increases emotional satisfaction and enhances the feeling of autonomy. Strategies to try include, remaining upright and mobile in early labour, bathing, breathing techniques and the presence of a support person in labour.

Pharmacologic methods of pain relief include the use of nitrous oxide, parenteral opioids and regional anaesthesia.

Nitrous oxide can be effective for 50% of women in labour. For maximal results, breathing of nitrous oxide (mixed with oxygen) should start 45 seconds before the contraction. This is difficult to time effectively. The low blood-gas solubility of nitrous oxide allows for a rapid onset and offset of action. It is important that the woman self administers the gas to maintain safety. The side effects include dizziness, excessive sedation and loss of awareness if there is prolonged self-administration. The most frequently used dose of nitrous oxide is 50% with a range of 0 to 70% for labour.

Pethidine (Meperidine) is the most frequently use parenteral opioid in labour in Australia. The dose is one to 1.5 mg/kg every four hours. The dose should be timed so that ideally, there is greater than four hours between the dose and delivery of the baby so as to avoid neonatal respiratory depression. If neonatal depression occurs, naloxone 0.1 mg/kg should be administered. Pethidine is effective in approximately 30 to 50% of women in labour. Another 30% of women will find the same dose ineffective. A dose of pethidine will take 30-45 minutes to have an effect. The common maternal side effects include, drowsiness, dizziness, disorientation and nausea. In a double blinded randomised, placebo controlled trial of intramuscular pethidine for first stage of labour pain in 50

women, Tsu et al showed a greater reduction of the VAS pain score in the pethidine group (-17mm) than in the intramuscular saline group at 30 minutes ($p=0.009$). The time to first request for subsequent analgesia was also greater in the pethidine group (232 minutes compared to 75 minutes). The authors concluded that systemic pethidine was more effective at relieving labour pain than placebo but that its analgesic effect was modest.

Regional analgesia for labour encompasses pudendal nerve block, paracervical block, spinal, epidural and combined spinal and epidural block. Regional anaesthesia is the most effective form of analgesia for labour.

Epidural analgesia

Epidurals are the most effective and consistently reliable way of relieving childbirth pain. An epidural will provide conduction anaesthesia of the spinal nerves and the spinal cord. (Neuraxial block) The aim is to provide analgesia by blocking the A-delta and C fibres of the spinal segments involved in the transmission of labour pain. However, because spinal nerves transmit motor, autonomic and other sensory impulses, they will be blocked too if a large enough dose of local anaesthetic is applied to them.

The conduct of epidural analgesia for labour requires the operator to explain the procedure and gain consent for the procedure. A skilled assistant should be in attendance during the insertion and after the block has been established. The assistant should help to position the patient and perform 5 minutely observations of maternal blood pressure and heart rate, height of the block and foetal heart rate for 20 minutes after a top up or the establishment of the epidural block. Where an epidural infusion is in use in labour and the block is stable, observations can be performed 1/2 hourly with continuous cardiography monitoring.

Intravenous access is established before the conduct of the epidural. A fluid bolus of at least 500 ml of balanced salt solution is given. Resuscitation drugs and equipment should be immediately available and checked.

Drugs used in the epidural space

The aim is to provide analgesia with little motor blockade. Pain free mobility requires the blockade of C and A-delta fibres whilst preserving A-alpha fibres. This is best achieved by using low concentrations of local anaesthetic agents and opioids. Modern epidurals will consist of high-volume low-concentration doses of anaesthetic. Apart from the differential blockade, this will also reduce the incidence of hypotension.

Traditionally bupivacaine was the local anaesthetic of choice for epidural analgesia. Its advantages are its long duration of action and potency. The disadvantages of bupivacaine are its relatively slow onset and its cardiac toxicity with inadvertent intravenous injection due to its rapid binding to and slow dissociation from cardiac sodium channels.

Newer single enantiomer drugs have been developed with the promise of lower cardiac toxicity. They are ropivacaine and levo-bupivacaine. Ropivacaine has been shown to be less potent and its therapeutic index, which is the margin between its effective dose and toxic dose, is smaller than for bupivacaine, so its safety advantage may not be as great as originally thought.

Centrally administered opioids act on the opioid receptors in the substantia gelatinosa of the dorsal horn of the spinal cord. They are more effective at C-fibre blockade than A-delta fibre blockade and are more effective for first stage pain relief than for delivery. They will not cause motor block or numbness or hypotension. The agents most commonly used are fentanyl or sufentanil, because they are very lipid soluble and penetrate the dura. This allows for a more rapid onset and shorter duration of action than morphine, which may take two hours to cross the dura and when given intrathecally, its effects may last 24 hours. The most common side effects of centrally administered opioids are pruritus, nausea and vomiting, urinary retention and respiratory depression. When given intrathecally, opioids may cause uterine hyperactivity and a self limiting foetal bradycardia. This is thought to be due to a decrease in maternal catecholamines. (Clarke VT, Smiley RM, Finster M. 1994)

Techniques

After positioning the patient in the lateral or sitting position, the skin is prepared with antiseptic solution. The correct spinal level for epidural insertion is identified (usually L3-4 or L4-5) and local anaesthetic is infiltrated into the skin and subcutaneous tissues. An 18 or 16G Tuohy needle is inserted with the bevel directed cephalad. A loss of resistance technique is used to identify the epidural space and a 20g catheter is fed so that 3-4 cm remains in the epidural space. The catheter can then be tested with a 3ml dose of local anaesthetic (generally 2% lignocaine) to ensure that it is correctly positioned. The total dose of local anaesthetic is then inserted in increments until the correct block height is attained. (T10 upper level for 1st stage of labour) This may take up to 20 minutes with longer-acting local anaesthetics such as bupivacaine or ropivacaine. An infusion of weak local anaesthetic with opioid is commenced to provide ongoing analgesia during the labour. Further top ups via the catheter may be given for breakthrough pain.

Loss of resistance to saline or air

The epidural space is best located in the lumbar area with a loss of resistance to fluid technique. Air has been used for many years but may present some problems. There is the potential for a large amount of air to be introduced into either the epidural or subarachnoid space, or indeed into an epidural blood vessel. As a result, the patient may end up with a patchy block, headache or neck pain, pneumocephalus or an air embolus. There is a smaller chance of dural puncture if saline rather than air is used for loss of resistance.

How far to thread the catheter

Most modern catheters are multi-orifice catheters and should be threaded into the epidural space far enough so that the catheter will not get dislodged during labour, yet not

so far that it emerges from an intervertebral foramen, which may cause a unilateral block. The optimal depth is 4 cm.

Test dosing

The catheter should be tested to ensure that it is not in the intrathecal space or intravascular. The recommended test dose is lignocaine 45mg, which will produce a spinal block if the catheter is intrathecal. It is important to allow enough time for the dose to be effective. Immediate testing (within one minute) will not produce a motor block. A 45 mg dose of intrathecal lignocaine will produce a motor block at S1 after 6 minutes. To test for intravenous placement in labour, the options include the use of epinephrine or fentanyl. The heart rate response in labour is unpredictable so fentanyl is preferred. An intravenous bolus will produce sedation within 5 minutes.

Options for the maintenance of the block:

Epidural bolus administration

All epidural regimens commence with a bolus dose to achieve analgesia. Ongoing analgesia can be managed with intermittent boluses by the anaesthetist or midwife, typically 0.5% or 0.25% bupivacaine is used. The problems associated with boluses include pain in between boluses, moderate to severe motor block and hypotension after bolus dosing.

Epidural infusions

It has become routine to use continuous infusions of dilute local anaesthetic plus lipid soluble opioids. The use of infusions (over intermittent boluses) has the advantage of better pain relief with less motor block. Common infusion solutions are: bupivacaine 0.125% with fentanyl 2 mcg/ml, ropivacaine 0.2% with fentanyl 2 mcg/ml or more recently, bupivacaine 0.0625% with fentanyl 2 mcg/ml at a rate of 10-12 ml/hr.

Patient Controlled Epidural Analgesia

PCEA may offer the advantages of greater patient autonomy and satisfaction, lower overall doses of local anaesthetic and reduced need for physician or midwife epidural top ups. Dilute solutions of bupivacaine (0.1%) or ropivacaine (0.1% to 0.2%) or levobupivacaine (0.1%) are used with or without opioid. The usual dose is 3-5 ml with a lockout of 10-20 minutes. A background infusion may be beneficial when labour is induced, as it is more likely to be a prolonged and more painful labour.

Side effects

The side effects of the epidural depend largely on the dose of local anaesthetic used. Any neuraxial block will block nerve conduction in motor, sensory and sympathetic fibres to some extent.

A loss of sensation is inevitable and some degree of motor block can be expected. This generally means the patient cannot ambulate, will require a urinary catheter and may require a lift-out forceps delivery.

The autonomic blockade will produce vasodilatation and may create hypotension. If the block extends to the T1-4 fibres, then bradycardia may also occur.

Shivering is very common. The cause is not clear, but there may be a degree of heat loss (although the women often do not complain of feeling cold) and it is more common with larger doses of local anaesthetic.

Side effects will also occur due to drug administration. For example, pruritus, nausea, urinary retention and respiratory depression may occur with the administration of epidural opioids.

Complications

The complications of epidural analgesia range from the more common but mild to the rare and catastrophic.

- **Incomplete epidural block**

- Incidence is about 10% (failed block 1%)

- Unilateral block –partially withdraw catheter and give top up with patient lateral, painful side down.

- Sacral pressure or pain, missed segments or back pain with contractions –try fentanyl 50 to 100 mcg via the catheter.

- Catheter migration, partial intravascular injection, subdural or paravertebral block
Are the patient's expectations too high

- **Total spinal anaesthesia 1:10,000**

- If a large dose of local anaesthetic has been administered into the subarachnoid space, then this will cause a high spinal block and will lead to refractory hypotension and a loss of consciousness requiring intubation and ventilation until the block wears off.

- Identification

- Sudden hypotension, rapid profound analgesia and motor block, nasal stuffiness

- Apnoea, unconsciousness, dilated pupils

- Precautions to avoid total spinal

- Carefully aspirate the needle or catheter

- Check for a falling meniscus

- Give a suitable test dose

- Management

- Apply oxygen, position on the side, assist ventilation, prepare for intubation

- Call for help

- Treat hypotension with rapid infusion and vasopressors

- Treat bradycardia with atropine

- Monitor the foetus, may require urgent delivery

- Provide anaesthesia to avoid awareness

- **Bloody tap**

Incidence with the needle 0.3% - 1.7%, with the catheter 2.8 – 9%. The incidence of intravascular injection occurs in 1:10,000

Management of bloody tap—Remove the catheter or needle

Re position one space higher

Further doses should be given by the anaesthetist and in increments of no greater than 3 ml of 0.25% bupivacaine to avoid intravascular injection

Local anaesthetic toxicity is another potentially severe complication. If injected intravenously, the large dose used to establish an epidural block may cause fitting and loss of consciousness. If a large dose of bupivacaine is injected intravenously into an epidural vein, cardiac toxicity will occur.

- **Dural tap**

Accidental dural puncture is usually recognized when it occurs by the free flow of CSF through the needle or catheter. The incidence is roughly 1 in 300 epidural insertions. When it is recognized, there are usually no serious complications. However, about 60% of the women will develop a post dural puncture headache, some of whom will require an epidural blood patch.

Incidence 0.2 – 2%

Occasionally unrecognised and PDPH is the first sign.

Headache occurs 12-36 hrs post partum

Management

- Consider using sub arachnoid analgesia

- All top ups should be given by the anaesthetist

- Remove the catheter after delivery and leave intravenous line for 24 hours

- Follow the patient up at least daily for 3 days

- Allow the patient to mobilize.

- If a headache develops, assess thoroughly

- Use simple analgesics first

- Offer an epidural blood patch

- **Convulsions**

- may be related to local anaesthetic toxicity (1:9000-1:20 000)**

The main threat to mother and baby is from hypoxia

Possible causes

- Pregnancy related (elcampsia)

- Anaesthetic related (Local anaesthetic toxicity 1:9000 to 1:20,000, intravenous injection)

- Coexisting disease (epilepsy, hypoglycaemia, cerebral pathology)

Management

Call for help

Attention to airway, breathing and circulation –protect the airway from aspiration and ensure oxygenation. In late pregnancy this means intubation. Use thiopentone to control the fit and suxamethonium to facilitate intubation.

Implement anti-convulsant therapy

Liaise with the obstetric team about the need for urgent delivery

- **Severe hypotension 1:1000**

Occurs due to the combination of autonomic blockade with subsequent vasodilatation with or without bradycardia if thoracic segments are blocked and hypovolaemia and aortocaval compression.

Management

Non-pharmacological

–Positioning,

–fluid loading

Pharmacological

–Anaesthetic technique

–Beta adrenergic agent: ephedrine

–Alpha adrenergic agents: metaraminol, phenylephrine

Epidural infection leading to abscess or epidural haematoma will cause compression of the spinal cord leading to paraplegia if the mass is not compressed within 6 hours. This is rare.

The incidence of permanent paralysis is rare and is of the order of 1: 80,000.

Neural injury due to parturition (obstetric palsy - often a foot drop or obturator nerve palsy from a difficult forceps delivery) occurs in one in 3000 deliveries. These are temporary and resolve within 6 weeks. Similarly, nerve root injury from needling of the epidural space may occur and are mostly temporary.

Backache occurs in up to 50% of women who have had a baby regardless of whether or not they have received an epidural. Most of this is related to changes in posture, relaxation of the pelvic joints and childbirth itself. Bruising and tenderness over the epidural needle insertion site is common. This is generally not a problem.

Does epidural analgesia slow the progress of labour?

Epidural analgesia in labour has been blamed for slow progress in labour and the increase in likelihood of caesarean section. It has been suggested that motor block in second stage increases the need for instrumental delivery. The problem is that women with abnormal presentations and long labours experience greater pain and become fatigued, necessitating regional analgesia so there is an association with instrumental delivery, but this does not necessarily imply causation. In a Swedish study, which looked at that country's medical

birth register during a two-year period, it was found that there was no clear association between epidural use and caesarean section or instrumental delivery. Therefore, there is no indication that the use of epidurals should be restricted in order to improve instrumental delivery rates.

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PHYSIOLOGIC CHANGES OF PREGNANCY

Pregnancy results in physiologic changes in many organ systems. These changes begin in the first trimester and continue until after delivery. Labour presents its own unique physiologic state and will be discussed below. Many of these changes will impact on anaesthesia.

Cardiovascular changes

Changes in the cardiovascular system prepare the mother for delivery. Intravascular blood volume increases. This increase begins in the first trimester and at term there is a 30-40% increase in total blood volume (about 1000 ml). There is an increase in plasma and red cell volume, but the increase in plasma volume is greater. This results in the physiologic anaemia of pregnancy. During a normal vaginal delivery, blood loss is about 500 ml, which is offset by the autotransfusion of blood from a contracted uterus. The pre-pregnancy intravascular volume is reached by 7-14 days post partum.

Cardiac output is increased by 40% at term due to systemic vasodilatation, increased contractility, myocardial hypertrophy and an increased stroke volume and heart rate. This increase in cardiac output is reached by the end of the 10th week of gestation. There is a progressive decrease in systemic vascular resistance throughout pregnancy and mean arterial blood pressure is preserved although systolic blood pressure is decreased. The uterus at term receives up to 20% of the maternal cardiac output.

The supine hypotensive syndrome is a decrease in maternal blood pressure that occurs in a proportion (about 10-15%) of pregnant women near term when they lie supine. The mechanism for this drop in blood pressure is due to the gravid uterus obstructing the inferior vena cava and thereby reducing venous return to the heart. When the inferior vena cava is obstructed, venous blood from the inferior half of the body is redirected through the paravertebral venous plexuses to the azygous veins and then the superior vena cava. Supine hypotension can be avoided by maintaining the pregnant woman in the left lateral position or by using left uterine displacement. Because the aorta may also be compressed in the supine position, uterine blood flow may be compromised. If there is any foetal distress, left uterine displacement should be used.

	Average change (%)
Intravascular fluid volume	+35
Plasma volume	+45
Red cell volume	+20
Cardiac output	+40
Stroke volume	+30
Heart rate	+15
Peripheral circulation	
Systolic blood pressure	No change
Systemic vascular resistance	-15
Diastolic blood pressure	-15
Central venous pressure	No change
Femoral venous pressure	+15

(Stoelting RK, Dierdorf SF)

Respiratory changes

The upper airway of the pregnant woman becomes oedematous due to capillary engorgement and requires the placement of a smaller endotracheal tube if general anaesthesia is required. Due to nasal obstruction and oedema, the placement of a nasal tube is not recommended as this may lead to epistaxis.

Minute ventilation increases early in pregnancy, presumably due to stimulation of ventilation by progesterone. By the end of the first trimester, minute ventilation is increased by about 50%. The resting arterial partial pressure of carbon dioxide (PaCO₂) decreases to near 30mmHg. The partial pressure of oxygen also increases, but the arterial pH is nearly normal due to the renal excretion of sodium bicarbonate.

Lung volumes change after the fifth month of gestation, probably due to the cephalad displacement of the diaphragm by the gravid uterus. There is a 20% decrease in expiratory reserve volume and residual volume. Functional residual capacity is therefore decreased by a similar amount. This has implications for anaesthesia, as it reduces the potential oxygen stores. Because of the 20-40% increase in oxygen consumption and the reduction in FRC, there is a tendency to hypoxia during periods of apnoea.

In the supine position, airway closure occurs. This normally does not lead to hypoxaemia unless there is concomitant supine hypotension, or obesity or respiratory disease. Airway resistance is decreased in pregnancy.

	Average change
Minute ventilation	+50%
Tidal volume	+40%
Respiratory rate	+10%
PaO ₂	+10 mmHg
PaCO ₂	-10 mmHg
pH _a	no change
Total lung capacity	no change
Vital capacity	no change
Functional residual capacity	-20%
Expiratory reserve volume	-20%
Residual volume	-20%
Airway resistance	-35%
Oxygen consumption	+20%

(Stoelting)

Neuronal changes

During pregnancy, the minimal alveolar concentration for volatile anaesthetics is reduced by 40%. This is apparent from the first trimester. The sensitivity to local anaesthetics increases. Lumbar lordosis, epidural vein engorgement, decreased volume of CSF and decreased volume of the epidural space all lead to greater spread of local anaesthetic administered either epidurally or spinally. The doses administered for an epidural should be reduced by 30-50%.

Gastro-intestinal changes

The parturient is at increased risk of regurgitation of acidic gastric contents and therefore the development of acid aspiration syndrome. The enlarged uterus displaces the pylorus, which retards gastric emptying and the angle of the gastro-oesophageal junction is also changed to produce relative incompetence and increase regurgitation. In addition gastric motility is reduced due to progesterone. The placenta produces gastrin, which increases gastric acid production. All of these changes mean that the airway needs to be protected with a cuffed endotracheal tube during general anaesthesia in pregnancy. It is recommended that a histamine receptor antagonist (such as ranitidine) and a non-particulate antacid (such as sodium citrate) be given before general anaesthesia (such as sodium citrate) to bring gastric pH towards neutral.

During labour, gastric emptying is delayed. This is worsened by the administration of opioids.

Renal changes

There is increased renal blood flow during pregnancy and an increase in glomerular filtration rate and creatinine clearance. The normal upper limits of the serum urea and creatinine levels are reduced by 50%. The renal calyces are dilated from the second trimester, which tends to lead to urinary stasis, putting the pregnant patient at risk for urinary tract infection.

Hepatic changes

A modest increase in the levels of hepatic enzymes can occur during any normal pregnancy and do not indicate liver disease. The colloid oncotic pressure falls, as does the serum albumin. Serum cholinesterase is reduced but is rarely of clinical significance.

Haematologic changes

There is an increase in red cell volume that does not match the increase in plasma volume resulting in a physiological anaemia. The white cell count increases, probably as a result of cortisol and oestrogen.

There is a tendency towards a hyper coagulable state as a result of increased fibrinogen, coagulation factors II, VII, VIII, IX, X, XII, reduction in plasminogen activator and increased number of platelets. The prothrombin time and activated partial thromboplastin time is decreased by 20%.

Labour

During labour, painful contractions increase minute ventilation by up to 300%, which leads to hypocarbia and alkalemia. Between contractions, the patient may hypoventilate, which can lead to foetal and maternal hypoxaemia.

Oxygen consumption tends to rise during labour, and it may increase by 100% during second stage.

There are marked fluctuations in the cardiac output during labour and second stage labour produces more than 100% increase in cardiac output compared to the non-pregnant state. Pushing increases venous return and elevates atrial pressures.

During uterine contractions, there is an autotransfusion of blood from the uterus to the maternal circulation. This can increase central blood volume by 25%. The blood pressure tends to rise during contractions. The cardiac output increases by 60% after delivery due to the closure of virtual arterio-venous fistula that is the placental circulation and relief of aorto-caval compression.

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MATERNAL CARDIAC DISEASE

Introduction

The incidence of cardiac disease in pregnant patients in developed countries is 0.2 to 3%. Rheumatic disease is less frequent but corrected congenital heart disease, cardiomyopathy and coronary heart disease is becoming more important.

Cardiac disease was the second most frequent indirect cause of maternal death in the Report of the Confidential Enquiries into Maternal Deaths in the United Kingdom 2000-2002. The leading causes of maternal cardiac death were peri partum cardiomyopathy, myocardial infarction, aortic dissection and secondary pulmonary hypertension. Patients with cardiac disease benefit from careful preoperative evaluation, medical optimisation and planned elective delivery. In most cases, assisted second stage is planned to avoid excessive pushing and to reduce the cardiovascular stress of delivery. Caesarean section is reserved for obstetric indications, as it is not without its own risks.

Physiologic changes during pregnancy

Changes in the cardiovascular system start in the first trimester. These changes are well tolerated until the 20th week, after which time further adaptation is difficult for the parturient with cardiac disease.

Intravascular volume increases by 50%. There is a relative anaemia due to the higher increase in plasma volume as compared with the red cell mass. There is a progressive decrease in systemic vascular resistance throughout pregnancy, cardiac output increases by 30-40% and mean arterial blood pressure is preserved although systolic blood pressure is decreased. The increase in cardiac output is achieved by systemic vasodilatation, increased contractility, myocardial hypertrophy and an increase in heart rate.

There are marked fluctuations in the cardiac output during labour and second stage labour produces more than 100% increase in cardiac output compared to the non-pregnant state. Excessive pushing increases venous return and elevates atrial pressures.

Coagulation factors VII, VIII, X, XII and fibrinogen increase during pregnancy causing a hypercoagulable state. Fibrinolytic activity and anticoagulant activity is decreased. Hypercoagulability of pregnancy increases the risk of arterial thrombosis and embolization in the cardiac patient.

Predictors of cardiovascular complications during pregnancy include earlier cardiovascular events or arrhythmias, New York Heart Association classification of more than 2 or cyanosis, mitral valve stenosis or aortic valve stenosis and ejection fraction of less than 40%.

Neuraxial blockade and cardiovascular changes

Neuraxial anaesthesia is considered safe for many cardiac patients if there has been careful assessment and optimisation and invasive monitoring is used.

During labour, pain increases cardiac output by 60% due to catecholamine release, which is abolished by adequate pain relief. Cardiac output increases further with each contraction due to autotransfusion of the uterine blood.

Neuraxial blockade reduces the cardiovascular stress response to pain, reduces the effects of the Valsalva manoeuvre by decreasing the pushing reflex and allows the level of analgesia to be adjusted according to the stage of labour. However, the sympathetic block reduces systemic vascular resistance due to arteriolar dilatation and cardiac preload due to veno-dilatation followed by reflex tachycardia. A low systemic vascular resistance is poorly tolerated in the patient with aortic and mitral stenosis and coronary artery disease. It can also reverse the pressure gradient across a left to right intracardiac shunt (eg VSD), which can lead to dangerous decreases in pulmonary blood flow.

It is important to consider the degree of cardiac failure, the use of concomitant cardiac medications and therapeutic anticoagulation, as these will influence the ability to safely provide neuraxial anaesthesia. Patients with significant cardiac disease should be delivered in an institution with cardiac and intensive care facilities where possible.

Neuraxial block is considered a risk for the cardiac patient due to the sympathetic block that decreases cardiac preload with subsequent hypotension and imbalance in the autonomic innervation of the heart, which may lead to arrhythmias. A sudden onset sympathetic block is potentially dangerous, so single-shot spinal techniques with local anaesthetic are not recommended. However, carefully conducted epidurals or combined spinal-epidurals are considered advantageous for labour and delivery even for the patient with severe cardiac disease.

A rapid onset of sympathetic block is avoided by using incremental dosing with invasive monitoring of arterial pressure and cardiac filling pressures.

The use of opioids for the first stage of labour, carefully titrated segmental epidural analgesia with low concentrations of local anaesthetic and opioids for second stage, and low spinal anaesthesia for vaginal instrumental delivery have been used with good results in patients with severe cardiac disease. (Gomar, Errando 2005).

Many cardiac diseases are associated with a reduced clearance of local anaesthetics, so reduction of doses for repeated boluses or infusions should be used. Intravascular volume load should be avoided in most cases, so hypotension should be treated with small doses of ephedrine, dopamine or phenylephrine. Lateral tilt to avoid aorto-caval compression becomes very important in the cardiac parturient.

Oxytocin, ergotamine and tocolytic beta-adrenergic drugs should be administered carefully due to their important cardiovascular effects. Most cardiac medications have no

relevant interaction with neuraxial blockade, but one should always check to see that the patient is not anticoagulated and provide antibiotic prophylaxis where indicated.

Congenital heart disease

With improved medical care for children with congenital heart disease, increasing numbers of patients with congenital lesions survive to adulthood and reproductive age. Patients with simple surgical corrections like atrial or ventricular-septum defects result in the largest number of successful pregnancies of those patients with congenital heart disease. Maternal cyanotic valvular defects lead to impaired utero-placental perfusion and diminished foetal oxygenation. In a retrospective analysis of 44 patients with cyanotic heart disease, the rate of live births was 43% and only 27% were born at term. The incidence of maternal arrhythmias, cardiac decompensation, thromboembolism and endocarditis was 32% but mortality was low. There was one death from endocarditis 2 months after delivery. (Presbitero 1994)

VSD

Small VSDs should not be a problem for the provision of neuraxial analgesia in the parturient but antibiotics should be given. In patients with a moderate sized VSD, pain and increased SVR may lead to increases in the left-to-right shunt and congestive cardiac failure. Epidurals should be carefully titrated to avoid a large drop in SVR, which can lead to reversal of left-to-right shunt and hypoxaemia.

Large defects lead to pulmonary vasoconstriction, which is initially reversible but gradually becomes irreversible with resultant pulmonary hypertension. In women with pulmonary hypertension, maternal and foetal mortality reaches 50%. Significant decreases in SVR caused by autonomic blockade may lead to Eisenmenger's syndrome. A CSE or segmental epidural early in labour is indicated. The use of air for the detection of the epidural space may lead to a paradoxical embolism if it is accidentally injected into a vein.

Tetralogy of Fallot

Patients with incomplete or no correction of tetralogy of Fallot do not tolerate a decrease in preload and systemic vascular resistance and neuraxial blockade should be avoided.

Eisenmenger's syndrome

This is defined as pulmonary hypertension at systemic levels with a reversed or bidirectional shunt through a large left to right communication or due to pulmonary artery occlusion. The size of the shunt will depend on the ratio of the systemic vascular resistance to the pulmonary vascular resistance.

Significant mortality can be expected in patients with either Eisenmenger's syndrome or pulmonary hypertension. The increasing cardiac load during pregnancy with an increase in circulating blood volume and cardiac output, lead to progressive right ventricular failure.

One should avoid significant drops in central venous pressure and systemic vascular resistance. A combined spinal-epidural technique is possible for labour analgesia by

using an initial injection of 25mcg of fentanyl with 2.5mg of bupivacaine in the intrathecal space, followed by an epidural infusion of dilute local anaesthetic with opioid. In this way a significant sympathetic blockade can be avoided.

Central venous pressure and arterial pressure monitoring should be extended into the post partum period, as most deaths occur several hours after delivery.

Aortic Coarctation

Aortic coarctation can worsen during pregnancy with obstruction of the left ventricular outflow, left ventricular failure and aortic rupture or dissection. Neuraxial blockade is not recommended as cardiac preload, systemic vascular resistance and heart rate should be kept normal or high. Caesarean section should be performed under general anaesthesia.

Valvular heart disease

Valvular stenosis is a flow obstruction with a pressure gradient between the atrium and left ventricle or the left ventricle and aorta. The cardiac output is fixed due to the flow obstruction and the pressure load on the left atrium or left ventricle. The valvular area will determine whether pregnancy will be tolerated or not.

Mitral stenosis

The most important symptom is dyspnoea on effort. This becomes worse when diastolic filling time is shortened by tachycardia.

The avoidance of tachycardia is most important as the diastolic filling time should be maximized. Segmental epidural analgesia and anaesthesia is recommended. Phenylephrine is the vasopressor of choice. Symptomatic patients should receive arterial and pulmonary catheter monitoring until at least 24 hours after delivery.

Aortic stenosis

Patients with aortic stenosis have a fixed cardiac output. The cardiac output depends on heart rate and adequate preload. The anaesthetic management must avoid both tachycardia and bradycardia and an adequate preload must be maintained. The patient may not be able to tolerate the reduction of preload and afterload following sympathetic blockade due to regional anaesthesia. Neuraxial analgesia is not absolutely contraindicated in these patients but should be performed with invasive monitoring.

Mitral regurgitation

Mitral regurgitation and prolapse are well tolerated in pregnancy because a decrease in SVR will reduce the regurgitant flow. Atrial arrhythmias and embolism remain a risk. The increase in systemic vascular resistance caused by pain is avoided by the use of epidural anaesthesia in labour. Adequate filling should be maintained and invasive monitoring is only indicated for the symptomatic patients.

Aortic regurgitation

Aortic regurgitation causes chronic volume overload of the left ventricle resulting in hypertrophy and dilatation. Myocardial oxygen requirements are increased due to the left ventricular hypertrophy. Anaesthetic goals are to reduce pain so as to avoid an increase in systemic vascular resistance and to avoid bradycardia, which will increase regurgitant flow. Epidural anaesthesia is recommended in labour and invasive monitoring should be used in the sympathetic patient.

Coronary artery disease

The incidence of acute myocardial infarction during pregnancy is one in 10 000 to 100 000 births, with an increasing frequency in the peri partum period.

The mortality of myocardial infarction is 50% in pregnancy and is even higher if delivery is within 2 weeks of infarction or the patient has a caesarean section. If the left ventricle is compromised, then invasive monitoring including a pulmonary artery catheter is recommended.

The use of ergotamine and PGF₂-alpha can lead to adverse cardiovascular conditions, which can precipitate myocardial infarction in those who have coronary artery disease.

Primary pulmonary hypertension

The maternal mortality is as high as 50% in patients with primary pulmonary hypertension, with most deaths occurring during labour or after delivery. Neuraxial blockade is not recommended due to the risk of producing severe decompensation as a result of reduced SVR. The patient will not tolerate a reduction in right ventricular volume from reduced venous return. It is important to avoid aorto-caval compression and invasive monitoring is required throughout labour and in the immediate post partum period.

Cardiomyopathy

Peri partum cardiomyopathy is a rare type of heart failure with a left ventricular ejection fraction of less than 45% occurring in the last month of pregnancy or within 5 months postpartum without any other identifiable cause. The mortality rates are from 20-85%. Patients with any sort of cardiomyopathy do not tolerate the cardiac changes resulting from pregnancy.

Idiopathic hypertrophic subaortic stenosis

Hypertrophic subaortic stenosis presents as a marked hypertrophy of the left ventricle and interventricular septum with left ventricular outflow tract obstruction by the hypertrophied muscle. Patients are treated with beta-blockers to reduce myocardial contractility and rate. A drop in systemic vascular resistance is not well tolerated and regional anaesthesia is not recommended but has been reported in the literature. Sufficient volume load as well as maintenance of the arterial blood pressure (with alpha-sympathomimetic agents) and avoidance of a tachycardia is important for successful epidural analgesia and anaesthesia for caesarean delivery.

Mode of delivery

In a stable patient, the main goal is to get the patient to term, so as to reduce foetal mortality. In severe disease, a planned operative delivery is performed because the required increase in cardiac output during vaginal delivery is not possible. Contraction-inducing drugs such as oxytocin and prostaglandin can cause significant haemodynamic stress. Emergency caesarean delivery should be avoided. If there is a need to deliver the baby prematurely (before 34 weeks), then an elective caesarean carries the least morbidity for the foetus. During vaginal delivery, early epidural analgesia combined with instrumentally assisted delivery could reduce the cardiovascular workload. (Cox et al, Current Opinion, 2005) If a caesarean section is performed, previous case series show no difference in outcome between regional and general anaesthesia. Large haemodynamic variations and high volume loads should be avoided.

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MATERNAL HAEMORRHAGE

Obstetric haemorrhage is a significant cause of major maternal morbidity and mortality. It is recommended that all obstetric units have a massive obstetric haemorrhage protocol in order to mobilise resources and achieve rapid resuscitation and transfusion with appropriate fluids and blood products, and medical or surgical treatment of the underlying cause of bleeding.

Classification

Antepartum Haemorrhage

The causes of antepartum haemorrhage include placental abruption and placenta praevia. Uterine rupture is most commonly an intrapartum event but may occur before or after birth.

Postpartum Haemorrhage

PPH is bleeding within six weeks after delivery and most commonly occurs within one or two hours of birth. It is the most common cause of serious blood loss in obstetrics. The causes of PPH include retained placenta, genital tract trauma, uterine atony and placenta accreta. Amniotic fluid embolism may present as a PPH with coagulopathy and disseminated intravascular coagulation.

Signs and symptoms associated with acute blood loss in the parturient

The pregnant patient at term has an increased blood volume (40%) with a dilutional anaemia and increase in coagulation factors. Her cardiac output is increased by 50% with 20% directed to the uterus.

(From Palmer, ASA refresher, 2000)

Modest bleeding	Up to 15 % blood volume (900 ml)	Mild tachycardia Variable pallor Normal blood pressure Normal respirations Normal urine output Normal capillary refill
Moderate bleeding	20-25% of blood volume (1200-1500 ml)	Tachycardia Diastolic hypertension, Decreased pulse pressure Moderate tachypnoea Urine output 25-40 ml/hr
Severe bleeding	30-35% of blood volume (1800-2100 ml)	Marked tachycardia (120-160) Cold clammy pale skin Hypotension Tachypnoea (respirations 30-50/min) Oliguria
Massive bleeding	Over 40% of blood volume (Over 2400 ml)	Profound shock Systolic BP <80 mmHg Absent peripheral pulses Marked tachycardia Circulatory collapse Oliguria or anuria

Management of massive obstetric haemorrhage

The goals of therapy are to replace circulating blood volume, maintain adequate tissue oxygenation and to control ongoing bleeding. This will require the administration of warmed crystalloids and colloids via two large bore intravenous cannulae whilst awaiting the arrival of blood. It is better to use a balanced salt solution rather than normal saline, which may lead to hyperchloraemic acidosis. All non-cellular fluids will cause a dilutional coagulopathy but some colloids may produce coagulopathy by other mechanisms. Gelatin based colloids will only cause a dilutional coagulopathy, whereas high molecular weight hydroxyethyl starch solutions may affect platelet function by decreasing glycoprotein IIb-IIIa availability.

Supportive measures should be undertaken including the maintenance of body temperature (which will help maintain coagulation), acid-base status, adequate ventilation and oxygenation, and the maintenance of an adequate cardiac output, which may require inotropic support. If the patient's level of consciousness is reduced, then intubation and ventilation may be required. Before delivery, left lateral tilt should be employed to alleviate aorto-caval compression. Head down tilt will aid venous return. Foetal monitoring with either cardiotocography or ultrasound may be required.

Maternal monitoring will include pulse, blood pressure, ECG, pulse oximetry, urine output and temperature. Baseline blood testing should include a full blood count, clotting, urea and electrolytes, and cross match. Frequent assessment of haemoglobin, platelet count, coagulation and electrolytes will guide therapy. Invasive blood pressure monitoring and central venous pressure monitoring can be inserted at the discretion of the anaesthetist but should not prevent the team from resuscitation and definitive treatment of the bleeding.

It is important that all senior members of the team are involved in the management of a bleeding patient. Each hospital needs to have a protocol for the management of massive obstetric haemorrhage. It is quite common for the junior members of the obstetric team to underestimate the amount of blood lost, as the parturient does not show signs of significant blood loss until over 1200 ml has been lost.

It is important to call for help early so that people are available to liaise with the blood bank, set up rapid infusion devices and to take samples to the blood bank and fetch blood products. Close communication with the blood bank and pathology services enables the planning of blood product administration. The services of a haematologist are very useful, particularly when there is ongoing blood loss and coagulopathy. (Pinder, Current anaesthesia and critical care, 2005)

The obstetric treatment of haemorrhage will depend on the cause. Massive antepartum haemorrhage will generally require delivery of the foetus, as the placental bed will continue to bleed until the uterus is empty. Post partum haemorrhage will usually involve the evacuation of any retained placental products, repair of genital tract trauma and treatment of uterine atony. Uncontrolled haemorrhage may require the ligation or embolisation of uterine arteries, hysterectomy and occasionally, ligation of the internal iliac arteries. In Victoria, Australia, the incidence of caesarean hysterectomy is rising, mainly due to treatment for post partum haemorrhage. In 2003, the incidence was one in 1300 deliveries. It is essential that high-risk mothers be delivered in an institution that has ready access to blood and pathology services. It must be remembered that coagulopathy may precipitate as well as result from massive obstetric haemorrhage.

Choice of anaesthesia

Regional anaesthesia can be used safely if there is no coagulopathy, bleeding is controlled, hypovolaemia is corrected.

When there is severe maternal haemorrhage and emergency caesarean delivery is required, general anaesthesia is indicated. Before induction, in addition to routine precautions, two large bore intravenous cannulae should be inserted, a rapid infusion device connected, left lateral tilt employed and blood should be immediately available in

the operating theatre. With 20% of the cardiac output going to the uterus, potentially major life-threatening haemorrhage can occur within minutes from an atonic uterus.

Manual removal of a retained placenta requires uterine relaxation and analgesia. If there is no haemodynamic instability, a regional anaesthetic is reasonable (such as a spinal or epidural). If uterine relaxation is then required, nitroglycerin can be used. A dose of 100 mcg to 200 mcg intravenously will relax the uterus within 35-45 seconds, which lasts only 60-90 seconds due to its short half-life. It may be associated with significant, but transient maternal hypotension. Alternatively a general anaesthetic can be performed, which will provide both analgesia and uterine relaxation.

Regional anaesthesia can be employed safely in the patient with placenta praevia undergoing an elective caesarean section, but one should be prepared to convert to a general anaesthetic if the patient's cardiovascular or conscious state should deteriorate. Parekh et al found significantly reduced blood loss and lower transfusion requirements with regional compared to general anaesthesia, no matter what the grade of placenta praevia or classification of the caesarean section. It would seem sensible though, to administer a general anaesthetic if the placenta is low lying and anterior, especially if there has been a previous caesarean section. A regional anaesthetic will unmask hypovolaemia due to haemorrhage due to the sympathetic blockade. Conversely general anaesthesia with volatile agents will relax the uterus, so the dose should be limited or propofol can be used instead.

Transfusion Therapy

Guidelines

In acute blood loss, the need for transfusion will depend on the estimated blood loss and the patient's ability to compensate for the amount of blood lost. Where there has been a 30-40% or greater loss of blood volume, rapid volume replacement is required with crystalloids and synthetic colloids and red cell transfusion is probably required. Transfusion "triggers" will depend on preexisting medical conditions. For the patient with ongoing blood loss, a haemoglobin of 10 g/L will likely require transfusion, but a lower haemoglobin of 7 g/L will be acceptable if there is not likely to be any ongoing loss.

Massive transfusion is defined as the replacement of the patient's entire blood volume within 24 hours or more than 20 units of red cells transfused within 24 hours. Death is more likely to occur from irreversible shock than to anaemia and reduction in oxygen carrying capacity. Therefore initial therapy should be directed to restoring circulating blood volume.

Pre-transfusion compatibility testing should be performed where possible. A group and screen for antibodies is recommended for all pregnant women. Full cross matching will take over 30 minutes which is not practical if the patient is exsanguinating. If the blood group is not known and the situation is life threatening, uncrossmatched group O Rh (D) negative red cells can be used. If the blood group is known, then group-specific blood is

acceptable (as the rate of transfusion reactions has been shown to be low in patients with no atypical antibodies). Where time permits, a full cross match is preferable.

Transfusion of large numbers of packed cell units will eventually result in a coagulopathy, which will require administration of platelets and coagulation factors (in the form of FFP). The amount of FFP and platelets should be guided by laboratory testing of coagulation and platelet count. For a rapidly exsanguinating patient, a formula based transfusion protocol may be required, as waiting for the results of such testing is not practical. As a guide, 2-4 units of FFP and one adult dose of platelets (4-6 units) should be given for every 10 red cell units transfused.

FFP should be considered if the prothrombin time or activated partial thromboplastin time is greater than 1.5 times normal. If the patient's group is not known, AB group FFP can be used (or A group if AB is not available).

Thrombocytopenia usually results from haemodilution but may occur due to increased consumption. There is a large amount of patient-to-patient variability in the situation of massive transfusion and it is recommended that platelet therapy be administered according to laboratory investigations. Platelets are indicated if the platelet count is less than $50 \times 10^9/L$ or if the count is less than $100 \times 10^9/L$ in the presence of diffuse microvascular bleeding.

In the presence of hypofibrinogenaemia (less than 1.0 g/L), cryoprecipitate may be indicated, but FFP should supply enough fibrinogen to correct most deficiencies.

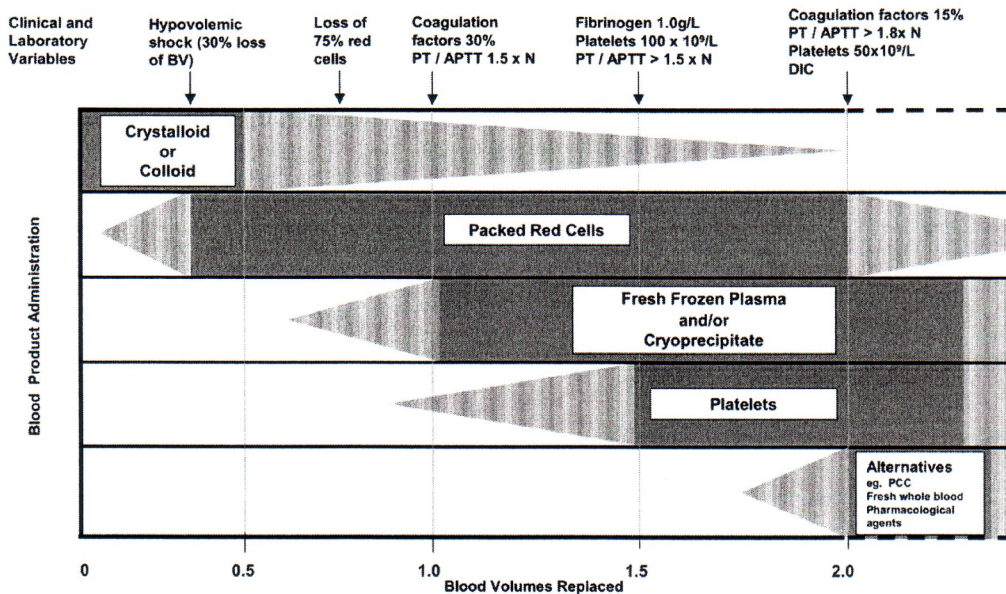


FIGURE 3 The management of massive transfusion in the elective surgical setting
 Reproduced with permission from *Erber WN*. Massive blood transfusion in the elective surgical setting. *Transfus Apheresis Sci* 2002; 27: 83-92.

Problems with transfusion

Blood banks collect blood from donors and then fractionate the donation to produce the different blood products. The products available are then packed red blood cells (in citrate as the anticoagulant), fresh frozen plasma, cryoprecipitate and platelets. The storage time is different for each of these products. Platelets are kept at room temperature and are kept for 72 hours. They require constant agitation. Packed red cells are kept refrigerated and the cells will gradually lose their membrane integrity and undergo lysis. FFP and cryoprecipitate will keep for many months and will require thawing before use. This may take up to one hour.

Potential major complications of massive transfusion include coagulopathy, hypothermia, citrate toxicity, acid-base abnormalities and hyperkalaemia. This is due to the rapid administration of large volumes of cold packed cells, particularly if they have been stored for a long period of time in the blood bank. ABO incompatibility, febrile reactions and other immune-mediated complications can occur.

Coagulopathy in massive transfusion can be due to haemodilution, hypothermia, acidosis, the administration of fractionated blood products and disseminated intravascular coagulation (DIC). Hypothermia below 35 degrees C slows the enzymatic process of coagulation and reduces the synthesis of coagulation factors, affects platelet function and fibrinolysis.

The administration of whole blood or modified whole blood used to be common practice in the past. There were few reported problems with dilutional coagulopathy. Plasma-poor red cell concentrates will cause a coagulopathy via citrate (which binds calcium and acts as an anticoagulant), via the low pH of red cell concentrates, and dilution. The hypocalcaemia associated with rapid massive transfusion will interfere with the coagulation cascade because calcium is required as a co-factor for many steps of the cascade. FFP and platelets need to be administered to maintain normal haemostasis. (Wojciechowski et al)

Acidosis leads to a coagulopathy but the mechanism is not clear. There is evidence that a pH less than 7.10 is a significant risk factor for the development of life-threatening coagulopathy.

Transfusion-related acute lung injury (TRALI) is a non-cardiogenic form of pulmonary oedema. It is a diagnosis of exclusion. It can lead to respiratory failure, which mimics acute respiratory distress syndrome. It is estimated to occur in one in 5000 blood transfusions, one in 7900 FFP transfusions and one in 432 whole-blood-derived platelet transfusions. (Toy et al) The onset is typically within one to two hours of transfusion, but can occur up to six hours later. The presentation is one of dyspnoea, hypoxaemia, cough and fever which may be followed by hyper or hypotension. More than 70% of patients will require mechanical ventilation. The chest x-ray shows diffuse bilateral infiltrates. Most cases will resolve within 96 hours and mortality is not common but may reach up to 6%. The treatment is supportive with ventilation. Diuretics are not indicated. The

pathophysiology is thought to be inflammation, leading to neutrophil adherence to the pulmonary endothelium followed by the passive transfer of neutrophil/granulocyte HLA antibodies from the transfusion, which leads to the release of oxygen free radicals and other non-oxidative products which in turn leads to capillary leakage and pulmonary oedema. (Williams and Gettinger)

Cell salvage

Although many obstetric units are using cell salvage, there are still concerns with its safety due to the potential for the reinfusion of amniotic fluid into the maternal circulation. Cell salvage involves the aspiration of blood from the bleeding site, which is then filtered, separated, heparinized, washed and returned to the patient as a red cell and saline suspension. The risk of contamination by amniotic fluid is reduced with the use of a separate suction system for the amniotic fluid and the use of leucocyte depletion filters.

Cell salvage is unlikely to reduce maternal mortality from massive obstetric haemorrhage because it is hard to process and return the blood rapidly enough and a dilutional coagulopathy will still develop. Its place may be for the avoidance of homologous blood transfusion in the Jehovah's Witness patient or in the elective situation where blood loss is predicted. It does help to avoid the use of donor red blood cell units.

Antifibrinolytics

Tranexamic acid and aprotinin are the most commonly used antifibrinolytic agents. They inhibit fibrinolysis by enzyme inhibition. There are limited case reports of their use in obstetric haemorrhage and they may pose a possible thromboembolic risk. Their use may be restricted to the case of massive obstetric haemorrhage that fails to respond to conventional measures.

Recombinant factor VIIa

Recombinant factor VIIa was originally developed for use as a pro-haemostatic agent for the treatment of bleeding in patients with haemophilia A or B with antibodies or inhibitors of factor VIII or IX. There have been several case reports of its successful use in cases of massive haemorrhage with coagulopathy, including in the obstetric patient. Recombinant factor VIIa replaces the missing clotting factor and also actively initiates and promotes the coagulation process by binding to tissue factor and activated platelets to result in a local thrombin burst. The intrinsic cascade, platelets and fibrin generation are activated. It acts at the site of vessel injury but not systemically. The dose is 90 g/kg as a single intravenous bolus dose, but larger and repeated doses have been reported. It is used in combination with replacement of the deficient coagulation factors, red cells, fibrinogen and platelets. The correction of acidaemia is also important. It is a very expensive drug and should only be used in consultation with a haematologist.

Radiological techniques

Uterine artery embolization has been reported to have a high success rate in the management of massive obstetric haemorrhage. It requires the skills of the radiologists and involves the movement of the patient to the radiology department for the placement of the catheters via the femoral arteries, which are then fed up to the bleeding point or the

uterine arteries. Embolization is performed with polyvinyl alcohol particles, gelatin sponge foam pieces or microcoils. The advantages of embolization include the high success rate and avoidance of a hysterectomy. The high success rate is due to the occlusion of blood vessels more distally than is possible with surgical techniques, so avoiding bleeding from collateral vessels. The complications include post-embolization ischaemia, pelvic infection and technical complications of angiography.

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DISSEMINATED INTRAVASCULAR COAGULATION

Disseminated intravascular coagulation (DIC) is a consumptive coagulopathy that results from the inappropriate and excessive activation of the coagulation cascade. There is formation of micro thrombosis in multiple vessels, which leads to organ failure, and a consumption of the coagulation factors and platelets, resulting in the coagulopathy.

DIC may be acute or chronic. The acute form is more overt and characterised by diffuse bleeding and is life threatening. The chronic form is more likely to be characterised by the formation of thrombus.

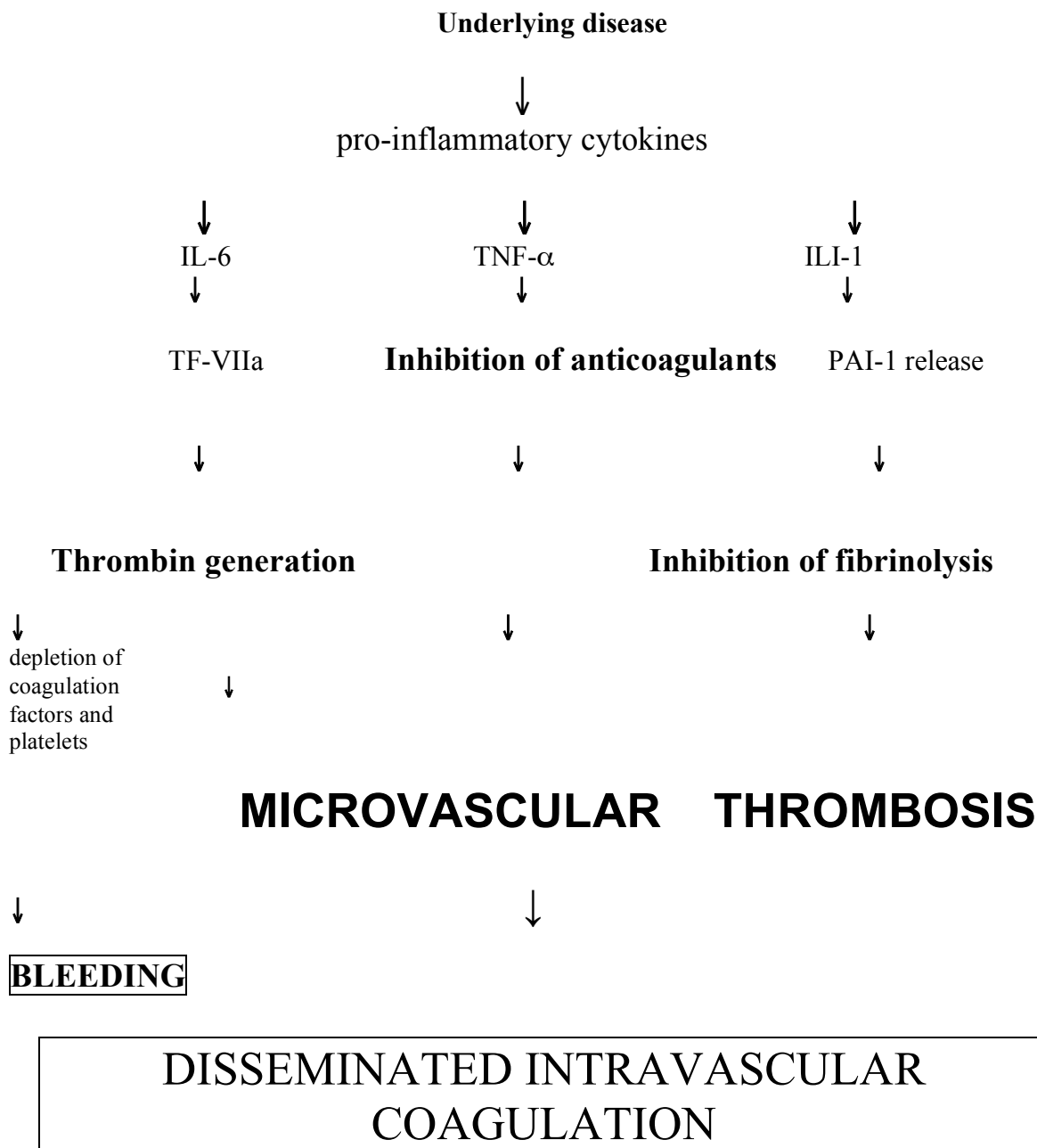
DIC is a disorder that occurs secondary to another systemic disease process. The conditions associated with DIC in obstetrics include; placental abruption, amniotic fluid embolism, haemorrhagic shock and abortions. Abruption is the most common cause of DIC during pregnancy. (Palmer ASA refresher 2000 –Anaesthetic management of obstetric emergencies) Chronic DIC can result from a retained dead foetus.

Non obstetric conditions leading to acute DIC include infection and sepsis (overt DIC is found in 25-50% of patients with significant sepsis and is indicative of a poor outcome), incompatible blood transfusion, acute promyelocytic leukaemia, disseminated prostatic carcinoma, stroke or cerebral haemorrhage, snake and spider bite, massive tissue destruction from trauma and heparin-induced thrombocytopenia with thrombosis (HITT). Chronic DIC can result from any chronic infection, inflammatory bowel disease, malignancy, aortic aneurysm or a giant haemangioma.

Pathophysiology

Inflammatory cytokines stimulate the expression of tissue factor on monocytes, neutrophils and platelet micro-particles leading to the formation of thrombin and activation of the coagulation cascade. The presence of procoagulant material in the circulation such as in amniotic fluid embolism syndrome may also cause direct activation of the coagulation cascade, leading to thrombin generation. In acute DIC there is an explosive generation of thrombin, which converts fibrinogen to fibrin, which is a potent platelet activator. This depletes the clotting factors and platelets and activates the fibrinolytic system. The natural anticoagulants such as antithrombin and the constituents of the protein C anticoagulant pathway are suppressed, resulting in increased thrombin generation.

Both the coagulation cascade and fibrinolysis are abnormal. Fibrinolysis is initially enhanced and then becomes significantly suppressed. The principal mediator of the activation of coagulation is interleukin-6 and tumour necrosis factor alpha inhibits the physiologic anticoagulation pathways and fibrinolysis. Bleeding then occurs into the subcutaneous tissues, skin and mucous membranes as well as occlusion of blood vessels due to the presence of fibrin in the microcirculation.



In chronic DIC the process is less rapid, allowing time for compensatory responses in the coagulation system to reduce the likelihood of bleeding but instead a hyper coagulable state occurs.

Diagnosis

Acute DIC leads to multiple bleeding sites, skin bruising, bleeding from mucous membranes, visceral haemorrhage and tissue ischaemia. The laboratory findings are prolonged prothrombin time, activated partial thromboplastin time, thrombin time, decreased fibrinogen levels and increased levels of fibrin degradation products (FDP), a low or falling platelet count and abnormal red cells on blood film.

Chronic DIC leads to signs of deep venous or arterial thrombosis or embolism, superficial venous thrombosis and multiple thrombotic sites. The laboratory findings include a slightly increased prothrombin time, abnormally long or short partial thromboplastin time, normal thrombin time and increased levels of FDP. The fibrinogen level or platelet count may be high, normal or low.

The diagnosis of acute DIC can be made based on:

1. The presence of an underlying disease known to be associated with DIC
2. A rapid decline in platelet count or a count below 100,000/ml
3. Prolonged clotting times
4. The presence of fibrin degradation products (FDPs) in the plasma
5. Low levels of coagulation inhibitors (such as antithrombin III)

In clinical practice the laboratory diagnosis is made using screening tests and confirmatory tests. The screening tests measure prothrombin time, activated partial thromboplastin time, platelet count and fibrinogen level. If all tests are abnormal, then the diagnosis of DIC is likely. The confirmatory tests are assays of fibrin degradation products (which measures plasmin-cleaved fibrinogen and fibrin) and the D-dimer assay (which measures plasmin-cleaved, insoluble, cross-linked fibrin). The FDP test is not as reliable as a positive D-dimer (which confirms the presence of both thrombin and plasmin), and in some patients with severe DIC, FDP may be normal.

The DIC committee of the International Society on Thrombosis and Hemostasis has proposed an algorithm to calculate a DIC score. A score of 5 or more is compatible with DIC. The scoring system has a sensitivity of 91% and a specificity of 97%. (Levi 2004)

1. Risk assessment

Does the patient have an underlying disorder known to be associated with DIC? If yes, proceed with algorithm, if no, do not use algorithm.

2. Order global tests
(Platelet count, prothrombin time, fibrinogen, soluble fibrin monomers, fibrin degradation products)
3. Score global coagulation test results
 - a. Platelet count (>100=0; <100=1; <50=2)
 - b. Elevated soluble fibrin monomer or FDP (no increase=0; moderate increase=2; strong increase=3)
 - c. Prolonged prothrombin time (<3 sec=0; >3-6 sec=1; >6 sec=2)
 - d. Fibrinogen level (>1 g/L=0; <1 g/L=1)
4. Calculate score
5. >5 =compatible with overt DIC, repeat scoring daily
6. <5=suggestive for non-overt DIC, repeat next 1-2 days

Treatment

Management of acute DIC is a medical emergency. If possible the trigger should be treated or eliminated, and general supportive measures undertaken. The advice of a haematologist is often valuable. In patients with thrombocytopenia and low levels of coagulation factors, replacement of platelets and coagulation factors is not indicated unless there is clinical bleeding or a need for an invasive procedure. Platelets should be given for counts less than 50,000/ml, fresh frozen plasma will replace most coagulation factors, but low fibrinogen levels are best managed with cryoprecipitate. Packed cells should be administered as required. Prothrombin complex concentrates should be avoided because they contain traces of activated coagulation factors that may worsen the coagulopathy.

The role of anticoagulant therapy remains controversial, but heparin therapy is recommended in the case of venous thromboembolism and marked microvascular obstruction. In the case of chronic DIC due to a retained dead foetus or vascular malformations, a heparin infusion should be considered.

There has been some work done on therapy aimed at restoring the natural anticoagulant pathways (antithrombin III, tissue factor pathway inhibitor) but the results do not support their routine use yet.

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PRE – ECLAMPSIA

The hypertensive disorders of pregnancy can cover a wide spectrum of diseases including pre-eclampsia, eclampsia, and the syndrome of haemolysis, elevated liver enzymes and low platelets (HELLP). Chronic hypertension can be superimposed on pre-eclampsia and indeed is a risk factor for the development of pre-eclampsia. Pregnancy induced hypertension implies the absence of systemic disease and has a better prognosis.

Pre-eclampsia is a multisystem disorder of uncertain aetiology. It is thought to occur due to an imbalance of placental prostaglandins. In pre-eclamptic patients a relative increase in thromboxane compared to prostacyclin causes vasoconstriction, platelet aggregation, uterine irritability and uteroplacental hypoperfusion. It is believed that placental ischaemia might cause trophoblastic fragmentation and the entry of trophoblasts into the maternal circulation. Platelets may then aggregate on these fragments which then release serotonin causing widespread vasospasm and endothelial dysfunction. The uterus also releases renin which catalyzes the conversion of angiotensinogen to angiotensin I, causing widespread arteriolar vasoconstriction. Aldosterone secretion causes renal reabsorption of sodium and water.

The incidence of pre-eclampsia is 1-4% in primiparas and 1% in multiparas. Eclampsia is rare in developed countries where it affects one in 2000 deliveries. Overall pre-eclampsia and eclampsia account for more than 50,000 maternal deaths per year.

The diagnostic features are an arterial diastolic pressure above 90 mmHg on more than one occasion greater than 4 hours apart or over 110mmHg on a single occasion and the presence of proteinuria over 300 mg/24hours. Elevation of serum uric acid levels aid in the diagnosis of pre-eclampsia.

Pre eclampsia is severe if there is a sustained increase in arterial pressure over 160/110 mmHg, proteinuria of over 5g per day, oliguria of less than 500 ml per day, pulmonary oedema, cerebral and visual disturbances, epigastric pain and coagulopathy. The presence of the HELLP syndrome indicates severe disease.

Risk factors for the development of pre-eclampsia include the presence of chronic hypertension, renal disease, a positive family history, twin pregnancy, age over 40, nulliparity and diabetes.

Because pre-eclampsia is characterised by the variability of its presentation and progression of disease, the only definitive treatment is delivery of the foeto-placental unit. The disease may continue to progress until 24 hours following delivery before there is recovery.

The key complications of pre-eclampsia include renal failure, fitting (eclampsia), stroke, coagulopathy, pulmonary oedema, hepatic or splenic infarction and HELLP.

Placental blood flow reduction may result in chronic foetal hypoxaemia and intra-uterine growth retardation. There is a higher incidence of poor foetal outcome and placental abruption is more common in women with pre-eclampsia.

Renal blood flow and glomerular filtration rate are normally increased during pregnancy as is creatinine clearance. In the pre-eclamptic patient, there is renal arteriolar vasoconstriction so that RBF and GFR are reduced and urea and creatinine concentrations are increased. Proteinuria contributes to a reduction in serum albumin and hyperuricaemia is usually present, which represents early deterioration in renal function. Oliguria after delivery lasting up to 6 hours is common but does not necessarily indicate volume depletion. Acute tubular necrosis is rare unless there has been another renal insult.

The central nervous system may show signs of irritability such as headache, visual disturbances and hyperreflexia. Seizures in late pregnancy represent eclampsia unless proven otherwise. Eclampsia complicates one in 2000 maternities in developed countries. Seizures may occur as a result of obstruction of the cerebral microcirculation or intense cerebral vasospasm. Cerebral oedema and hypertensive encephalopathy may also occur. Cerebral haemorrhage accounts for up to 40% of the deaths due to pre-eclampsia. (Santos)

Normal pregnancy creates a hypercoagulable state. The platelet count is increased above 200,000 platelets/ml and fibrinogen concentrations are elevated. In the pre-eclamptic patient, a drop in platelet count and function can occur. The presence of thrombocytopenia (below 100,000) indicates more severe disease. This represents a concern for the administration of epidural anaesthesia. Consumption coagulopathy is relatively rare unless placental abruption has occurred or HELLP syndrome is present.

The circulating blood volume is expanded relative to the non pregnant state in the woman with pre-eclampsia, but not as much as in the normal pregnant patient. Capillary permeability is increased, leading to extravasation of fluid and a low oncotic pressure. Pulmonary oedema may occur in up to 2% of severely pre-eclamptic women due to a combination of ventricular dysfunction, low colloid osmotic pressure, increased intravascular hydrostatic pressure or increased pulmonary capillary permeability. (Sibai, 1987)

The cause of hepatic dysfunction in pre-eclampsia is not clear but may result from periportal hepatic necrosis, subcapsular haematoma or fibrin deposition in hepatic sinusoids. Spontaneous liver rupture is a rare but life threatening complication (Mushambi, 1996).

HELLP is the syndrome of haemolysis, elevated liver enzymes and low platelets and it complicates 0.3% of all pregnancies and 4 to 20% of those with severe pre-eclampsia. It carries a high maternal (24%) and foetal mortality (33%) and usually occurs at less than 36 weeks gestation. 30% of cases occur in the postpartum period. (Mushambi) It is characterised by malaise, epigastric pain, proteinuria, jaundice, hypertension, nausea and

vomiting, and a flu-like illness. It may lead to haematuria, disseminated intravascular coagulation, liver and renal failure. The platelet count is less than 100,000. Treatment is delivery of the pregnancy. Platelet transfusion is recommended for counts less than 20,000 for vaginal delivery and for counts less than 50,000 for caesarean delivery. There is evidence that postpartum intravenous dexamethasone hastens recovery and reduces the severity of the disease. (10 mg given every 12 hours) (Levy, 2005)

The assessment of the pre-eclamptic patient should include a clinical assessment of the cardiovascular system (BP, hydration status, evidence of pulmonary oedema), central nervous system (reflexes and cerebral irritability), renal system (urine output, proteinuria), hepatic system (epigastric pain, jaundice) and haematological system (evidence of bleeding and haemolysis). Laboratory testing should include a full blood count (and coagulation studies if there is a low platelet count), liver function tests, uric acid determination and urea, creatinine and electrolytes if there is a concern about renal function. Special attention should be given to airway assessment as pre-eclamptic women may have airway oedema.

The definitive management of pre-eclampsia is delivery of the foetus and placenta. Before this can safely occur, the mother needs to be stabilized. The aims of therapy are to avoid eclampsia, restore normal haemodynamics and treat coagulopathy.

Magnesium sulphate therapy should be used to avoid eclampsia, and may be useful for the treatment of a fit. In the event of a fit, clear the airway, give 100% oxygen and relieve aortocaval compression. An attempt to avoid trauma to the mother or foetus needs to be made. If the fit is not self-limiting, a loading dose of 5 g of magnesium sulphate over 5 minutes can be used. If a magnesium is already in use a further 2 g load can be used. Alternatively diazepam 10 mg can be given over 2 minutes. The use of phenytoin is no longer recommended. Magnesium sulphate will be discussed in more detail below.

The circulating blood volume is reduced compared with the normal pregnant patient. Careful fluid administration is recommended. In the patient with severe pre-eclampsia, invasive monitoring of cardiovascular filling may be required, particularly if there is pulmonary oedema, refractory hypertension and low urine output.

Antihypertensive agents should be used to improve haemodynamics and prevent cerebral haemorrhage. A blood pressure above 170/110 mmHg requires urgent treatment but equally, in order to preserve renal and placental perfusion, the blood pressure should not be allowed to fall acutely to below 130/90 mmHg. The blood pressure may be treated with the use of an epidural, magnesium sulphate infusion and vasodilators. Nifedipine is a calcium channel blocker and is in widespread use in obstetrics as is labetalol, which is a mixed alpha and beta antagonist. Hydralazine is a potent vascular smooth muscle dilator that can be given as an infusion for the control of blood pressure. Its effect has an onset of 10 to 20 minutes and duration of up to 6 hours. In conjunction with fluid administration, it can result in an increase in the cardiac index.

Analgesia for labour and delivery can be provided with lumbar epidural anaesthesia. It is important to restore circulating blood volume, control the blood pressure and check the platelet count before insertion of a lumbar epidural. Intervillous blood flow in the placenta of pre-eclamptic patients increases by up to 75% with epidural anaesthesia. (Jouppila et al)

Because of the risk of spinal haematoma with regional anaesthesia in a patient with a low platelet count, the patient with pre-eclampsia should have a platelet count determined prior to the insertion of a spinal or epidural. In a patient with a platelet count over 100,000/ml, an epidural or spinal can be safely performed. In those patients with a count between 75,000 and 100,000, a coagulation screen should be performed before regional anaesthesia can be considered.

Both epidural and spinal anaesthesia have been used for caesarean delivery in the pre-eclamptic patients. The major concern in the past has been a large fall in blood pressure with the onset of a sympathetic block and therefore a reduction in placental blood flow and maternal cardiac output. It has been found that the magnitude of hypotension in the pre-eclamptic women undergoing caesarean section under spinal anaesthesia is less than in the normal parturient. It is important that the total dose of local anaesthetics for regional anaesthesia is monitored as maternal clearance of the local anaesthetic agents may be reduced due to a reduced hepatic blood flow.

The use of general anaesthesia may be required for the patient with a low platelet count or if there has been maternal haemorrhage. The major concerns are difficult intubation due to airway oedema, the pressor response to intubation, which may lead to cerebral haemorrhage and the interaction of magnesium sulphate with neuromuscular blockers.

The use of magnesium sulphate in obstetrics

Magnesium Sulphate was first used to prevent eclamptic seizures by Horn in Germany in 1906, who injected it intrathecally. Intramuscular injections were later found to be useful for the control of convulsions associated with tetanus and this led to its use for the prevention of recurrent seizures in women with eclampsia in 1926. The intravenous route was first used for preeclamptic women in 1933.

Magnesium has been used for the prevention of eclampsia for over sixty years in the United States. In the UK, however, only 2% of obstetricians surveyed were using it in 1992. Since then, there have been some large studies comparing Magnesium with Diazepam and Phenytoin for pre-eclampsia, which have demonstrated its superiority.

Administration

A suggested protocol for eclampsia prophylaxis is the administration of a 50% Magnesium Sulphate solution via a syringe pump. A 4 g bolus is given over 15 minutes (8 ml at 32 ml/hr for 15 min), followed by an infusion of 1-2 g/hr (2-4 ml/hr) until 24 hours after delivery. Magnesium levels are checked every 6 hours (therapeutic 1.7 – 3.5

mmol/l) and the patient is monitored for clinical signs of toxicity, including the loss of patellar reflexes and respiratory rate. Eclampsia is treated with a 1-2 g bolus over 5 minutes i.v.

Pritchard popularised the intramuscular regimen used widely in many countries. A continuous intravenous loading dose of 4 g (as a 20% solution) is given over five minutes, followed by 5 g of 50% solution as a deep i.m. injection into each buttock. Maintenance consists of a 5 g i.m. injection every four hours until 24 hours after delivery.

Zuspan's intravenous regimen consists of a 4 g (or 5g) intravenous load followed by an infusion of 1 g/hr until 24 hours after the last fit.

A further load of 2-4 g i.v. over 5 minutes is given if fitting recurs.

Distribution and plasma levels

Magnesium is distributed rapidly through the extracellular fluid, and some is taken up by bone. An i.v. load of 4-6 g results in an immediate but transient plasma level of 2.1-3.8 mmol/l. Within 90 minutes, 50% moves into the bones or into cells. Intramuscular magnesium requires 90-120 minutes to reach peak plasma levels.

Levels are usually less than 1.7 mmol/l with infusions of 1g/hr but are between 1.7 and 3.3 mmol/l with 2 g/hr infusion rates, suggesting that a rate of at least 2 g/hr is required to reach therapeutic levels.

There is no single accepted therapeutic level, but in general it is considered to be between 2 and 4 mmol/l for eclampsia.

Excretion

Magnesium undergoes renal excretion, with 50% of the dose being excreted in the urine after four hours. The renal clearance increases linearly with an increase in plasma level. If there is oliguria the infusion rate should be reduced and levels monitored frequently.

Toxicity

There is frequently hot flushing on commencement of magnesium, which does not necessarily herald serious toxicity, and this is usually transient. The loss of the tendon reflexes is the first sign of toxicity.

4-6.5 mmol/l

- nausea and vomiting
- somnolence
- double vision
- slurred speech
- loss of patellar reflex

6.5-7.5 -muscle paralysis

>7.5 -respiratory arrest and CNS depression
-sinoatrial and atrioventricular blockade

>12 -cardiac arrest

Laryngeal reflexes remain intact for much longer than with diazepam, so affording some protection against aspiration pneumonia.

Toxicity is treated with calcium chloride (5 ml of 10%) or calcium gluconate (10 ml of 10%). This should be administered as a slow i.v. injection (over 10 min) to avoid hypotension and bradycardia.

Contraindications

There are few contraindications to magnesium except myasthenia gravis and heart muscle damage associated with conduction defects.

Effects on CNS

The mechanism of action of Magnesium in the treatment and prevention of eclampsia may be due to its ability to reduce both systemic and cerebral vasospasm by antagonism of calcium.

The NMDA receptor is blocked by the magnesium ion, which may account for its anticonvulsant effect as well as its ability to reduce opioid requirements in the postoperative patient.

Eclamptic seizures are characterised by intense cerebral vasospasm. Belfort *et al* demonstrated that magnesium vasodilates the middle cerebral artery when given to women with pre-eclampsia, when measured by doppler flow studies.

Magnesium increases the production of prostacyclin and protects against injury by free radicals to endothelial cells *in vitro*, which may account for some of its effects in eclampsia and in neuroprotection of the fetus.

CNS depression occurs with magnesium and will reduce the MAC of volatile agents.

Effects on neuromuscular junction

ECF Mg causes a reduction in acetylcholine release at the neuromuscular junction and reduces the sensitivity of motor end plates to acetylcholine. The amplitude of motor end plate potentials is reduced. There is potentiation of non-depolarizing neuromuscular blockade, the dose of which should be reduced to about 1/3. The effect on depolarizing blockade is probably an increase in the blockade but this does not seem to be clinically significant. Fasciculations and potassium release are reduced.

Smooth muscle

There is a relaxation in smooth muscle tone, which results in a reduction of systemic vascular resistance and a transient reduction in blood pressure with boluses and high infusion rates. The mechanism is probably via its effect on the movement of calcium across membranes. The vasodilator effects seem to be confined to resistance rather than capacitance vessels.

Studies of parturients and cardiac patients have demonstrated that magnesium sulphate is useful for blunting the cardiovascular response to intubation. (40mg/kg)

Placental transfer and effects on the foetus

Magnesium readily crosses the placenta and may cause transient drowsiness, hypoventilation and reduced muscle tone in neonates. A reduction in short term foetal heart rate variability has been observed in those women receiving magnesium, which does not seem to indicate foetal distress, as it does not correlate with a reduction of scalp pH.

Labour and placental blood flow

Labour outcomes such as oxytocin stimulation, administration-to-delivery intervals, prolonged second stage, forceps and caesarean delivery have been shown to be unaffected by maternal treatment with magnesium compared with those who received phenytoin for eclampsia prophylaxis by Leveno *et al.*

Studies on isolated human maternal uteroplacental arteries and on experimental animals show that magnesium infusion increases uterine and placental blood flow.

Evidence for the use of magnesium for eclampsia and pre-eclampsia

The recent MAGPIE trial investigated over 10,000 women with hypertension and proteinuria. They were randomized to receive either magnesium or placebo. The women in the magnesium arm had half the incidence of eclampsia as those in the placebo arm but the number needed to treat (to prevent one patient from fitting) was 91. (Magpie collaborative group, 2002)

Eligibility for entry in to the Magpie trial was the presence of pre-eclampsia, irrespective of whether or not the patient had already received an anticonvulsant and the presence of uncertainty about whether or not to use magnesium. The patients had to be antepartum or 24 hours or less post partum. The exclusion criteria were hypersensitivity to magnesium, hepatic coma with a risk of renal failure or myasthenia gravis. Women with oliguria (urine output less than 25 ml/hr) were eligible but the treatment dose was halved.

Patients received either an intravenous or intramuscular regimen of either magnesium or placebo, and a rescue pack of magnesium sulphate was included for use in the event of eclampsia. Magnesium levels were not monitored, as the maintenance dose was 1 g per hour and instead, reflexes and respiration were monitored at least every 30 minutes.

The primary outcomes were eclampsia and death of the baby before discharge. The study was not expected to have enough power to detect a reduction in maternal mortality. Secondary outcomes were measures of serious maternal morbidity (including respiratory arrest, respiratory depression, pneumonia, cardiac arrest, coagulopathy, renal failure, liver

failure, pulmonary oedema and cerebral haemorrhage), magnesium toxicity and other side effects of magnesium sulphate.

The results of Magpie showed that the groups were well balanced and that 26% had severe pre-eclampsia and 16% had imminent eclampsia on entry. There were significantly fewer eclamptic fits in the women allocated magnesium than those in the placebo arm of the trial (40 or 0.8% as opposed to 96 or 1.9%). This represented a 58% lower relative risk of eclampsia with a number needed to treat of 91. The NNT for women with severe pre-eclampsia was 63. The rate of side effects was 24% in the magnesium group as opposed to 5% in the placebo group, with very few life threatening side effects. Maternal mortality was lower among the women in the magnesium group, but the overall numbers were small. There was no clear difference in the risk of the baby dying for women randomized before delivery. There was a lower risk of placental abruption in the magnesium group. (27% lower relative risk in the magnesium group) (Magpie collaborative group)

Lucas, Leveno, Cunningham, 1995

Comparison of magnesium sulphate with phenytoin for the prevention of eclampsia.

- Randomized controlled trial
- Women with BP > 140 systolic and >90 diastolic
- Delivery not imminent and no eclampsia already
- No epilepsy

Randomized to MgSO₄ 10 g I.M.I. then 5 g I.M.I. every 4 hours until 24 hours post delivery or to Phenytoin 1000 mg I.V. load and 500 mg orally 10 hours later.

BP controlled with Hydralazine 5-10 mg 15 minutely if diastolic > 110 mmHg.

Results

- less eclampsia in Mg group 0/1049 Vs 10/1089
- no maternal deaths in either group
- BP control equal
- Eclampsia risk after Mg 1/750

Collaborative Eclampsia Trial 1995

- Multicentre randomized controlled trial
- comparing magnesium sulphate, diazepam and phenytoin
- 1680 patients
- exclusion criteria contraindication to one of the study drugs

Randomized to MgSO₄ intravenous loading followed by either an infusion or regular intramuscular injections, or to diazepam loading 10 mg i.v. over 2 min then 40 mg over 24 hours then 20 mg for 24 hours or to phenytoin (diazepam given i.v. for control of seizures) then 1g i.v. over 20 min with monitoring followed by 100 mg every 6 hours for 24 hours.

Results

- recurrent seizures less likely in the magnesium treated group compared with either diazepam or phenytoin.
- when compared with phenytoin, there were fewer intensive care admissions, less pneumonia, fewer blood transfusions, neonatal intubations and less need for maternal ventilation in the magnesium group.
- there was a trend toward lower maternal mortality in the magnesium group when compared to both diazepam and phenytoin groups. This was not statistically significant.

The use of hydralazine in obstetrics

Hydralazine is an arterial vasodilator which acts directly on arterial muscle to produce smooth muscle relaxation. The mechanism is unclear but thought to involve the release of NO from arteriolar endothelium. It produces a reduction in BP, but as with other arterial vasodilators, may induce a reflex tachycardia. It is the most widely used hypotensive agent for the acute control of blood pressure in pre-eclampsia. It is inexpensive and there has been extensive experience with its use in obstetrics.

Pharmacokinetics

Hydralazine has a 20-30 minute onset of action, and an elimination half life of 3 hours. It undergoes extensive first pass metabolism, but may be administered orally. It is metabolized partially by acetylation, which results in a variable response to treatment and half life in the fast and slow acetylators.

Dosage and administration

An infusion of hydralazine can be given. 20 mg is made up to 20 ml in normal saline. A 5-10mg bolus is given over 5-10 minutes and an infusion of 5mg per hour is used according to blood pressure response (140-160/90-100 mmHg). The BP is measured at five minute intervals for 20 minutes. Alternatively, a 5-10 mg i.v. bolus may be given every 20 minutes.

Effects on maternal and placental haemodynamics

Gudmundsson, Gennser, and Marsal (Acta Obstet Gynecol Scan, 1995) used doppler ultrasonography to measure blood velocity in the arcuate and umbilical arteries in 12 women before and after starting oral hydralazine (50 mg b.d.) and found an increase in heart rate and decreased BP but no effect on placental blood velocity waveforms.

Side effects and toxicity

Headache, tremor, vomiting, which can be indistinguishable from impending eclampsia are well known side effects of hydralazine therapy. Severe hypotension, tachycardia, flushing and palpitations can occur, as can sodium retention and tachyphylaxis to its hypotensive effect. With prolonged therapy, a reversible drug induced Lupus syndrome is well described, and other immunological effects can occur (including serum sickness, haemolytic anaemia, vasculitis and glomerulonephritis). The dose is therefore limited to 200 mg per day.

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ANAESTHESIA FOR CAESAREAN SECTION

The rate of caesarean section has increased over the past few decades. The overall caesarean section rate is approximately 25% in developed countries. At the Royal Women's Hospital (RWH) in Melbourne in 2003, there were 4882 deliveries. 28% were via caesarean section. At the private hospital, which is co-located with the RWH 46% of 2666 deliveries were via caesarean section.

The indications for caesarean section include: uterine dystocia, cephalopelvic disproportion, maternal haemorrhage, acute foetal distress, previous caesarean section, placenta praevia, prolapsed cord, hypertonic uterus, abnormal presentation and deteriorating maternal medical illness (eg pre-eclampsia, heart disease, respiratory disease).

Delivery via caesarean section will avoid severe trauma to the baby by avoiding a difficult mid forceps or a vaginal breech delivery. The increased use of monitoring of foetal wellbeing in labour has made it easier to identify a foetus in distress, which accounts for the largest proportion of emergency caesarean sections.

Caesarean section is most commonly performed under regional anaesthesia in the United Kingdom, USA and Australia. At the RWH in Melbourne in the year 2000, 12% of caesarean sections were performed under general anaesthesia (GA) whilst 88% were done under regional anaesthesia. In the UK in 1997, a survey of obstetric units found that of 60 455 caesarean sections, 78% were performed under regional anaesthesia. 72% of the emergency caesarean sections were performed under regional anaesthesia.

Regional anaesthesia

Maternal mortality is higher with caesarean than with vaginal birth. Maternal mortality rates are between 0 and 105 cases per 100,000 operations.

Anaesthetic mishaps account for about 2.4% of maternal deaths. This has been halved over the 1980-1990 decade due to the increased use of regional anaesthesia. The anaesthetic related maternal mortality rate is approximately 0.17 per 100,000 live births.

In the 1970s, obstetric anaesthesia was the 3rd most common cause of direct maternal death. Most of the deaths followed general anaesthesia, particularly for emergency caesarean section.

The risk of a serious life-threatening complication with GA occurs in approximately 1:350 cases and of attempted regional anaesthesia in 1:11 900 cases (mainly due to inadequate anaesthesia requiring conversion to GA).

The other advantages of regional over general anaesthesia include: avoidance of awareness under general anaesthesia, post operative analgesia, a reduction in the incidence of deep venous thrombosis, less neonatal depression, a reduction in blood loss,

quicker return of gastro-intestinal function, improved maternal bonding and the ability of both parents to participate in the birth.

There are relatively few contraindications to regional anaesthesia, the absolute contraindications are: maternal refusal, coagulopathy, infection at the injection site, uncorrected hypovolaemia and raised intracranial pressure due to a space occupying lesion.

Maternal haemorrhage (abruption, uterine rupture) produces cardiovascular instability which usually necessitates general anaesthesia. Severe foetal compromise (cord prolapse, severe foetal distress) favours the use of general anaesthesia due to the shorter time to surgical readiness in a time-critical situation.

The patient for caesarean section requires a routine pre-operative visit. Special attention should be paid to; the airway, fasting status, pregnancy-related complications, obstetric history, obstetric ultrasound, and blood group and screen (a cross match should be performed if there is a high risk for bleeding).

The patient should have the risks and side effects of the procedure explained to her and she should be told what sensations she might experience during the operation. Consent for regional anaesthesia should be obtained during the pre-operative visit.

Aspiration prophylaxis

A pregnant patient is at a higher risk of aspiration pneumonitis than the non-pregnant patient. All patients for caesarean section, regardless of the planned anaesthetic technique should receive prophylaxis against aspiration. The patient should fast for 6 hours after a light meal and be given ranitidine 150 mg the night before surgery (or 6 hours before surgery if it is an afternoon case). The dose of ranitidine should be repeated 90 mins prior to surgery and a non-particulate antacid should be given on leaving the ward for theatre. At our hospital we use 0.3M sodium citrate 30 ml.

In an emergency, give 50 mg ranitidine intravenously when the decision to perform a caesarean is made and administer a non-particulate antacid on leaving the ward.

Patients should be fasting in labour (allowing sips of clear fluid), particularly if they are at high-risk for an operative delivery because gastric emptying is delayed in labour.

Spinal anaesthesia

In order to reduce the risk of post dural puncture headache the smallest pencil point needle available (27 to 25G) should be used. If using a cutting needle, align the bevel parallel to the fibres of the dura. This reduces the risk of headache.

Inject Bupivacaine (plain or hyperbaric) 0.5% 2.2-2.5 ml with fentanyl 10-20 mcg. The use of an opioid allows for the reduction of the dose of local anaesthetic and provides early post-operative analgesia. Sufentanil (5-10 mcg) can be used in place of fentanyl.

To reduce hypotension after the induction of spinal anaesthesia, co-load with 500 ml of balanced salt solution or a colloid. Monitor the blood pressure and heart rate. Treat hypotension with metaraminol or phenylephrine. Ephedrine is a less effective, but widely used alternative. The mother should be positioned with a wedge under her right hip to achieve 15 degrees of left lateral tilt in order to minimise aorto-caval compression.

Epidural

A working labour epidural can be readily topped up to provide surgical anaesthesia for caesarean section using lignocaine 2%. Adding adrenaline 1:200,000 and bicarbonate (2 ml of 8.4%) will speed up the onset of the block. Fentanyl may be added to allow for a reduction in the dose of local anaesthetic and improve post-operative analgesia. Inject 3 ml to 5 ml of local anaesthetic at a time. One may need up to 25 ml to establish surgical anaesthesia.

One of the advantages of an epidural over a spinal for caesarean section is the ability to titrate the level of the block. This reduces the risk of profound and sudden hypotension. The other obvious advantage is the unlimited duration of action if the catheter is used post operatively for analgesia. This is particularly useful for the pre-eclamptic patient.

Some of the problems with the use of an epidural for caesarean section are: the risk of inadvertent intravenous or subarachnoid injection, an increased time to surgical anaesthesia (particularly if the epidural is being inserted de novo before the caesarean section), an increased risk of post dural puncture headache if the dura is breached and a failed block in 2-6% of cases.

An inadequate block for surgery is more likely with an epidural than with a spinal. The anaesthetist needs to warn the patient of what sensations to expect during surgery. That is, some discomfort, particularly during the delivery of the baby when fundal pressure may be used. Not all sensation will necessarily be blocked. The patient can expect some sensation of touch and movement but not pain. Test for light touch as well as for cold sensation when establishing the block. The sympathetic block will be 2 segments higher than the sensory block. In order to block the pain of the incision, the dermatomal level should extend to T10-12. In order to achieve surgical anaesthesia for caesarean section one needs to block the peritoneum, which requires the block to be extended to T4.

CSE

The advantages of a combined spinal and epidural are the same as for an epidural with the added benefit of a rapid onset due to the spinal component. The dose of local anaesthetic in the spinal can be low and then extended with the epidural if necessary.

Side effects of regional anaesthesia

Hypotension is a common side effect of regional anaesthesia. A baseline maternal tachycardia may indicate relative hypovolaemia and an increased likelihood of hypotension. I personally load with fluid whilst the spinal is being inserted and use vasopressors (alpha agonists) to treat hypotension. A prophylactic infusion of phenylephrine 100 mcg per min can be used. Ephedrine has been shown to increase foetal acidosis but is a reasonable option where alpha agonists are not available. Bradycardia should be treated early with atropine.

Nausea and vomiting is usually associated with hypotension or the use of opioids.

A reduced VC and ineffective cough can occur with a block extending to the thoracic segments. The patient may complain of dyspnoea due to intercostal muscle paralysis. The anaesthetist should maintain oxygenation by providing supplemental oxygen via a facemask and reassuring the patient. Diaphragmatic function is preserved so long as the block does not extend to C4. It is important to check upper limb power to exclude the possibility of an impending total spinal.

Itch occurs due to the use of neuraxial opioids. Although shivering is common, particularly with an epidural, the mechanism is not known. It can be treated with small doses of pethidine 20-25 mg or clonidine 25-50 mcg intravenously.

Complications and risks of neuraxial blockade

Unintended high or total spinal block is more common with the use of epidurals because a large volume of local anaesthetic is required to establish a block. The risk of a high or total spinal is 1:10 000. Large doses of local anaesthetic also present the problem of local anaesthetic toxicity. The risk of intravascular injection of local anaesthetic with an epidural is 1:10 000.

Headache occurs due to ongoing cerebrospinal fluid leak after the dura has been breached. If there is an unintentional dural puncture with an epidural needle, the risk of developing a headache is 80%. The risk of a headache after spinal anaesthesia is reduced to roughly 1:200 with the use of small-gauge pencil-point needles.

The risk of obstetric palsy including obturator nerve, femoral nerve and common peroneal nerve injury is 1:3000. The risk of neurological damage with neuraxial blockade is 1:13 000.

A spinal or epidural haematoma or abscess may lead to permanent paralysis as can needle insertion and injection into the spinal cord. The risk of permanent paralysis with the use of a neuraxial blockade is quoted at 1:1 000 000.

The spinal cord terminates at the level of L1-2 in most adults but may end at L2-3 in some patients. Tuffier's line is an unreliable as a way of identifying the correct vertebral level, particularly in the obese. One may have miss-judged the level by 2 segments and given that the spinal cord may be at L2-3, one should avoid inserting a needle above L3.

Post operative analgesia

A simple regimen for post-operative analgesia after caesarean section is usually best. There are several options for analgesia. Epidural or spinal morphine is common in some people's practice and provides good analgesia for up to 24 hours. However, there is an increased risk of itch, nausea and vomiting and most importantly, delayed respiratory depression. Patient controlled intravenous morphine is another option for post-operative analgesia but is cumbersome.

In Melbourne, it is common practice to use a combination of regular paracetamol, rectal or oral diclofenac and rectal or oral oxycodone. Oxycodone is as effective as a neuraxial opioid and far safer. It is simple and inexpensive, with less need for nursing intervention. One does need to bear in mind that other opioids should not be administered within 6 hours of a dose of oxycodone due to the risk of respiratory depression.

In the pre-eclamptic patient, an ongoing epidural infusion will not only provide post-operative analgesia, but will help with blood pressure control. One should check that the coagulation is normal before the epidural catheter is removed.

General anaesthesia

The most common indications for general anaesthesia include: a contraindication to regional anaesthesia, the failure of regional anaesthesia and when there is a need for urgent delivery within 10 minutes such as might occur with severe foetal distress, cord prolapse, and placental abruption.

The advantages of general over regional anaesthesia include a more rapid induction, less hypotension, less maternal anxiety and its application in situations where there is a contraindication to regional anaesthesia.

Potential problems

1. Aspiration pneumonitis
2. Failed intubation (your first responsibility is to the mother)

3. Stress response to intubation
4. Rapid desaturation (pre-oxygenate the patient before induction)
5. Supine hypotension
6. Neonatal depression (Lower APGAR scores at one minute are related to sedation. Regardless of the anaesthetic technique, uterine incision-to-delivery time of greater than 3 minutes produces more asphyxia.)
7. The incidence of maternal awareness is reduced with the use of an increased dose of induction agent and the increased use of volatile agents.
8. Uterine relaxation and maternal bleeding.

Conduct of General Anaesthesia

Reduce the risk of acid aspiration by fasting the patient for at least 6 hours from solids and 3 hours from clear fluids, give antacid prophylaxis as already described and perform a rapid sequence induction with a good assistant to provide cricoid pressure after the loss of consciousness.

Supine hypotension is common at term due to aortocaval compression. This is reduced by left lateral tilt of 15 degrees.

Due to the increased incidence of blood loss under general anaesthesia, it is important to secure large-bore intravenous access. In order to reduce the induction to delivery time, insert a urinary catheter and ask the surgeon to prepare and drape the abdomen before induction of the anaesthetic. Allow the surgeon to start operating as soon as the endotracheal tube is inserted and its position confirmed.

Hypocapnia induces uterine vasoconstriction, therefore avoid hyperventilation of the patient. The patient should be extubated when her airway reflexes return to avoid aspiration of stomach contents on emergence.

Failed intubation is the leading cause of anaesthetic maternal mortality. The incidence is greater than in the general surgical population (up to one in 200). Ensure you have assessed the airway and called for assistance if it looks difficult. Pre-oxygenate the patient in order to allow yourself more time for intubation. Always have a back up plan for failed intubation and know a technique for cricothyroid puncture.

Emergency caesarean section

The rate of emergency CS varies depending on the definition of an emergency but has been reported to be 61%.

The time required for surgical readiness in emergency caesarean section is slightly longer (17min) with a spinal compared with a general anaesthetic. This time is reduced in more experienced hands. In any case, the time difference for surgical readiness for emergency

caesarean section does not justify a general where a spinal can be performed. That depends on your definition of an emergency....

The indications for an emergency caesarean section can be grouped into maternal and foetal indications. Maternal indications include a deteriorating medical condition, haemorrhage and trauma. The most common foetal indication is acute severe foetal distress. The other foetal indications are a prolapsed presenting part and foetal injury.

How urgent is urgent?

Anoxia and brain injury in the rhesus monkey

In an early study, hypoxia was deliberately induced in the foetus of the rhesus monkey by clamping the umbilical cord for different periods of time and the severity of foetal brain injury was determined. Less than 10 minutes of anoxia produced no brain injury. With 10-20 minutes of anoxia the foetus survived but had neuronal injury especially in the basal ganglia, thalamus and brain stem. Over 20 minutes of anoxia caused death.

Post mortem caesarean section and neonatal sequelae

Delivery interval	Neurological sequelae
< 5 minutes	0%
5-10 minutes	13%
10-15 minutes	17%
>15 minutes	82%

Grading of urgency of caesarean section

I	Immediate threat to life of mother or baby	1-10 minutes	GA
II	Maternal or foetal compromise which is not life threatening	10-30 minutes	Spinal
III	Needing early delivery but no maternal or foetal compromise.	30-60 minutes	Regional
IV	At a time to suit the patient and staff	1-24 hours	Regional

In the UK, the Association of Anaesthetists of Great Britain and Ireland, the Royal College of Obstetrics and Gynaecology and the Royal College of Midwives, recommend that when a decision is made to deliver a baby by caesarean section because of foetal distress, the baby should be delivered within thirty minutes. In a series of audits done in a large obstetric unit in the UK, it was found that delivery within thirty minutes is achievable in only two of three cases but that the delay in delivery made no difference to the rate of admission to special care for babies over 36 weeks.

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