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Editors: Iain Wilson and Bruce McCormick

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Editorial

Welcome to Update in Anaesthesia number 21!
This edition of Update has been produced by the World Anaesthesia Society, and has been generously funded by the Publications Committee of the World Federation of Societies of Anaesthesiologists.

Update 21 covers a number of topics which the editorial team hope will prove practical to our readers. In particular the articles on ketamine, local anaesthesia and post-partum haemorrhage are all important topics and have been requested by different readers. Please continue to send requests for articles.

Readers of Update will be delighted to hear that a series of on-line tutorials are being produced on the website www.anaesthesiaworld.com. These are available free of charge, and in time will form an entire curriculum of anaesthesia based topics. The tutorials are produced on a weekly basis, and cover a range of topics including clinical anaesthesia, obstetric and paediatric anaesthesia, basic sciences, regional techniques and intensive care.

The tutorials can be downloaded from the website or received weekly by email by contacting carol@world-anaesthesia.org. We look forward to feedback on this new venture which is proving very popular. Some of the tutorials are reproduced as articles in this edition of Update.

The WFSA is also trying to increase the numbers of books and journals donated to developing world anaesthetists. If you are working without access to books and journals, and would like to request a book donation, please email carol@world-anaesthesia.org with details of yourself and your hospital.

I am delighted to let all our readers know that from the next edition of Update in Anaesthesia, Dr Bruce McCormick will take over as the editor. I have greatly enjoyed developing and editing Update in Anaesthesia since 1992, and have very much appreciated all the feedback from different parts of the world. I would like to thank the WFSA for their kind support, Angela Frost who has typeset the journal and Media Publishing who have printed and distributed the journal for us.

I hope that you enjoy this edition.

Please inform us if you change address in order to keep our records up to date.

Best wishes,

Iain Wilson
Bruce McCormick

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FETAL COMPROMISE

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The management of the compromised fetus is a challenging task and often prompts performance of an emergency caesarean delivery. One important aspect in the care of the compromised fetus is the well-coordinated team. The team members should clearly understand the medical terms used to describe fetal status and the urgency of the necessary intervention. Fetal distress is a poorly defined term and may result in unnecessary emergency caesarean deliveries under general anesthesia.

This article reviews the pathophysiology, diagnosis, terminology and anesthetic management of the compromised fetus.

Pathophysiology of fetal asphyxia

Fetal asphyxia results from failure to maintain gas exchange. During normal labor, hypoxemia occurs transiently with uterine contractions. The healthy fetus tolerates this well.

There are four basic causes of asphyxia in the intrapartum period¹:

1. Inadequate perfusion of the maternal side of the placenta (severe maternal hypotension, aortocaval compression).
2. Interruption of gas exchange across the placenta (placental abruption).
3. Interruption of umbilical blood flow (cord compression).
4. Inability to withstand transient, intermittent hypoxia that occurs with uterine contractions of normal labor in the compromised fetus (anemic or growth retarded fetus).

At the onset of asphyxia, the fetus reacts with a remarkable series of responses. First there is redistribution of blood flow to vital centres to limit the deleterious effects of oxygen limitation in the brain, heart and adrenal glands. A further compensatory response is that overall fetal oxygen consumption declines to values as low as 50% of the control. This level can be maintained for periods up to 45 minutes and is completely reversible on cessation of hypoxia. There is accumulation of lactate in the vascular beds with limited oxygen supply due to anaerobic glycolysis leading to gradual development of a metabolic acidosis².

Diagnosis of intrapartum asphyxia

The diagnosis of intrapartum asphyxia is normally made by alterations in the fetal heart rate or scalp blood gases.

Changes in fetal heart rate (FHR) characteristics and patterns³:

- The normal FHR is between 110 and 160bpm. Persistent **fetal tachycardia** may be associated with fetal hypoxia or be caused by fever, chorioamnionitis, administration of anticholinergic agents, beta sympathomimetic agents, or fetal anemia. Persistent **fetal bradycardia** may be associated with fetal hypoxia (most common cause), congenital heart block and administration of beta- adrenergic blocking agents.
- **Baseline variability - short-term or beat-to-beat variability** is the difference in fetal heart rate between successive beats which is measured via fetal scalp electrodes. **Long-term variability** can be detected with external or internal monitors, and appears as crude sine waves of 3-6 cycles per minute. Normal long-term variability is more than 6bpm. The presence of both long-term and short-term variability indicates normal interaction between sympathetic and parasympathetic control of FHR and an absence of cerebral hypoxia. Acute hypoxia may initially increase FHR variability. Persistent hypoxia causes loss of variability which may also occur from other factors such as maternally administered medications. These include central nervous system depressants (volatile anesthetics, barbiturates, propofol, benzodiazepines, magnesium), local anesthetics (lidocaine, chloroprocaine), narcotics, anticholinergics, and beta sympathomimetics. There is strong evidence that the presence of normal fetal heart rate variability represents normal central nervous system integrity, including adequate oxygenation¹.
- **Periodic changes.** Early, late, or variable FHR decelerations may occur.

Early decelerations occur simultaneously with uterine contractions and usually are less than 20 bpm below baseline. The onset and offset of each deceleration coincides with the onset and offset of the uterine contraction. Early decelerations are not ominous, and in humans, thought to result from reflex vagal activity secondary to mild hypoxia.

Late decelerations begin 10 to 30 seconds after the beginning of a uterine contraction and end 10-30 seconds after the end of the uterine contraction. Late decelerations represent a response to hypoxia, and when combined with absent or decreased FHR variability is an accurate, ominous signal of fetal distress⁷.

Variable decelerations vary in depth, shape, and/or duration. Clinical studies suggest that partial or complete umbilical cord occlusion results in variable decelerations.

- **Reactivity** is acceleration in response to fetal movement. During the antepartum period, FHR accelerations in response to fetal movement signal a healthy fetus. During the intrapartum period, the presence of fetal accelerations most likely precludes significant fetal metabolic acidosis.

Fetal acid-base status

Although FHR monitoring is very accurate (99%) in predicting a healthy fetus, it suffers from lack of specificity. Abnormal FHR tracing has a poor positive predictive value for abnormal outcome. The prediction of fetal compromise has a 35-50% false positive rate. Therefore, when FHR monitoring suggests the presence of fetal compromise, fetal scalp blood pH determination may be used to confirm or exclude fetal acidosis. In general, fetal scalp blood pH of less than 7.20 is considered abnormal and delivery should be expedited. Relative contraindications to fetal scalp blood pH sampling include intact membranes and unengaged vertex, infections such as HIV or herpes simplex virus and fetal coagulopathy.

Meconium passage in utero - controversy exists over its relative importance on fetal status.

Passage of meconium into the amniotic fluid (in utero defecation) is accepted as an indicator of fetal distress. Recent experimental and clinic studies have suggested that meconium passage into the amniotic fluid (AF) alone was not necessarily a sign of fetal distress. The human fetus exchanges the amniotic volume totally by urinating, swallowing, and respiratory tract secretions every 24 to 48 hours in the last trimester. Swallowing serves to stabilize the AF volume and plays a major role in the clearance mechanism. It has been shown that fetal swallowing is suppressed under fetal distress conditions. Therefore, it is suggested that meconium-stained AF is not related to meconium passage after fetal distress; rather it reflects impaired clearance of AF, which already contains meconium caused by physiological in utero defecation⁴.

Meconium-stained AF causes amniotic epithelial destruction and vascular damage resulting in further impairment of the transamniotic clearance mechanism. It also produces umbilical vein contraction⁵ causing fetal hypoperfusion, thus distress. Both of these factors aggravate the impaired clearance mechanism and create a vicious cycle during intrauterine life.

The relationship between peripartum asphyxia and cerebral palsy

At the time FHR monitoring was introduced, it was felt that virtually all intrapartum deaths and neonatal cerebral palsy were due to intrapartum asphyxia, yet the prevalence of cerebral palsy has not decreased

since the advent of fetal electronic monitoring.⁶ A multivariate analysis of risk revealed that the leading factors associated with cerebral palsy are maternal mental retardation, birth weight less than 2000g, and fetal malformation. Other factors involved are breech presentation, severe proteinuria in the second half of pregnancy, third trimester bleeding and a gestational age of 32 weeks or less⁷. Although severe asphyxia can cause cerebral palsy, it is now clear that the proportion of cerebral palsy caused by birth asphyxia is relatively small. The incidence of cerebral palsy due to intrapartum asphyxia is of the order of 0.025% (1000 fold less than the incidence of variant FHR patterns during labor)⁸.

How quickly should the baby be delivered when there is fetal compromise?

“Fetal distress” is a widely used term indicting the need for an urgent caesarean section, but it is a poorly defined, nonspecific term. It is clear that we should no longer accept the term fetal distress as a sufficient description of fetal condition.⁹ This confusion of definition compounds the difficulty of making an accurate diagnosis and initiating appropriate treatment. Better terminology is:

- **Fetal asphyxia** is a non-reassuring fetal status. The term non-reassuring fetal status describes a condition arising from compromised fetal gas exchange (diminished but persisting gas exchange) and there is usually time to place a regional block.
- The term **fetal anoxia** describes a condition resulting from complete cessation of gas exchange (complete cord occlusion, sustained bradycardia, tetanic uterine contractions, uterine rupture); which can be lethal in <10 minutes. The desired time frame from the diagnosis to delivery in cases with presumed fetal anoxia is strictly as soon as possible.

Planning anaesthesia

Fetal anoxia (e.g. cord prolapse with fetal bradycardia) can be lethal in less than 10 minutes however the speed and effects of fetal asphyxia are highly variable. Some brief episodes of mild asphyxia, on the other hand, may reverse spontaneously. Therefore, **it is always advisable to check the FHR in the operating room before proceeding with the caesarean delivery.** When deciding which anesthetic technique to use, the anesthesiologist must clarify with the obstetrician the nature of the asphyxia to determine the urgency of the caesarean section.

Pregnant airway and changes in airway during labour

Major maternal risks of general anesthesia are failed intubation, failed ventilation, and pulmonary aspiration of gastric contents. A recent study indicates that the case-fatality risk ratio for regional anesthesia for obstetrics is 16.7 times less than for general anesthesia, primarily because of decreased

number of complications associated with regional anesthesia¹¹. Therefore, general anesthesia should be used only when it is absolutely necessary and in most hospitals regional anesthesia is preferred during pregnancy. However in resource poor environments where drugs and equipment may be in short supply, different principles may apply.

Early assessment and communication with the anaesthetist for patients who may be at risk of requiring operative intervention allows airway and other preoperative assessment. In some units epidural analgesia is encouraged in patients thought to be at high risk for operative delivery including multiple gestation, preeclampsia, diabetes, IUGR, macrosomia, morbid obesity (caesarean delivery rate > 50%).

The result of an airway assessment in early labor, however, may no longer be valid after a period of active labor, especially after prolonged strenuous bearing down efforts. Deterioration in Malampati scores has been reported due to edema, which is explained on the basis of the intermittently raised venous pressure in the upper body.¹² Therefore, airway assessment should be repeated prior to initiation of any major obstetric anesthesia.

Intrauterine treatment for abnormal fetal heart rate patterns

As soon as fetal compromise is suspected, maternal and fetal factors that may contribute to this compromise should be identified. There are therapeutic measures that may successfully resuscitate the fetus in-utero and allow time for placement of regional anesthetic (or delivery of the fetus vaginally, if imminent). Maintaining effective uterine blood flow is a priority.

$\text{Uterine blood flow} = \frac{\text{uterine artery pressure} - \text{venous pressure}}{\text{vascular resistance}}$
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Correctable maternal factors to improve uterine blood flow

- **Hypotension.** Normal maternal blood pressure and uterine artery pressure should be maintained by left uterine displacement to avoid aortocaval compression, intravenous fluid replacement, and giving vasopressors (ephedrine, phenylephrine) if indicated.
- **Excessive uterine activity.** Uterine contractions constrict the uterine spiral arteries and cause decreased placental perfusion and oxygen delivery. Oxytocin infusion may result in uterine tetany. Oxytocin has a plasma half-life of 1 to 6 minutes. Therefore, after stopping the infusion of oxytocin, tocolytic agents such as terbutaline and nitroglycerin may be necessary to relieve the tetanic contraction.

Supplemental Oxygen

Although there is little objective evidence that maternal supplemental oxygen improves neonatal outcome in cases of fetal distress during labor¹⁸, most obstetricians advocate oxygen 4–6lpm by facemask to these mothers. Maternal supplemental oxygen increases fetal transcutaneous PO₂ slightly and seems unlikely to cause uterine vasoconstriction.

Correctable fetal factors to improve uterine blood flow

- **Transient umbilical cord compression** (causes variable decelerations). Oligohydramnios is a risk factor for cord compression. Changing maternal position may relieve the compression and correct fetal compromise. Amnioinfusion may also relieve the compression. This is done by infusing about 800ml lactated Ringer's solution at a rate of 10-15ml/min initially. This may be followed by repeated boluses of 250ml at a rate of 2-3ml/min. Correction of abnormal FHR pattern requires 20-30 minutes. Amnio-infusion by gravity rather than by means of a pump prevents uterine over distension. Maternal infection and fatal amniotic fluid embolism have occurred during amnioinfusion.
- **Increased fetal oxygen consumption** Hyperglycemia increases fetal oxygen consumption and leads to neonatal hypoglycemia after delivery. Therefore, administration of a large bolus of glucose-containing solution is contraindicated. Maternal fever should be treated with acetaminophen, antibiotics and cooling of the mother.

Emergency cesarean sections have been divided into three categories as follows:¹⁰

Stable: There is stable maternal and fetal physiology. The patient requires caesarean delivery before destabilization occurs. The preferred anesthetic technique is regional anesthesia (spinal, epidural or combined spinal/epidural). Examples include chronic uteroplacental insufficiency or footling breech presentation with ruptured membranes and not in labor.

Urgent: There is unstable maternal and/or fetal physiology, but not immediately life-threatening to the mother or fetus. Regional anesthesia is preferred using the preexisting epidural catheter, single shot spinal, or combined spinal epidural. Examples include cord prolapse without fetal distress or variable FHR decelerations with prompt recovery and normal FHR variability.

Emergency: Immediate life-threatening condition exists for the mother and/or fetus. Preferred anesthetic technique is general unless epidural anesthesia can be established quickly using a pre-existing epidural catheter. Examples include prolonged fetal bradycardia or late FHR decelerations with absent FHR variability.

Regional anesthesia for emergency caesarean section

Hospitals should be able start a caesarean delivery within 30 minutes of the decision to operate.

Examples of indications that may require more rapid delivery include prolonged fetal bradycardia and late FHR decelerations with no FHR variability, cord prolapse, uterine rupture or maternal hemorrhage such as in placenta previa.

If an epidural catheter has been placed earlier for labor, and the patient is hemodynamically stable, extension of the block with 3% 2-chloroprocaine, 2% lidocaine or 0.5% bupivacaine are appropriate choices for emergency caesarean section. After an initial 2-3ml bolus of local anaesthetic (to exclude intrathecal migration of the catheter), the remaining medication, usually 15-20ml, can be given in increments of 5ml every 2-3 minutes, until an adequate level for surgery is achieved. The patient should receive an intravenous bolus of Ringer's lactate because the local anaesthetic has a fast onset of action. This rapid onset also ensures that the anesthetic level will be adequate for incision when the surgeon is ready. Chloroprocaine is rapidly metabolized by both the mother (25 seconds) and fetus (45 seconds) making it the authors' first choice. If 2-chloroprocaine is not available, 2% lidocaine with epinephrine (1 in 200,000) may be administered. The onset of anesthesia is shown to be only 2 minutes slower than 2-chloroprocaine when bicarbonate (2ml of 8.4% sodium bicarbonate per 20ml of lidocaine) and 1:200,000 epinephrine is added¹³.

If an epidural catheter is not already in place, spinal anesthesia may be given safely in most urgent cases. When fetal compromise is present, the anesthetist should consider the possibility of placental abruption, concealed hemorrhage and unrecognized hypovolemia.

Fluid preloading with Ringer's solution through a large bore (18 or 16G) intravenous access should be started. A 25G pencil point spinal needle is preferred to avoid post dural puncture headache. Usually 10-12mg of hyperbaric bupivacaine (2-2.4ml of 0.5%) injected intrathecally provides rapid onset of spinal anaesthesia. Prophylactic administration of ephedrine 10-15mg IV may avoid episodes of significant hypotension. If the anaesthetist is not expert at performing spinal anaesthesia, or there are delays in establishing the block, the plan should change to general anaesthesia.

Some high-risk patients (morbidly obese, difficult airway) require a reliable and controllable regional anesthetic technique and some anaesthetists use an **intrathecal catheter** (using a spinal microcatheter) followed by incremental bolusing.^{14,15} For caesarean section, we use incremental doses (0.3-0.5ml) of 0.5% hyperbaric bupivacaine to achieve an adequate block. In most cases an adequate block is achieved with 1.6-2.0ml of this solution.

Characteristics of regional anesthetic techniques suitable for Caesarean section

	Spinal	Continuous Epidural	Continuous Spinal
Rapid onset	+	-	+
Controllable duration	-	+	+
Consistently effective	+	-	+
Controllable level	-	+	+
Low dose of local anesthetic	+	-	+

Source: Mallan PT, Johnson MD. *Difficult airway in obstetric anesthesia J Clin Anesth.* 1988;1:107

General anesthesia

General anesthesia with rapid sequence induction is required for many emergency cesarean deliveries due to fetal condition or unstable maternal condition. When there is fetal compromise anesthetists must be prepared to provide anesthesia quickly, but safely. Patients should receive normal antacid medication according to local protocols.

- **Difficult intubation.** The incidence of failed intubation in pregnancy is 1:250-1:750, which is ten times that of nonpregnant patients¹⁶. Difficult intubations are encountered in 5% of general anaesthetics in obstetrics¹⁷. A pregnant patient has not only a more difficult airway, but desaturates more rapidly (3 times faster than a nonpregnant person) due to increased oxygen consumption and decreased functional residual capacity. A difficult intubation kit with airway devices to provide emergency oxygenation such as combitube, laryngeal mask airway, percutaneous cricothyrotomy kit should be readily available in the obstetric suite.
- **Unrecognized difficult airway.** When attempts at intubation fail after the three or four attempts with repositioning of the head/neck, applying external pressure over the thyroid cartilage and using different laryngoscope blades (optimal intubation attempts), it is important to stop further manipulations and reassess the situation. Ask yourself:
 1. Is there severe fetal compromise (fetal anoxia) or a maternal obstetric emergency?
 2. Is the maternal airway okay and is there adequate gas exchange by mask?

If there is no fetal compromise or obstetric emergency, and the patient is stable, the patient should be woken up. Continue assisted mask ventilation with 100% oxygen and cricoid pressure until awake. Once the patient is awake,

the options include awake regional anaesthesia or an awake fiberoptic intubation.

If there is severe fetal compromise or an obstetric emergency and mask ventilation with cricoid pressure is adequate, one may proceed with 100% oxygen and volatile agent such as halothane. In order to minimize passive regurgitation, the surgeon should avoid fundal pressure and uterine exteriorization.

If the patient cannot be intubated or ventilated by mask, the priority is to maintain ventilation and provide oxygen rapidly to the mother using the following rescue options. Surgery should wait until the patient is stabilized.

- LMA
- Combitube
- Percutaneous cricothyrotomy
- Surgical cricothyrotomy

Case history

35 year old, obese (130kg, 5'2"), woman (G4P0), at 34 weeks gestation is rushed to the operating room for an emergency caesarean section for "fetal distress". The obstetrician insists on general anaesthesia.

She has a large tongue, and a Mallampati IV airway classification. What should the anaesthetist do?

- Ask the obstetrician the reason for concern in more specific terms.
- Check the FHR in the operating room.
- When faced with a patient who has potentially difficult airway, communicate your concerns to the obstetrician and look for therapeutic measures that may successfully resuscitate the fetus in utero and allow time for placement of regional anaesthetic.
- If general anaesthesia is the only choice, call for help and:
 - Optimize the position of the patient's head and neck to facilitate successful endotracheal intubation.
 - Ensure the availability of airway devices to provide O₂ rapidly such as laryngeal mask airway, combitube, percutaneous cricothyrotomy kit.
 - If intubation fails, and the mask ventilation with cricoid pressure is adequate, you may proceed with 100% oxygen and volatile agent when there is severe fetal compromise or other obstetric emergency.
 - If the patient cannot be intubated or ventilated by mask, the priority is to maintain the ventilation and oxygenate the mother. The mother's life always takes priority.

The consequences of poorly managed perinatal emergencies can be devastating. Clear communication between the anaesthetist and the obstetrician is vital in selecting the optimal anaesthetic care for these patients. Most maternal deaths under anaesthesia occur during emergency caesarean deliveries.

Work with your obstetrician to develop strategies to minimize the need for emergency induction of general anaesthesia for caesarean delivery.

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CARDIAC OUTPUT MONITORS

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Cardiac output can be measured in a number of ways, from simple clinical observation to invasive haemodynamic monitoring. Estimation of cardiac output has an important role in patient management during anaesthesia and critical care. This ranges from monitoring the predictable changes of anaesthetic induction to assessing cardiac output during anaesthesia for major surgery or resuscitation of trauma victims and critically ill patients. Advanced monitoring techniques are often used when clinical signs are difficult to interpret.

DEFINITIONS

Cardiac output is the volume of blood ejected from each of the ventricles of the heart per minute, and is therefore the product of stroke volume and heart rate. The unit of cardiac output is l/min. **Cardiac index** is the cardiac output of a patient referenced to their body surface area and has units of l/min/m². The stroke volume is the volume of blood ejected by each contraction of the ventricle and is determined by the **preload**, the **contractility** and the **afterload**.

Preload describes the tension developed in the ventricle wall at end-diastole (i.e. at maximal filling just prior to contraction). This tension is difficult to measure and end-diastolic pressure is taken as a surrogate measurement.

Contractility refers to the amount of work the heart can generate, at given levels of preload and afterload, and is estimated by the maximum rate at which the ventricle can generate a change of pressure over time. Inotropy is used to explain an increase in the work done by the heart, that is independent of heart rate, preload and afterload.

Afterload is the tension that needs to be generated in the ventricle wall in order to eject blood into the arterial system during systole. This is largely determined by the resistance of the arterial system – **the systemic vascular resistance** (SVR). It is calculated by:

$$\text{SVR} = \frac{\text{mean arterial pressure (mmHg)} - \text{central venous pressure (mmHg)}}{\text{cardiac output (l/min)}} \times 8$$

(Recall that Ohm's Law describing electrical resistance is analogous to this: $V=IR$)

The units of the SVR are dyne second/cm⁵.

The cardiac output is determined by, and therefore can be manipulated by, alterations to the **heart rate**

or **rhythm**, the **preload**, the **contractility** and the **afterload**.

Cardiac output informs us of global blood flow and therefore oxygen delivery (the product of cardiac output and blood oxygen content) and does not describe delivery of oxygen to each organ, whose function must be assessed individually.

An appreciation of how information is measured and derived using a cardiac output monitor is essential in order to use the information accurately and appropriately.

Thorough assessment of a patient's clinical status strongly influences interpretation of the measurements made. For example, cardiogenic shock and obstructive shock due to tamponade will both give a low cardiac output, but can be differentiated by the patient's clinical signs. There is a wide variability between practitioners in the measurement and interpretation of cardiac output data, using the various techniques that are currently available. For this reason, clear evidence that they benefit patient outcome is difficult to obtain.

MEASURING CARDIAC OUTPUT

The interpretation of data from invasive haemodynamic monitoring is made in light of the clinical examination. Heart rate, blood pressure, pulse strength at various sites, patient colour, respiratory rate and core to peripheral temperature gradient all give an indication of a patient's haemodynamic status. A patient's ability to compensate for a haemodynamic insult is highly variable, depending on age, premorbid status and other comorbidities. An example is the rise in the diastolic pressure in early hypovolaemic shock, associated with peripheral vasoconstriction, that is usually only seen in young fit individuals. In addition, clinical parameters such urine output, capillary refill time and cognitive function give a guide to end organ perfusion.

Measurement of lactate and base deficit in arterial blood and, in particular, the trend of these variables over time gives non-specific information about a patient's organ perfusion. The oxygen saturation

in central venous blood ($S_{cv}O_2$) also gives a global indication of haemodynamic status, is useful in directing fluid therapy¹ and is a reliable surrogate of mixed venous oxygen saturation (see under pulmonary artery flotation catheters, PAFC - below).

Oesophageal Doppler

Theory of technique

A Doppler probe is inserted into the distal oesophagus and is directed to measure the blood flow in the descending aorta at about 35 to 40cm from the incisors. The monitor calculates cardiac output using descending aorta diameter, which is either obtained from an age-related nomogram or measured directly (in newer machines). The ventricular ejection time corrected for heart rate (the corrected flow time, FTc) gives an indication of preload, and the peak flow velocity (PV), estimates the contractility of the ventricle. Newer probes incorporating M-mode Doppler measurement may improve accuracy and reliability.

Practical application

The technique is straight-forward, easily learned, and relatively non-invasive. The disposable probes are easy to insert, however some expertise must be gained in recognition of intracardiac and pulmonary artery signals. Continuous measurement is possible, although frequent positional adjustments are needed. Some user variability is inevitable.

Advantages

The system is small and relatively portable, but requires an electrical power source. The calculated cardiac output correlates well with that of the PAFC. The cardiac output data is best used as a trend to guide the effectiveness of interventions such as fluid challenges. Paediatric probes are available.

Disadvantages

Few complications have been described, but oesophageal injury is possible. Oesophageal Doppler use is contraindicated in the presence of oesophageal varices. When patients are positioned on their side for surgery, movement of the mediastinum with ventilation (particularly during thoracotomy) makes reliable probe positioning impossible. The probe is poorly tolerated in awake patients, although thinner nasal probes are available.

Transoesophageal Echocardiography (TOE)

Theory of Technique

A specialized oesophageal probe is inserted into the oesophagus, providing real-time, high resolution ultrasound images. Both qualitative and quantitative values for cardiac output are available, using a two dimensional cross-sectional area measurement, a Doppler flow measurement at that point and the heart rate.

Practical application

A multiplane transducer is inserted into the oesophagus and stomach, where various standardized views are gained.

Advantages

A large amount of haemodynamic information is available beyond just cardiac output.

Disadvantages

The probes are still expensive and the machinery is large and bulky. Various levels of examination skill are required and these take time and resources to learn. A full study can take over twenty minutes. Some form of local pharyngeal anaesthesia or sedation is required to tolerate the probe. There is a risk of trauma from the probe, although the risks are low in patients with no oesophageal disease. The probes generate a degree of heat and are therefore not suited to continuous measurement. As the technology advances and costs decrease, TOE may find more applications in theatre and the ICU.

Lithium Dilution Monitoring – Lidco and PulseCO and Lidcoplus

Theory of Technique

This technique combines the techniques of lithium dilution (Lidco and Lidcoplus) and pulse contour analysis (PulseCO). A small dose of lithium is injected into a peripheral vein and an ion selective electrode is attached to a peripheral arterial line. The area under the curve of a plot of lithium concentration against time allows accurate calculation of the cardiac output. This information is then used to calibrate the PulseCO which provides 'beat-to-beat' cardiac output measurement, using pulse contour analysis of the arterial waveform.

Practical Application

The convenience of this system is that it uses catheters which are likely to be already in place or are likely to be needed in a critically-ill patient. The system requires some familiarity to set up, but is relatively quick. The total dose of lithium is small and is clinically insignificant. Calibration is recommended every 8 hours, or after any significant change in the patient's clinical condition.

Advantages

A figure for stroke volume variation is produced and provides an indicator of volume responsiveness to fluid therapy.

Disadvantages

The system cannot be used for patients taking lithium and those who have recently received vecuronium or atacurium. The monitor performs poorly in the presence of atrial fibrillation and other tachyarrhythmias. The system is prone to technical difficulties related to damping and resonance within the measurement system.

Thermodilution Pulse Contour Monitoring – PiCCOplus

Theory of Technique

This technique uses arterial pulse contour analysis (PulseCO) to measure cardiac output and correlates well with the PAFC (below). ‘Stroke volume variation’ (the mean difference between the highest and lowest arterial pressure wave peaks over 30 seconds) gives an indication of the blood volume status of the patient.

The system is calibrated using intermittent cold transpulmonary thermodilution, where cold fluid is injected through a central venous catheter and traverses the pulmonary circulation. A curve of blood thermodilution is measured in a systemic artery and, in addition to cardiac output, other data is derived. The calculated extra-vascular lung water (EVLW) gives an indication of the water content of the lungs and is increased in left ventricular failure, pneumonia and sepsis. The normal range is 3-10ml/kg and values greater than 14ml/kg are associated with an increased mortality. The intra-thoracic blood volume index gives an indication of blood volume status (normal value 850-1000 ml/m²).

PiCCOplus replaced the original PiCCO machines in 2002 and have improved displays, automated features and allow the use of room-temperature injectate for calibration.

Practical Application

A specialised arterial catheter, inserted into either the brachial artery or femoral artery is required, along with either a thoracic or femoral central line. Some centres use treatment algorithms based on these variables, to guide use of fluid and inotropes in an attempt to maximize intravascular filling, without increasing the EVLW and causing pulmonary oedema. The use of EVLW as an endpoint for resuscitation has not been validated.

Advantages

The arterial line can be simultaneously used for blood pressure monitoring and for blood sampling. The system is relatively easy to set up and calibrate.

Disadvantages

The arterial catheter is relatively large gauge and expensive, although few complications have been reported. Recalibration is required every 12 hours or following a major change in the patient’s clinical condition.

Pulmonary artery flotation catheters (PAFC)

Dye dilution is the gold standard for measurement of cardiac output, but is impractical for clinical practice. Thermodilution using a PAFC uses similar principals. However, use of PAFCs has been hotly debated in recent years and use in the United Kingdom is currently low. The recent PAC-Man trial showed no improvement in survival for patients randomised to

have a PAFC inserted, compared to those who were not².

Theory of technique

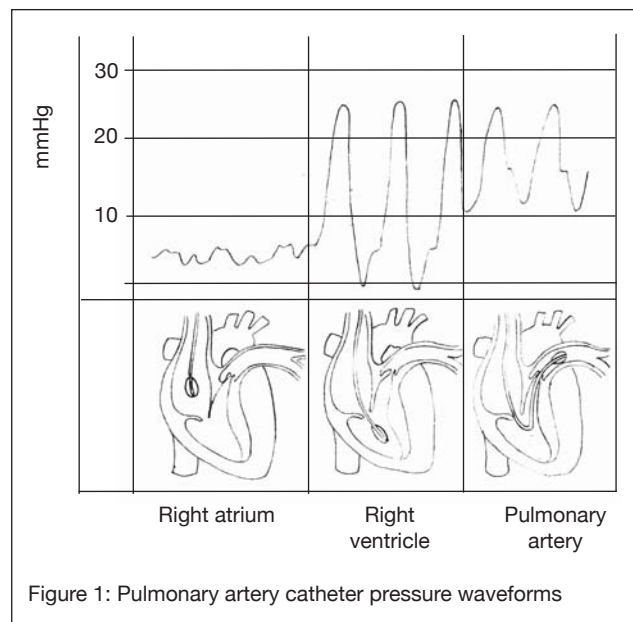
A flexible balloon-tipped, flow-directed catheter is inserted via a wide-bore catheter sited in a central vein. The catheter is ‘floated’ through the right atrium and ventricle to enter the pulmonary trunk. From this position it can intermittently be ‘wedged’ in one of the pulmonary arteries.

The catheter allows a number of variables to be measured and others to be derived.

The measured variables are pulmonary artery pressure, pulmonary capillary wedge pressure (PCWP), cardiac output and mixed venous oxygen saturation. Traditionally, cardiac output is measured by thermodilution of 10ml iced water injected through the proximal lumen of the catheter. Measurement of the fall in blood temperature against time from injection, as the cooled blood passes the distal end of the catheter allows calculation of the cardiac output of the right (and therefore the left) ventricle. Semi-continuous cardiac output measurements are now available which use warming coils in the right ventricular portion of the catheter. A sequence of heating and recording gives an averaged cardiac output after a short delay.

Practical Application

The catheter is inserted with reference to the waveforms seen (see figure 1). Insertion may take several attempts and is more difficult in patients with a low cardiac output.



Advantages

Measurement of cardiac output is probably the most reliable of the variables measured using a PAFC and is therefore a valuable guide to interventions introduced to increase cardiac output. The numerous

assumptions made in interpretation of the PCWP as a measure of preload or ventricular filling make the PCWP a less reliable measurement. Some units use the mixed venous oxygen saturation, measured using a sample taken slowly from the pulmonary artery aperture of the catheter, as a further indicator of a patient's overall tissue perfusion.

Disadvantages

This invasive monitor is associated with a number of potential complications. The PAC-Man study recorded non-fatal complications in 10% of insertions. In addition to the usual complications of central venous access, PAFCs may cause arrhythmias, heart block, rupture of the right heart or pulmonary artery, thromboembolism, pulmonary infarction, valvular damage and endocarditis.

Partial CO₂ rebreathing Fick monitoring or NICO

Theory of Technique

The NICO monitor uses a rearrangement of the Fick equation for CO₂ elimination. It is relatively non-invasive, although it can only be used for patients who are intubated.

Practical Application

A small, disposable plastic loop is placed between the ventilator Y-piece and the patient. It contains a rebreathing valve, a differential pressure pneumotachograph and mainstream infrared CO₂ analyser. Only one calibration is required for setup. A bedside computer induces episodes of re-breathing every 3 minutes, each lasting 50 seconds. This raises the end-tidal CO₂ by 0.4-0.6 kPa. By a rearrangement of the Fick principle for CO₂ elimination, a value for the total pulmonary blood flow (i.e. cardiac output) can be calculated. Assumptions are made about the shunt fraction and PaCO₂ being equal to end-tidal CO₂.

Advantages

These include the easy setup. Various pulmonary volumes, such as dead space are available.

Disadvantages

Although sold as non-invasive it requires the patient to be ventilated, and preferably have access to arterial blood measurements. Its main area of use has been in cardiac surgical patients and in relatively stable ICU patients.

Thoracic Bioimpedance

Theory of technique

The technique depends on the change in bioimpedance of the thoracic cavity during systole.

Practical application

A series of ECG type electrodes are placed on the thorax and neck. A small, non-painful current is passed and measurements made.

Advantages

Derived stroke volume is calculated and cardiac output computed. Thoracic fluid content is also measured. This is the least invasive method of cardiac monitoring and was initially conceived for space flight monitoring.

Disadvantages

It is not useful with significant aortic regurgitation and open chest procedures. The correlation with PAFC in critically ill patients is inconsistent.

SUMMARY

At present no perfect system exists, but each of the monitors above, can aid the clinician when uncertain about the patient's condition. The information gained must be understood in the context of how it was gathered and interpreted alongside clinical evaluation of the patient. Only then can it be safely used to guide subsequent therapeutic strategies.

Further reading

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RHEUMATOID ARTHRITIS AND ANAESTHESIA

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SELF ASSESSMENT

- You go to assess a rheumatoid patient pre-operatively. She has a hoarse voice. Why might this become significant during anaesthesia?
- What percentage of patients affected with atlanto-axial instability have symptoms or clinical signs of the condition?
- Patients often have extra-articular manifestations of disease. Which organ systems can rheumatoid disease affect?
- Patients with rheumatoid disease affecting the lung may have a restrictive pattern of disease in spirometric studies. Which pathological conditions may cause this?
- A seropositive rheumatoid patient has a routine FBC; it reveals neutropenia, anaemia and thrombocytopenia. What clinical signs would you look for in association with this? If the patient does not have any associated clinical signs, what may also be causing this pattern on the FBC?

DEFINITION

Rheumatoid arthritis is a chronic inflammatory disorder. It is characterised by a chronic polyarthritis that primarily affects the peripheral joints and related periarticular tissues. It usually starts as an insidious symmetric polyarthritis, often with non-specific systemic symptoms.

PREVALENCE

Prevalence ranges from 0.5–1.5% of the population in industrialised countries. Rheumatoid arthritis occurs more frequently in women than men (ratio 3: 1).

PROGNOSIS

The course of rheumatoid arthritis is variable with a range of disease patterns and progression. Over years, structural damage occurs, leading to articular deformities and functional impairment. Patients may also have multisystem disease as a result of the continuing inflammatory process. Rheumatoid arthritis shortens life expectancy.

ARTICULAR DISEASE

Assess joint deformities prior to anaesthesia. Special consideration must be paid regarding positioning. If regional anaesthesia is being undertaken, can the patient move their limbs into the required position for the technique? Manual dexterity is needed to use patient controlled anaesthesia devices post-operatively.

Temporomandibular joint: If the patient is unable to open their mouth, intubation may become a problem. It may be necessary to conduct a nasal fibroscopic intubation or avoid general anaesthesia.

Cricoarytenoid: Fixation of the cricoarytenoid joints may lead to voice changes, hoarseness, or even stridor from glottic stenosis. Minimal oedema may lead to airway obstruction postoperatively.

Spine: Joints of the cervical spine are often affected. This may lead to atlantoaxial subluxation or, less commonly, subluxation at lower levels, with subsequent compression of the spinal cord. The earliest and most common symptom of cervical subluxation is pain radiating up into the occiput. Other symptoms include paraesthesia, sudden deterioration in hand function, sensory loss, abnormal gait, and urinary retention or incontinence.

Atlantoaxial subluxation (AAS): AAS occurs in 25% of severe rheumatoids. Only 25% of affected patients will have any neurological signs or symptoms such as paraesthesia in the hands/feet or neck pain. Assess the range of movement in the neck. Excessive movement may lead to cervical cord compression and should be carefully avoided.

- Anterior AAS: 80% of all AAS. This is where C1 moves forward over C2 from destruction of the transverse ligament. A gap >3mm between the odontoid peg and the arch of the atlas is significant as seen in lateral flexion radiographs. Atlantoaxial extension should be avoided.
- Posterior AAS: C1 backwards on C2 resulting from destruction of the odontoid peg.
- Vertical AAS: Destruction of lateral masses of C1. The odontoid moves upwards through the foramen magnum to compress the cervicomedullary junction.
- Lateral AAS: Arises from involvement of the C1 C2 facet joints. >2mm difference in lateral alignment is significant. Requires a frontal open mouth view to assess.

EXTRA-ARTICULAR MANIFESTATIONS OF RHEUMATOID ARTHRITIS

Rheumatoid nodules: These can affect between 20%-30% of patients. Most common at sites of pressure; the extensor surfaces of the forearms and the posterior surface of the Achilles tendon. Rarely, nodules may arise in visceral organs, such as the lungs, the heart, or the sclera of the eye.

Vasculitis: Disease of small and sometimes larger blood vessels may be caused by deposition of immune complexes in the vessel walls. This can lead to digital infarction, skin ulcers, and mononeuritis because of damage to the vasa nervorum.

Eye: Sjogren's syndrome results in dry gritty eyes with slight redness but normal vision. It is usually a late feature in women with seropositive rheumatoid arthritis. Patients have a variable expression of disease in other exocrine glands: characterised by dry skin, decreased perspiration, dry vaginal membranes, or a non-productive cough. Commonly, there is also a polyclonal lymphoproliferative reaction characterized by lymphadenopathy and splenomegaly. This can mimic and rarely transform into a malignant lymphoma.

Episcleritis is ocular irritation with nodules. Vision is normal. Scleritis causes severe pain and occasionally reduces vision. There is diffuse or nodular redness, and the end stage of the condition is healing, with atrophy producing a bluish-grey sclera.

Felty's syndrome: This is a combination of seropositive rheumatoid arthritis (often with relatively inactive synovitis) with splenomegaly and neutropenia. It is associated with serious infections, vasculitis (leg ulcers, mononeuritis), anaemia, thrombocytopenia and lymphadenopathy.

Neurological complications: These include entrapment of peripheral nerves (carpal tunnel, ulnar, lateral popliteal, tarsal, etc), mononeuritis multiplex, peripheral neuropathy either associated with the disease or caused by drugs, compression of nerve roots and compression of the cervical region of the spinal cord.

Liver: Tests for liver function may give abnormal results in patients with rheumatoid arthritis. Serum concentrations of transaminases and alkaline phosphatase may be moderately elevated when the disease is active.

Pulmonary: There are several pulmonary manifestations of rheumatoid arthritis:

- Pleurisy with or without effusion
- Intrapulmonary nodules
- Rheumatoid pneumoconiosis (Caplan's syndrome)
- Diffuse interstitial fibrosis; anti-rheumatic drug reactions in the lung may be associated
- Bronchiolitis obliterans organising pneumonia (BOOP)
- Bronchiectasis
- Pulmonary hypertension

Cardiovascular: Cardiac involvement occurs in many patients with severe seropositive rheumatoid arthritis. The most common manifestation is pericarditis. This

can be associated with pericardial effusion and the development of acute or chronic pericarditis with tamponade, although most cases are asymptomatic. The restrictive pericarditis of rheumatoid arthritis responds poorly to medical therapy and generally requires pericardectomy.

Rheumatoid nodules may affect the pericardium, myocardium, and endocardium. Disease affecting the heart valves can lead to valvular regurgitation. The mitral valve is most commonly affected, but all can be involved. Myocardial nodulosis and myocarditis have been associated with conduction defects and congestive heart failure. Rarely, rheumatoid vasculitis affecting the coronary arteries leads to angina or myocardial infarction.

Detecting limitations in exercise tolerance is difficult due to problems in mobility. Check for signs of raised venous pressure.

Skin: Palmar erythema, cutaneous vasculitis and pyoderma gangrenosum are all associated.

Renal: Renal disease is rare but may occur as a result of secondary renal amyloidosis due to long standing chronic inflammation. It is often related to treatment with nonsteroidal anti-inflammatory drugs (NSAIDs), anti-rheumatoid drugs or vasculitis. Renal manifestations include glomerulonephritis, uraemia, interstitial nephritis, and papillary necrosis.

Haematological: The majority of patients with rheumatoid arthritis have a normochromic-normocytic anaemia of chronic disease. Thrombocytosis may be apparent as a result of acute and chronic inflammation. Some patients may also be deficient in iron, folic acid, or vitamin B12 causing a mixed picture on haematological analysis. Active rheumatoid disease is generally associated with an elevated erythrocyte sedimentation rate and CRP. The risk of lymphoma in patients with rheumatoid arthritis is independent of immunosuppressive therapy and is two to three times that of the general population.

Drug therapy

Patients are commonly prescribed a variety of drugs in order to control their pain, limit disease progression and suppress active inflammation. These include

- Disease Modifying Antirheumatoid Drugs (DMARDs) e.g. methotrexate, azathioprine, gold.
- Steroids
- NSAIDs
- Analgesics

There is potential for DMARDs to increase the risk of infection and prolong wound healing. This has to be balanced against the likelihood of flare-ups around the time of surgery.

Steroids: A full description of pharmacological and physiological actions is beyond the scope

of this article. However, important side effects of chronic steroid use relevant to patients undergoing anaesthesia include:

- Hypothalamic adrenal corticoid suppression requiring replacement therapy
- Immunosuppression
- Diabetes
- Obesity
- Poor wound healing
- Osteoporosis
- Nerve entrapment syndromes

NSAIDs: Aspirin has irreversible effects on platelet function and should be stopped 10 days prior to major surgery. Other NSAIDs should be continued to enable early mobilisation, but should be stopped if there is excessive bleeding, shock or deterioration of renal function.

INVESTIGATIONS AND PREOPERATIVE ASSESSMENT

All patients with significant disease undergoing surgery should have a FBC, creatinine, electrolytes, LFTs, ECG and chest Xray if symptomatic.

- ECG may indicate conduction disorders/ischaemic heart disease or LV strain or hypertrophy as a result of disease.

- CXR may show evidence of pleural effusion, nodulosis, infection, bronchiectasis or fibrotic lung disease.
- Cervical spine Xrays are controversial. Any patients with neurological symptoms from the cervical spine should have a careful Xray and assessment. Most patients however are best managed by carefully noting the degree of comfortable preoperative cervical spine movement and ensuring that during anaesthesia this is not exceeded. Patients wearing collars should bring them to theatre and have them replaced during surgery, after intubation.
- Cardiac ECHO may reveal regurgitant valves secondary to nodulosis or pericardial fibrosis. This should be done if there is a murmur or if the patient has symptoms of cardiac disease.
- Pulmonary function tests should be carried out in patients with dyspnoea or radiological evidence of pathology. Investigation may reveal a restrictive pattern of disease in fibrotic disorders, although an obstructive pattern may be present with emphysematous disorders which are commonly potentiated by rheumatoid disease.
- An ENT opinion should be sought and nasendoscopy performed if there is hoarseness or symptoms and signs of respiratory obstruction.

Patients currently taking regular steroids

Recommended guidelines for steroid replacement:		
<10mg prednisolone/day	Assume normal hypothalamic pituitary axis	No additional steroid cover required
>10mg prednisolone/day	Minor surgery e.g. hernia	Routine preoperative steroid or hydrocortisone 25mg IV at induction
	Intermediate surgery e.g. hysterectomy	Routine preoperative steroid plus hydrocortisone 25mg IV at induction. Postoperative hydrocortisone 25mg IV 6 hourly for 24hrs
	Major surgery e.g. cardiac	Routine preoperative steroid plus hydrocortisone 25mg IV at induction. Postoperative hydrocortisone 25mg IV 6hourly for 48-72hrs
High-dose immunosuppression	Should continue usual immunosuppressive equivalent dose until able to revert to normal oral intake e.g. 60mg predisolone/24 hr= 240mg hydrocortisone/24h	
Patients formerly taking regular steroids		
< 3 months since stopped steroids - treat as if on steroids		
> 3months since stopped steroids - no perioperative steroids necessary		

- DVT prophylaxis. RA patients tend to be slower to mobilise and follow a protracted course of recovery secondary to their presurgical disability.

ANAESTHESIA

Many rheumatoid patients have undergone repeated surgery and anaesthesia. They may have specific requests or drugs which they prefer to avoid – listen and take these comments into account.

Each patient requires individual assessment and planning with regard to their airway. Take care of the neck at all times during anaesthesia to ensure that a neutral position is maintained, especially during transfers and on positioning the patient. Unless it is certain that there are no neck problems, manual in-line stabilisation must be carried out during airway manipulation. If there is AAS, awake fibreoptic intubation is preferred by some anaesthetists.

Careful positioning and padding of affected joints is necessary. Patients often have fragile skin; special attention must be given to avoid skin tears or pressure areas developing. Assess any deformities before induction and try to maintain limbs in this position so as not to stress joints overtly. Veins are often extremely fragile and may cross fixed joints.

Regional techniques provide effective postoperative pain relief but may be technically difficult due to problems in positioning patients in order to put in blocks, spinals or epidurals. Patients may not be able to move into the ideal position due to reduced range of movement or pain. If a patient is required to remain awake during anaesthesia under regional blockade, they may become uncomfortable as a result of their joint disease.

A smaller endotracheal tube may be required due to crico-arytenoid disease, ensure a small tube is available.

Hypothermia may increase the risk of wound infection, so should be avoided.

Strict asepsis must be maintained due to immunosuppression from the disease and drug therapy.

POSTOPERATIVELY

Pain should be controlled adequately to ensure early mobilisation. All regular analgesic medications should be recommenced, and tailored appropriately to the increased requirements postoperatively. Patients may require continuation of their NSAIDs. In the elderly check renal function and watch for gastro-intestinal side effects such as haemorrhage.

Ensure DVT prophylaxis until mobility improves.

Physiotherapy is an essential adjunct. Prolonged periods of immobility can cause stiffening of affected joints; this can lead to a protracted course of recovery. Early mobilisation helps to prevent this, and in doing so reduces risks of DVT and pneumonia.

Fluids should be balanced accordingly. Renal function should be checked regularly for signs of deterioration. Renal dysfunction may be multi-factorial, thus a close monitoring is essential for early detection and appropriate treatment. Drug toxicity is more likely at this time due to the number of adjuvant stressors.

Restart DMARDs. These drugs are commonly omitted only for two days post-operatively as there is little evidence for discontinuing them prior to surgery reduces the incidence of postoperative complications. However if there is a leucopenia (associated with azathiopine), withdrawal may be required 2-3 weeks prior to surgery.

SELF ASSESSMENT ANSWERS

You go to assess a rheumatoid patient pre-operatively. She has a hoarse voice. How might this become significant during anaesthesia?

Fixation of the cricoarytenoid joints may lead to voice changes, hoarseness, or even stridor from glottic stenosis. A small endotracheal tube may be required.

What percentage of patients affected with Atlanto-axial instability have symptoms or clinical signs of the condition?

AAS occurs in 25% of severe rheumatoids. Only 25% of affected patients will have any neurological signs or symptoms such as paraesthesia in the hands/ feet or neck pain. Assess the range of movement in the neck. Excessive movement may lead to cervical cord compression and should be carefully avoided.

Patients often have extra-articular manifestations of disease. Which organ systems can disease affect?

- Cardiovascular
- Pulmonary
- Gastrointestinal - All of them!
- Central nervous system
- Skin
- Renal
- Haematological
- Eyes

Patients with rheumatoid disease affecting the lung may have a restrictive pattern of disease in spirometric studies. Which pathological conditions may cause this?

- Rheumatoid pneumoconiosis (Caplan's syndrome)
- Diffuse interstitial fibrosis, anti-rheumatic drug reactions in the lung may be associated
- Bronchiolitis obliterans organising pneumonia (BOOP)

A seropositive rheumatoid patient has a routine FBC; it reveals neutropenia, anaemia and thrombocytopenia. What clinical signs would you look for in association with this?

This may be Felty's Syndrome. Look for a patient who has seropositive disease, neutropenia and splenomegaly. They may have signs of vasculitic disease, immunosuppression and lymphadenopathy.

The above patient does not have any associated clinical signs, what may also be causing this pattern on the FBC?

Many of the DMARDs can cause bone marrow suppression: Methotrexate, Leflunomide, Sulfasalazine and Gold. There are many potentially serious complications as a result of taking long term immunosuppressant and cytotoxic drugs. Patients are closely monitored whilst taking these medications to observe for signs of marrow suppression.

KETAMINE IN ANAESTHETIC PRACTICE

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Consider the following real life cases and how you might manage them:

Case 1

A 22 year old man has been admitted with a gunshot wound to the abdomen. He is shocked from major internal bleeding and requires a laparotomy. You have a very small supply of inotropes and want to try not to use them. What will you do for induction and maintenance of anaesthesia?

Case 2

A 2 year old boy needs repair of his hernia. He is extremely frightened of the hospital and its staff. You think that obtaining intravenous access will be very difficult and that a gas induction will be difficult as well because of his agitation. How will you anaesthetise this child.

Case 3

A 37 year old woman is recovering from 45% burns, she needs dressing changes every two days which are very painful. She has very few sites left for IV access and you don't want to use them as she has further surgery to come. She is also very scared of needles. How will you manage the sedation she requires for her dressing changes?

Case 4

Your laparotomy patient (case 1) is back on the ward. He has severe postoperative pain but you have been unable to get any morphine this month. How can you manage his postoperative pain?

Case 5

A 25 year old man has had his leg amputated after a motorbike accident. He is suffering from lots of problems with phantom limb pain. You have tried giving him amitriptyline and carbamazepine but without effect. What could be your third line option?

Case 6

An 18 year old girl has been admitted with severe asthma. You have been asked to see her as she has not

improved with subcutaneous injections of salbutamol or intravenous aminophylline. She is getting tired and her oxygen saturation is falling. Can you do anything to help?

Introduction

Ketamine is the only anaesthetic available which has analgesic (pain relieving), hypnotic (sleep producing) and amnesic (short term memory loss) effects. When used correctly it is a very useful and versatile drug.

Ketamine is available in three different concentrations 10mg/ml, 50mg/ml and 100mg/ml. 50mg/ml is most commonly stocked since it can be used for i.m. administration or diluted for IV use.

Routes of Administration

Ketamine may be given intravenously (induction 1-2mg/kg, maintenance 0.5mg/kg) or intramuscularly (induction 5-10mg/kg, maintenance 3-5mg/kg) for anaesthesia or orally (15mg/kg for a child to a maximum of 500mg for an adult) for sedation.

Effects of Ketamine on the Body

Respiratory System

With ketamine the airway is usually well maintained and it also preserves the laryngeal and pharyngeal reflexes to some degree. This is not always guaranteed however and standard techniques, where required, for prevention of aspiration and maintenance of a patent airway must be used. When ketamine is given slowly respiration is usually well maintained, after rapid i.v. injection the breathing may stop for a short while but usually restarts within a minute. For this reason ketamine is a very useful anaesthetic agent in areas where there is no oxygen or only limited oxygen available. Ketamine is an effective bronchodilator.

Cardiovascular System

With ketamine there is an increase in both blood pressure and heart rate. This usually reaches a maximum about 2 minutes after injection and settles over 15 – 20 minutes. There is wide variation in individual response and occasionally there can be

a large rise in blood pressure. The risk of this is not related to a preoperative history of hypertension. This rise in blood pressure usually responds to further doses of IV diazepam (1-2mg for an adult).

This increased workload for the heart means that ketamine should be avoided, if possible, in those patients with ischaemic heart disease. Patients with diabetes should have an ECG, if available, to rule out "silent" ischaemia (ischaemia without chest pain), since this is a common feature of poorly controlled diabetes.

Central Nervous System

Ketamine produces dissociative anaesthesia (detached from surroundings). Unlike other anaesthetic agents, patients who have had ketamine may have their eyes open and make reflex movements during the operation. It has a slower onset after an IV bolus (1-5 minutes). The duration of action depends on the route of administration (20-30 minutes for IM and 10-15 minutes for IV).

Ketamine provides very good analgesia and may be used without any other analgesics intraoperatively. However, consideration does have to be given to postoperative pain relief. Co-administration of opiates or tramadol intraoperatively can reduce the amount of ketamine required for maintenance of anaesthesia and therefore reduce the incidence and duration of postoperative hallucinations. This does however increase the risk of the patient's breathing stopping during the operation.

In recovery the patient may be agitated – this is due to the frequent occurrence of hallucinations after ketamine anaesthesia. These hallucinations can be reduced by premedication with benzodiazepines (usually diazepam 0.15mg/kg orally 1 hour pre-operatively or 0.1mg/kg IV) and by recovering the patient in a quiet area.

Ketamine increases the intracranial pressure and for this reason should be avoided wherever possible in those patients with recent head injuries.

Gastrointestinal Tract

Ketamine increases salivation. This can lead to airway problems due to laryngeal spasm or obstruction. It may also make the taping of endotracheal tubes more difficult. To reduce this salivation atropine is usually given either as a premed (20mcg/kg IM) 30 minutes preoperatively, or at the time of induction IV (10-20mcg/kg).

Skeletal Muscle

Ketamine increases skeletal muscle tone. This is most prominent after the initial iv bolus and gradually decreases. It is improved by administration of benzodiazepines. It is rarely a problem intra-operatively.

Eyes

Ketamine increases intraocular pressure. The eyes also commonly move continually during ketamine anaesthesia (nystagmus). This makes it an unsuitable anaesthetic for eye surgery.

Placenta

Ketamine crosses the placenta. Newborn infants after caesarean section under ketamine anaesthesia will therefore be partially anaesthetised and should be cared for accordingly.

Some Practical Examples:

Case 1: IV ketamine for induction and maintenance

This gunshot victim is shocked and requires a laparotomy, you have limited inotropes. Ketamine would be an ideal anaesthetic agent in this case due to its cardiovascular effects of raising the blood pressure and heart rate - all other anaesthetic agents tend to have a cardiac depressant effect.

Induction can be performed with IV ketamine (1-2mg/kg), atropine (10-20mcg/kg) and diazepam (0.1mg/kg). It is still possible to perform a modified rapid sequence intubation with ketamine, despite its slower onset time.

There are several options for maintenance:

- 1) intermittent boluses of IV ketamine (0.5mg/kg) given according to patient's response - pupil size, heart rate, blood pressure, movement etc.
- 2) ketamine infusion. Put 500mg of ketamine in a 500ml bag of saline or dextrose. Run this at 1-2mls/min (1-2mg/min). Some patients may require more and others less depending on what other drugs have been given and the type of surgery.

Generally the ketamine will need to be discontinued 20-30 minutes before the end of the operation to avoid a long wait for the patient to wake up.

This technique for laparotomy is best used with non-depolarising muscle relaxants (avoid pancuronium as combined with ketamine may have very high blood pressure increases). It is however possible, although more difficult, to perform the laparotomy under ketamine alone.

Case 2: use of IM ketamine

This child is clearly going to be uncooperative and either IV access or gas induction will be difficult. In these circumstances intramuscular ketamine is very useful.

There are two possible options:

- 1) induce anaesthesia with IM ketamine (5-10mg/kg) + atropine (20mcg/kg) + diazepam (0.1mg/kg) - these may all be mixed in the same syringe. Onset of anaesthesia will start about

5 minutes after injection. The disadvantage of this technique is that it requires a relatively large IM injection. While most textbooks quote 8-10mg/kg for induction it has been my experience that in many cases a much smaller dose (5mg/kg) is sufficient.

- 2) sedate with IM ketamine (2mg/kg) + atropine (20mcg/kg) + diazepam (0.1mg/kg). After 5 minutes you will have a docile child who can cooperate with either cannulations or a gas induction.

The author's preference is for option 2 since the IM injection is smaller and it can be performed safely in the waiting area on the mothers lap rather than in theatre and is therefore less traumatic.

In either case IV access should then be obtained. If IV access is impossible then anaesthesia can be maintained with IM ketamine (3-5mg/kg).

Case 3: oral ketamine sedation

This woman requires recurrent sedation for painful burns dressings. IV ketamine is possible but in burns patients there are often limited sites for cannulation and these are best saved for trips to theatre. IM ketamine is also an option but requires relatively large painful IM injections. Instead the intravenous preparation of ketamine can be given orally.

For an adult give 500mg of ketamine + diazepam 5mg.

For a child use 15mg/kg ketamine + 0.2mg/kg diazepam (you can use the IV preparation but it tastes very bad and may have to be hidden in juice).

The dressing change can usually start after 20-30 minutes. Responses can sometimes be unpredictable and onset time may be slower. There should always be equipment for suction and face mask ventilation available and if possible, oxygen and a pulse oximeter.

Case 4: ketamine for postoperative analgesia

Ketamine is a very good analgesic and can be a solution for severe pain when morphine is not available. Its use postoperatively is limited by the occurrence of hallucinations, however these are less of a problem when relatively low doses are used. For adult patients

in severe pain a loading dose of 0.5-1mg/kg IM may be given. This can then be followed by an infusion of 60-180mcg/kg/hr (4-12 mg/hr for a 70kg adult).

A reasonable regime is to put 50mg ketamine in a 500ml bag of saline or dextrose (0.1mg/ml ketamine) and run this at 40-120mls/hr (i.e. over 4-12 hours for a 70kg adult). This regime is relatively safe since even if the whole infusion were to be given quickly by accident the patient is unlikely to become deeply anaesthetised but the patient should still be closely monitored and anaesthetic help should be available if needed.

Case 5: use of ketamine for patients with chronic pain

Many patients with amputations or patients with spinal cord injuries have problems with chronic pain. The nature of this pain is often neuropathic (this means originating from an injury to the nerves) and has an unpleasant burning or shooting quality to it. When traditional first line treatments for neuropathic pain such as amitriptyline or carbamazepine have failed ketamine may also be added and has been shown to have success.

A standard dosing regime for an adult is 50mg orally (use the intravenous preparation) three times per day. This may be increased to 100mg tds. Problems with hallucinations and salivation are rare. The ketamine may be discontinued after about 3 weeks of good pain control, reducing the dose gradually to see if any pain symptoms reoccur. The authors have found this regime useful in postoperative amputation patients to try and prevent the onset of phantom limb pain. In this setting it seems the ketamine need only to be taken for about a week.

Case 6: ketamine for the treatment of asthma

Ketamine is an effective bronchodilator and can be used for the patient who is not responding to conventional bronchodilators such as salbutamol and aminophylline. The doses of ketamine required are very low and problems with hallucinations rare. A loading dose of 0.2mg/kg IV is given initially followed by an infusion of 0.5mg/kg/hr for 3 hours. This may be continued if necessary. Close monitoring of the patient is required and an anaesthetist should be available if necessary.

OBSTETRIC HAEMORRHAGE

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Hemorrhage is a leading cause of maternal mortality. It is the underlying cause in at least 25% of maternal deaths in the developing world.¹

In pregnancy there are physiologic adaptations in preparation for blood loss:

- Blood volume increase (1000-2000mls) and increased red blood cell mass.
- Hypercoagulable state (increased clotting factors, including fibrinogen).
- Involution of uterus following delivery has a 'tourniquet effect' on the spiral arteries of the gravid uterus.

Blood loss can occur rapidly because gravid uterine blood flow at term is 600-900ml/minute, and when there uterine atony occurs, more than one unit of blood is lost every minute.

Resuscitation may be inadequate during post partum hemorrhage because:

- Precise measurement of blood loss during cesarean section is almost impossible because of difficulties quantifying amniotic fluid. Blood loss in women with primary post partum hemorrhage tends to be grossly underestimated. In a study of Prasertcharoensuk et al² the mean visually estimated blood loss in the third stage of labor was approximately 100ml less than measured blood loss. The magnitude of underestimation increased as the blood loss increased.
- There may be no change in the maternal systolic blood pressure until more than 25% of the blood volume is lost in pregnancy.
- Pregnancy causes increased susceptibility to disseminated intravascular coagulation (DIC).

Causes of Obstetric Hemorrhage:³

- Antepartum hemorrhage is seen in 4% of pregnancies and is caused by placenta praevia, abruptio placenta or uterine rupture.
- Early postpartum hemorrhage is seen in 10% of deliveries and is caused by uterine atony (1:20 incidence), genital lacerations, retained placenta, uterine inversions (1:6400 incidence).

Uterine atony is the most common cause of significant bleeding in pregnant women after delivery. High risk situations are:

- Over-stretched uterus: As seen in multiple gestation, macrosomia, polyhydramnios.

A Case Report

A 22-yr-old Gravida 1 Para 0, was brought to the operating room after failed induction of labor with oxytocin for 20 hours. Following the delivery of baby she continued to bleed with estimated blood loss (EBL) approaching 2000ml. The obstetrician stated the uterus was atonic.

How should you manage this emergency?

- Tired uterus: As seen in high parity, prolonged labor, prolonged oxytocin use.
- Sick uterus as seen in chorioamnionitis.

Drugs in Postpartum Haemorrhage

Uterotonic therapy, most commonly with oxytocin and/or ergot alkaloids, is one component in the treatment of postpartum hemorrhage. The first line therapy in patients with postpartum hemorrhage (PPH) is oxytocin, which stimulates the force and frequency of uterine contraction. It has an immediate effect and a half-life of 5 to 12 minutes. Intramuscular oxytocin is circulating in the blood within 2-3 minutes.⁴

The main preservative that is used in Syntocinon ampoules (oxytocin) is chlorobutanol and it has a negative inotropic effect on the cardiac muscles.^{5,6} Since Syntocinon has a direct effect on the heart, it is recommended to be used intravenously as an infusion in a concentration of 20-40units/l. Oxytocin given as a bolus IV or fast IV infusion produces a decrease in systolic and diastolic blood pressures. It also produces flushing, reflex tachycardia, and an increase in peripheral blood flow. The use of oxytocin has been associated with pulmonary edema, subarachnoid hemorrhage, cardiac arrhythmias, and anaphylactic reaction.

Ergometrine, an ergot alkaloid derivative, increases both the force and the frequency of uterine contraction probably via alpha-adrenergic receptors, tryptaminergic receptors, or both. This drug produces constriction of arteries and veins, raising the blood pressure when administered in therapeutic dosage of 0.2mg intramuscular. The intensity of the pressor response is enhanced when the blood pressure is already elevated, therefore its use is contraindicated in women with hypertension and necessitates routine assessment of blood pressure before its administration. The ergot alkaloids can produce coronary vasoconstriction, and are often associated with anginal pain and ischaemic electrocardiographic changes in patients with history of ischaemic heart

disease.⁷ There is also a relatively high incidence of nausea and vomiting.

Ergometrine is used alone or in combination with oxytocin (Syntometrine) in the prevention and treatment of PPH.⁸ Syntometrine has the advantage of rapid onset of action of oxytocin combined with the sustained myometrial response of ergometrine. However, the higher incidence of the side-effects when compared with oxytocin makes it less favorable for routine use in the third stage of labor. Syntometrine (ergometrine 500 mcg combined with oxytocin 5 units) should also be avoided when there is hypertension, pre-eclampsia or cardiac disease.

Oxytocin and ergometrine should not be exposed to high temperatures and light. Studies have found that 90% of the active ingredients are lost after 1 year of storage at 21-25°C.⁹ These storage requirements are an important barrier to the effective use of oxytocics in the developing world.

It has been suggested that prostaglandins may be the ideal agents for routine prophylactic use in the third stage of labor. Unlike ergometrine-related agents, prostaglandins do not cause hypertension¹⁰, and have strong uterotonic effects. Misoprostol, the prostaglandin E1 analogue, is the most recent drug to be identified as a useful agent in the prevention and treatment of PPH.

The vaginal route of misoprostol is more potent and side-effects are lower compared to the oral route, but the vaginal route could be inappropriate because of bleeding. It has been reported that misoprostol 800-1000 mcg given rectally^{11,12} is an effective intervention in women with severe PPH. Almost all the studies report shivering and pyrexia as side effects of misoprostol and those are shown to be dose-related with a duration of up to 12 hours after administration.

Although misoprostol should not be first choice in the routine management of third stage of labor, in developing countries where resources may be limited and refrigeration of drugs is a problem, misoprostol offers the advantages of being cheap, easy to administer, not requiring special storage and has a long shelf life of several years.

The short duration of action of natural prostaglandins, coupled with a high incidence of side effects, prompted the development of methylated prostaglandin derivatives. Hemabate (15-methyl-PGF₂ alpha) 250mcg, is as effective as Syntometrine in the treatment of refractory atony¹². When administered as an intramyometrial injection it has an onset of action of 5 minutes, while its intramuscular use has an onset of action of 45 minutes before maximal effect is seen.¹³ Hemabate is expensive and has a high incidence of adverse gastrointestinal side effects such as diarrhea. Asthmatic patients are particularly

sensitive to Hemabate since it has the potential to cause bronchoconstriction and intrapulmonary shunting.¹⁴

Non-pharmacological Management of Postpartum Hemorrhage

The treatment for uterine atony starts with simple interventions but may progress to a hysterectomy if continuous bleeding persists. The treatment options include:

- *Uterine massage.* The first and most accessible option available to the obstetrician in the operating room following a cesarean section is massaging the uterus. Hemostasis following placental separation is initially a mechanical process where the myometrium constricts the spiral blood vessels to stop bleeding. If this does not occur, hemorrhage ensues. Continuous communication between the obstetrician and the anesthesiologist during this time is extremely important. Uterotonics should be given and fluid replacement initiated without delay.

- *Uterine packing.* Packing the uterus with thrombin packs or gauze is a simple and non-invasive technique to attempt to tamponade the bleeding. This technique can be used following vaginal or cesarean delivery. There are concerns regarding infection and prophylactic antibiotics should be administered.

- *Compression sutures.* Alternatives to packing the uterus were sought secondary to concerns regarding infection and pressure necrosis. Lynch et al. used vertical sutures to envelope and compress the uterus. By opposing the anterior and posterior walls of the uterus, blood flow is reduced.¹⁵ This is a simple procedure but evidence is limited to case reports. A modification of this technique makes it possible to apply compression sutures without opening the uterus.¹⁶

- *Internal iliac (hypogastric) artery ligation.* Bilateral internal iliac artery ligation has been advocated as an effective means of controlling hemorrhage in the postpartum period. Although pelvic blood flow is only reduced by 49%, the pulse pressure is reduced by 85% creating a much reduced pressure and promoting hemostasis.¹⁷ Bilateral hypogastric artery ligation is found to be a relatively easy, safe and successful procedure that can be attempted as an initial surgical approach for severe PPH, especially when uterine conservation is desired.¹⁸ Aortic angiographic studies have identified anastomotic branches of the lumbar, sacral and rectal arteries as the origin of the main collateral vascularisation preventing ischemia and tissue necrosis in bilateral hypogastric artery ligation.¹⁹ A systematic policy of attempting a conservative approach whenever possible is likely to decrease hysterectomy rate, especially when performed early when basic haemostatic procedures have failed. After failure of primary conservative procedure, hysterectomy should be performed promptly.¹⁹

- In recent years *uterine tamponade* has been used to gain hemostasis and determine whether further surgical measures will be needed to control the bleeding. Inserting a Sengstaken-Blakemore esophageal catheter into the uterus and inflating it with normal saline will create a tamponade. A Foley catheter has also been described for this technique however the balloon is often too small (30cc) to create a tamponade in a uterus immediately postpartum. This technique has been used successfully in cases of uterine atony^{20,21} as well as placenta accreta.²²

- **Uterine artery balloon occlusion.** Catheter arterial embolization has been a recognized method of controlling hemorrhage since the 1960's and more recently, has been used successfully to control postpartum hemorrhage. Uterine artery embolization has several advantages including identification of the specific bleeding site, preservation of the uterus and fertility, and less bleeding from collateral circulation because of more distal occlusion of the bleeding vessels.²³ The technique has good success and low complication rates.²⁴ One recent review found that embolization was successful in 95% of the 138 published cases of postpartum hemorrhage with a complication rate of 8.7%.²⁵ The most common complication was a low-grade fever. Some practical issues that need to be considered are the need for a trained interventional radiologist and a fully equipped x-ray department 24 hours a day. Embolization obviates the need for a laparotomy and if need be, arterial ligation can be attempted afterward if bleeding persists. A team approach between the anesthesiologist and the obstetrician can prove useful in identifying patients at high risk for hemorrhage who may benefit from having a prophylactic catheter placed to expedite the embolization technique if needed. Currently it is unclear as to the optimal timing for embolization. However where facilities exist, it is suggested that it should be incorporated into the algorithm at an earlier stage after more conservative measures have failed.²⁶

- **Hysterectomy.** In life-threatening hemorrhage, hysterectomy is the most definitive treatment. This procedure is technically difficult and should not be delayed until the patient is unstable and deteriorating quickly. Early action should be taken to obtain large bore intravenous access, start infusions of crystalloid and colloid, and call for blood products. Maintenance of body temperature with a warm air blower and fluid warmer is essential. An arterial line may be useful and vasopressors should be available. Obtain laboratory studies (full blood count, clotting values, electrolytes) and monitor urine output closely. Patients who are under regional anesthesia may require conversion to general anesthesia if they are hemodynamically unstable or requiring large volume transfusions. Intravenous anesthetics may be necessary (ketamine is ideal) as all volatile agents worsen uterine atony.

A subtotal hysterectomy is an acceptable alternative as long as bleeding is not from the cervical branch of the uterine artery or from tears in the lower uterine segment.²⁷

Other Treatments

Factor VIIa

Human recombinant factor VIIa is a vitamin K-dependent protein that has been approved by the United States FDA for the treatment of bleeding in Hemophilia A or B patients, acquired inhibitors, and congenital factor VII deficiency. Recombinant factor VIIa promotes clotting through the extrinsic pathway by forming a complex with tissue factor located on the subendothelial surface of damaged blood vessels.²⁸ This complex then activates factors IX and X which go on to generate thrombin.²⁹ Currently there are several case studies published where factor VIIa has been used in cases of intractable postpartum hemorrhage.³⁰ This being said, there is little scientific evidence and it is considered an "off-label" use of the product. It is not currently approved by any health authority for use in obstetrics. In all of the case studies the factor VII was given as a bolus in doses ranging from 60 to 120mcg/kg, effects were seen in as little as ten minutes. The major drawbacks of Factor VIIa are the short half-life (two hours) and the high cost (\$ US 1400 per milligram).³² Repeat dosing may be necessary in cases of ongoing hemorrhage adding the already high cost. Reported adverse effects of recombinant factor VIIa include disseminated intravascular coagulopathy, thrombosis, and myocardial infarction.³³ Clinical conditions that are mediated by tissue factor exposure may carry an increased risk of thrombotic events. In DIC, there is systemic tissue factor exposure to the circulation and administration of factor VIIa could theoretically lead to a more severe coagulopathy and microvascular thrombosis.³⁴ This is significant in hemorrhaging patients because DIC may develop quickly. While it appears that recombinant factor VIIa may prove useful in life-threatening postpartum hemorrhage when conventional surgical, interventional and blood product support measures have failed,³⁵ its safety and efficacy is yet to be determined.

Cell Saver

Intra-operative cell salvage has been considered relatively contraindicated in obstetrics because of the fear of amniotic fluid contamination and embolism. In fact, the manufacturer of the equipment states that the use of cell saver is contraindicated in obstetric cases. Because the exact mechanism of the syndrome is not known, the adequacy of the washing process cannot be thoroughly evaluated. A tissue factor derived from amniotic fluid may be responsible for the disseminated intravascular coagulopathy that develops.³⁶ Other investigators believe that other fetal components may be involved such as fetal squames, lanugo, and/or phospholipids.³⁷ Without knowing what exactly causes amniotic fluid embolism, we cannot be certain we are removing it with the washing process.

Case Report

A 36 year old female, gravida 6, para 5, Jehovah's witness with five previous abdominal deliveries presents with complete placenta praevia. At 37 weeks gestation, she is scheduled for a caesarean section and preoperatively her Hb is 10g/dl.

The following are risk factors for placenta accreta³⁹:

- Placenta previa
- Previous cesarean section
- Advanced maternal age (after age 35)
- Multiparity
- Previous uterine curettage

This patient has almost all of the risk factors for developing placenta accreta. The American College of Obstetrics and Gynecology warns that the rate of placenta accreta following 2 or more caesarean sections and an anterior or central placenta praevia is 40%⁴⁰. After five cesarean sections, the incidence of placenta accreta is 50%. As anesthesiologists, our main concern must be the patient's risk of hemorrhage.

The antepartum period should be used to optimize and prepare the patient for the operating room. Imaging investigations would be useful to confirm abnormal placentation. This can be done with an MRI or less expensively with vaginal color Doppler sonography. Color Doppler is 96% specific, giving a positive predictive value in high-risk patients of 87% and a negative predictive value of 95%.⁴¹ At least two large bore intravenous catheters should be placed. If the facilities are available, this patient would be a good candidate for a prophylactic femoral catheter placement in preparation for uterine artery embolization should hemorrhage ensue.

Cell saver should be arranged for intraoperative use as most Jehovah's witnesses will accept cell saver blood if it is kept in a closed circuit.

Although hysterectomy is the standard management when intractable bleeding from placenta accreta occurs⁴⁷, this has devastating consequences for future fertility. In 1986, Arulkumaran and colleagues⁴⁸ first described a conservative method of management of placenta accreta, in which they used systemic methotrexate 50mg as an intravenous infusion, administered on alternate days with a total dose of 250mg. The placenta was expelled on day 11 postpartum. Several similar cases have been reported using methotrexate, however the route of administration, treatment schedules and total doses vary considerably⁴⁹. Although the conservative treatment of placenta accreta with methotrexate seems to be an acceptable alternative for radical surgery, an agreed protocol must be developed. 49 Prophylactic antibiotics should be administered for the entire duration of the procedure.

In 2000, Waters et al looked at cell saver blood from a cesarean section after filtration through a leukocyte depletion filter.³⁷ The blood was then compared to a maternal blood sample drawn from a catheter placed slightly above the uterine veins in the vena cava. A significant reduction in particulate contaminants (lamellar bodies, fetal squamous cells) was found using the filter although the filtered blood did have increased fetal red blood cells. Because fetal blood cells routinely enter maternal circulation during delivery, it is believed that only in the case of Rhesus incompatibility will this be significant. To prevent isoimmunization, anti-D immune globulin should be administered to the mother. The leukocyte depletion filter appears successful in further reducing contamination of particulate matter in cell saver blood but in cases of obstetric hemorrhage it also reduces the flow rate of the intravenous system to 30ml/min or 80ml/min using a 300mmHg pressure bag. This is an obvious disadvantage during massive hemorrhage. Though unproven, another safety measure to decrease contamination is the use of a double suction set up where the cell saver suction device was used only after delivery of the placenta and the fetal membranes.

It is important to remember that because the incidence of amniotic fluid embolism is rare, 1:8000 to 1:80,000 deliveries,³⁷ the studies and case reports that are currently available in the literature are insufficient to assess the risk of using cell saver blood in obstetric hemorrhage. It is unlikely that the safety of cell salvage in obstetrics will ever be firmly established. Cell saver use should be limited to times when it is the only way to increase oxygen-carrying capacity and sustain life as in the following case report.

Uterine Inversion

Uterine inversion is a rare complication which is associated with profuse hemorrhage and shock. It occurs when fundal pressure and inappropriate traction on the cord is applied during the third stage of labor in the presence of atonic uterus with open cervix, particularly if there has been fundal implantation of the placenta. The usual clinical presentation is major hemorrhage and abdominal pain. The fundus cannot be palpated and the uterus may fill the vault or protrude from the vagina. Uterine inversion is classified by its extent as incomplete or complete, depending on whether the fundus extends beyond the cervix. It is also classified by its duration as acute or subacute, depending on whether cervical contraction has occurred.⁴²

Inversion of the uterus produces profuse and continued post partum bleeding. Bleeding from the placental site is exaggerated as a consequence of restricted venous outflow from the uterus. The degree of blood loss is related to the time the uterus remains inverted. The initial cardiovascular response may reflect a vasovagal reflex due to traction on the

peritoneum, resulting in hypotension and bradycardia. The inverted uterus may also exert traction on the sympathetic nerves thereby contributing an element of neurogenic shock.^{43, 44}

Uterine inversion therefore presents a unique problem for the anesthesiologist. First, hypovolemia must be treated and an attempt must be made to restore the intravascular volume and hemodynamic stability. Secondly, anaesthesia is often necessary to allow the obstetrician to perform the maneuvers necessary in replacing the uterus. Third, if manual replacement is not possible and the cervix has already begun to contract, pharmacological intervention may be necessary to achieve rapid relaxation of the uterus to facilitate its reinsertion. The anesthesiologist may therefore face the difficult situation of having to provide analgesia and rapid uterine relaxation with a volatile inhaled anesthetic or nitroglycerine (GTN) in a hypovolemic patient.

Because profuse hemorrhage will continue from the exposed inverted uterus until it is replaced, time is a critical factor in the patient's treatment. While the obstetrician provides manual external pressure on the inverted uterus, rapid intravenous fluids and vasopressors may be required to maintain or improve the arterial blood pressure.

Prompt repositioning requires anesthesia as the patient is often in severe pain, and the choice between a general and regional anesthetic technique needs to be made. Regional block causes sympathetic blockade which is dangerous in the presence of inadequate intravascular volume.

General anesthesia with a potent inhalation anesthetic relaxes the uterus, and use of higher than usual concentrations of potent volatile inhalation agents are often necessary for optimum uterine relaxation for these procedures with the attendant risk of cardiovascular system depression.

Nitroglycerine causes rapid and reliable uterine relaxation, and its use may avoid the need for general anesthesia. Several reports have described the safety and efficacy of intravenous nitroglycerin for uterine relaxation.^{45,46}

Nitroglycerine has the advantage of a rapid onset of action (30-40 seconds) in combination with a short-lived effect of approximately one minute. Doses of 50-200 mcg have been used successfully to achieve relaxation without causing significant hypotension or other unwanted side effects.⁴⁷ The rapid onset of action of intravenous nitroglycerine creates uterine relaxation in a much shorter time than would otherwise be achieved if an anesthesiologist were relying on the uptake of inhaled anesthetics. The short duration of action allows it to dissipate, obviating the need for reversal.

In patients where epidural anaesthesia was used for

labor and delivery, administration of small incremental doses of intravenous nitroglycerine in combination with epidural local anesthetics achieve uterine relaxation and comfort while maintaining stable hemodynamics.

Sublingual GTN is easily and rapidly administered and has demonstrated an equally fast onset of action and, in addition, the preparation is more readily available. The onset of action after sublingual administration is seen within 30-45 seconds which peaks at 90-120 seconds and lasts for up to 5 min.⁴⁸ It has been reported that the administration of 800mcg of sublingual GTN has resulted in complete relaxation and reduction of a partially re-inverted uterus within approximately 30 seconds.

Terbutaline and magnesium sulphate have been used for uterine relaxation in this setting. The onset of action of these drugs may be unacceptably long for an acute medical condition, particularly for magnesium sulphate which takes at least 10 minutes to take effect. Moreover, the duration of action is also long and the uterine effects of magnesium sulfate and terbutaline may need to be subsequently reversed.

Once the uterus is replaced, all medications that were administered to produce uterine relaxation should be stopped and uterotonic agents should be administered.

Summary

Postpartum hemorrhage is a major cause of maternal morbidity and mortality. In fact, in many developing countries, postpartum hemorrhage is the leading cause of maternal mortality. Several treatment options are available. Whereas in the past, postpartum hemorrhage almost inevitably lead to hysterectomy and therefore loss of fertility, today, more conservative alternatives can be used with preservation of fertility. These conservative approaches have proven to be useful, especially when performed early when basic haemostatic procedures have failed. However, hysterectomy should not be delayed when the conservative approach fails particularly in remote areas where supplies of fluids and blood may be limited. Close monitoring, good teamwork and timely clinical decision making are vital.

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OBESITY & ANAESTHESIA

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Self Assessment

1. You are asked to assess a 42-year-old woman who requires an emergency extensor tendon repair to her left hand. There is no neurovascular deficit. She is 158cm tall and weighs 102kg. She last ate 2 hours ago. What factors will you especially need to consider in her pre-assessment?
2. A 55-year-old man with a Body Mass Index (BMI) of 37 is having an anterior resection for colon cancer. Twenty minutes into the case you notice his oxygen saturations are falling and are now 88% despite FiO₂ 0.5. What actions can you take to improve his oxygenation?
3. A 65-year-old woman with a BMI of 41 is 24 hours post an elective total knee replacement. She has been given intramuscular morphine 2 hourly overnight. She is hypoxic with a SpO₂ of 87% on room air. Her respiratory rate is 8 breaths per minute. What is your diagnosis and action plan?

Key Points

- Calculate a BMI for all patients.
- BMI >30 is obese, BMI >35 is morbidly obese.
- Obesity is a multi organ disease.
- Significant cardiorespiratory disease is particularly common.
- Perioperative mortality and morbidity increases with BMI.

Introduction

Approximately 7% of the worldwide adult population is obese. Obesity is a global health problem and the prevalence varies with socio-economic status. In affluent cultures, the poor have the highest prevalence (27% of the US population and 17% of the UK population are obese). In the developing world it is the affluent that are at the highest risk. There is also a recent trend to an increasing prevalence of obesity in adolescents and children. Importantly 60-85% of obese schoolchildren will remain obese as adults.

The difference between normality and obesity is arbitrary but the Body Mass Index (BMI) is normally used to define obesity. It can be calculated by dividing the patient's weight in kilograms by their height in metres squared (kg/m²).

Interestingly, the regional distribution of excess fat is thought to be more predictive than BMI for

BMI (kg/m ²)	
<25	Normal
25-29	Overweight
30-35	Obese
>35	Morbidly Obese

morbidity and mortality. Excessive abdominal fat, "central obesity" is particularly predictive for NIDDM, dyslipidaemia and cardiovascular disease. Waist circumferences need to be sex and race specific. The table below is specific for Caucasian waist circumferences.

	Risk of obesity-associated metabolic problems	
	Increased	Substantially increased
Men	≥94cm (37inches)	≥102cm (40 inches)
Women	≥80cm (31.5 inches)	≥88cm (34.5 inches)

Since obesity is a multisystem disease affecting all organs, there are a number of implications relevant to the conduct of anaesthesia.

Respiratory system

Obstructive Sleep Apnoea (OSA)

At least 5% of morbidly obese patients will have OSA particularly if they have associated risk factors such as large collar size (over 16.5 inches), evening alcohol consumption and pharyngeal abnormalities. The disease is caused by passive collapse of the pharyngeal airway during deeper planes of sleep, resulting in snoring and intermittent airway obstruction. Resultant hypoxaemia and hypercapnia results in arousal and disruption of quality sleep thus causing the characteristic daytime somnolence. Pulmonary and systemic vasoconstriction, polycythaemia, right ventricular failure and cor pulmonale can all occur. Indeed the relative hypoventilation can cause a progressive desensitisation of the respiratory centres to hypercapnia with resultant Type 2 respiratory failure. Formal diagnosis is by sleep studies and treatment includes removal of precipitants, weight loss and nocturnal CPAP.

Specific Implications for Anaesthesia: Take a very careful preoperative history looking particularly for evidence of the characteristic increasing snoring and subsequent apnoea (ask a relative) and daytime somnolence. Avoid sedative premedication. Maintenance of the airway might be difficult. Airway obstruction is very likely to occur in the postoperative period – nurse in an HDU/ ICU setting, sit up if at all possible, give oxygen and apply CPAP if required. Regional techniques and short acting anaesthetic agents are ideal to reduce postoperative drowsiness. OSA occurs most frequently during rapid eye movement (REM) sleep, which predominantly occurs on the second night post surgery. Consider nocturnal oxygen for up to 5 days following major surgery if available.

Airway

Obese patients tend to have short, fat necks making both mask ventilation and direct laryngoscopy technically more challenging. A BMI of 46 is associated with a 13% risk of difficult intubation. The increased bulk of soft tissues in the upper airway make them prone to partial obstruction with the loss of consciousness.

Specific Implications for Anaesthesia: Always assess the airway with the simple, quick bedside tests such as Mallampati, thyromental distance, incisor gap and the ability to sublux the mandible. Combinations of tests improve the positive predictor value. Difficult mask ventilation can sometimes be transformed by placement of an oral airway. Obese women are more likely to have large breasts, which can interfere with easy placement of the laryngoscope, therefore aim for a degree of head-up tilt, avoid folding the arms across the chest and, if necessary, apply traction on the breasts to allow placement of the laryngoscope. Given the increased risk of aspiration (see later) and difficult intubation, a rapid sequence induction will often be the safest form of induction. Have all available intubation aids such as bougies and a variety of laryngoscope blades close to hand. Ensure there are adequate numbers of staff should the patient require turning. If a fibrescope is available, consider awake intubation but be wary of using any additional sedation.

Ventilation

The increased body mass and metabolically active adipose tissue leads to increased oxygen consumption and carbon dioxide production. Minute ventilation is thus increased to achieve normocapnia. There is reduced chest wall compliance (of up to 30%) due to the heavy chest wall, increased pulmonary blood volume and splinted diaphragm. This reduction in compliance, together with increased respiratory demand results in an increased work of breathing.

In addition, the functional residual capacity (FRC) declines exponentially with increasing BMI. The closing capacity in these patients can encroach on

the FRC even when conscious; therefore the onset of anaesthesia, a supine position and the abnormally high elevation of the diaphragm (due to increased visceral and abdominal wall fat) all combine to cause ventilation-perfusion mismatch, right-to-left shunting and arterial hypoxaemia.

Specific Implications for Anaesthesia: These patients are prone to hypoxia even when conscious and will desaturate particularly rapidly once apnoeic as their oxygen reserve is reduced (reduced FRC), and oxygen utilisation increased, thus necessitating meticulous pre-oxygenation. Ideally this should be done with the patient semi erect to increase the time to desaturation.

Due to the reduced chest compliance and sheer mass of the chest wall, higher inflation pressures are required to ventilate such patients. Such high pressures preclude the use of the laryngeal mask airway (LMA) for ventilation. Hypoventilation will often occur when breathing spontaneously via an LMA/ facemask and thus these techniques are not recommended. Application of PEEP via an endotracheal tube is particularly useful in improving oxygenation by reducing small airways collapse.

Extubation is usually best performed with the patient in the sitting position as awake as possible to allow maximal diaphragmatic excursion. Otherwise the left lateral position is very safe initially but abdominal splinting might subsequently lead to hypoxia. Sit up once awake.

The postoperative mortality of the obese patient is double that of the non obese. As previously stated, these patients are prone to hypoxia due to small airways collapse and shunt. This may be exacerbated if analgesia is inadequate. However, over-sedated or narcotised obese patients are even more likely to develop partial airway obstruction. For this reason obese patients should be maintained on oxygen, humidified if possible, on the ward postoperatively with continuous pulse oximetry.

Postoperative physiotherapy/incentive spirometry and use of regional techniques such as epidural analgesia should reduce atelectasis and postoperative respiratory failure. Early postoperative mobilisation is vital.

Cardiovascular system

Obesity is associated with a number of cardiac risk factors. These include hypertension, ischaemic heart disease (IHD), cardiomyopathies, cardiac failure, arrhythmias, sudden cardiac death and dyslipidaemias. Venous insufficiency, cerebrovascular and peripheral vascular disease exacerbated by atherosclerotic processes may also be present. Increased visceral fat is a cardiovascular risk factor even when the BMI is normal.

Hypertension is particularly common in obesity. These patients also have an increased absolute

blood volume and increased cardiac output. Thus left ventricular stroke work is increased and left ventricular hypertrophy can result. Left and right cardiac failure can both occur. Given the high prevalence of associated coronary artery disease, the tendency to hypoxia, tachycardia (increases in line with increasing cardiac output) and biventricular strain, the aetiology for ischaemic coronary events is strikingly apparent.

Venous return is also reduced. An obese abdomen will directly compress venous return from the legs (also increasing the risk of deep vein thrombosis (DVT) and pulmonary embolism). Once ventilated, higher inflation pressures and application of PEEP further reduces venous return, which may result in a fall in cardiac output.

The risk of pulmonary embolus and DVT is doubled in the obese. Other causative factors for this increase include hypoxia-induced polycythaemia, cardiac failure, decreased fibrinolysis and immobilisation.

Specific Implications for Anaesthesia: Perform a thorough preoperative assessment looking for evidence of IHD and cardiac failure on history, examination and ECG. Chest X-ray and echocardiography may be technically difficult but potentially useful tests. Measure non-invasive blood pressure with the correct sized cuff. The sphygmomanometer cuff should be 20% greater than the diameter of the upper arm (remember, if the cuff is too small, the BP will be over-estimated). In the morbidly obese, invasive BP monitoring is advisable. Continue cardiac drugs throughout the perioperative period. Heparin prophylaxis, TED stockings and early mobilisation are some measures to reduce the incidence of DVT. Postoperative oxygen may particularly reduce nocturnal ischaemic events.

Gastrointestinal, endocrine and other systems

There is an increased incidence of hiatus hernia in the obese. The volume and acidity of gastric contents is often increased and as stated earlier, intubation might be difficult. Thus the risk of aspiration is particularly increased. Non-insulin dependent diabetes mellitus (and its associated microvascular and macrovascular changes) is much more common in the obese, caused by insulin resistance and inadequate insulin production. Hypercholesterolaemia, hypothyroidism, gout, osteoarthritis, back pain, hepatic impairment, gallstones, abdominal herniae, breast and endometrial malignancies are all more common in the obese.

Specific Implications for Anaesthesia: Prescribe oral H₂ receptor antagonists (e.g. ranitidine 150mg) or proton pump inhibitors (e.g. omeprazole 20-40mg) routinely 1-2 hours preoperatively, and if in doubt, perform rapid sequence induction with cricoid pressure at induction and extubate when fully awake. Perform a random blood sugar test on all obese patients. Ensure good perioperative sugar control to reduce infection and risk of myocardial events.

Continue statins over the perioperative period as they might improve coronary plaque stability.

Drug handling in obesity

In the obese patient, volumes of distribution, binding and elimination of drugs are unpredictable. This uncertainty necessitates that the anaesthetist pay more attention to the clinical end points of drug action such as loss of verbal contact, tachycardia etc. rather than focusing specifically on whether to dose on ideal, lean or actual body weight.

Some pharmacological certainties are a reduction in total body water, higher fat mass, relatively higher lean mass, higher GFR, increased renal clearance and normal hepatic clearance. The apparent volume of distribution for a fat-soluble drug such as thiopentone is increased because of its lipophilic nature and therefore the dose should be increased but a raised volume of distribution also results in reduced elimination resulting in prolonged effects. Recent work suggests that suxamethonium should be given at a dose of 1mg/kg actual body weight.

Slow emergence after use of fat-soluble volatile agents may be due to central sensitivity as much as due to delayed release from adipose stores. If available, use relatively insoluble agents as much for speed of reversal as to reduce postoperative drowsiness. The risk of halothane hepatitis may be higher in obese patients, although overall it is still very low.

Regional anaesthesia

Good regional anaesthesia may reduce opioid and inhalational requirements intraoperatively in thoracic and abdominal surgery and may also be used as the sole technique in peripheral surgery. However it is technically harder because of the loss of landmarks, increased movement of the skin and the need for long

DRUG	DOSING GUIDELINE
Propofol	Dose between lean and actual body weight
Thiopentone	Dose between lean and actual body weight
Suxamethonium	Up to 1mg/kg actual body weight
Atracurium	Dose according to actual body weight
Vecuronium	Dose according to lean body weight
Fentanyl	Dose according to actual body weight
Morphine	Dose according to lean body weight. Titrate to effect

needles. Initial failure rate is higher in the obese. The sitting position is usually easier for spinal and epidural placement. In the absence of clear bony landmarks the 7th cervical prominence and gluteal cleft will indicate the midline and patients also can assist by verbally redirecting the needle when it strikes the lamina. It is relatively uncommon for the epidural space to be more than 8cm deep. Leave extra catheter in the space as it may be subject to drag as the flexed patient relaxes.

Due to the engorged extradural veins and extra fat constricting the potential space, less local anaesthetic is needed for epidurals. 75-80% of the normal dose may well be sufficient.

Venous access, as a routine part of any anaesthetic technique is also technically more difficult in the obese, especially central venous access, where ultrasound is particularly useful if available.

Surgical and mechanical issues

Surgery is technically more difficult due to reduced surgical access, difficult visualisation of underlying structures and excess bleeding. This leads to longer operating times, with subsequent exacerbation of many of the factors already mentioned. There is a higher risk of infection. The poor blood supply to the fatty tissues increases the chance of both wound infection and wound dehiscence. There may also be impaired immune system function due to neurohumeral factors.

Special equipment may need to be ordered for the very obese patient. Most theatre tables have a weight limit of approximately 130kg and can often be too narrow for these potentially very wide patients. "Overflow" from the side of the table increases the risk of pressure sores or nerve damage, as the patient is "wedged" in place to ensure they do not fall off. This may also interfere with the tipping/tilting function of some tables. The sheer mass of the patient means they are harder to position, and present an increased risk to theatre staff during handling/lifting. Given such problems it is preferable to induce anaesthesia in theatre to avoid such transferring.

Day case surgery is not contraindicated in the obese. Rather than having a rigid cut off based on BMI, it is preferable to have a policy based upon the type of surgery to be performed. It has been shown that with careful selection patients with a BMI over 35 have similar outcomes to "normal" patients.

Bariatric surgery is defined as surgery specifically for severely obese patients. It is increasingly considered for the treatment of morbidly obese patients who have serious comorbidity or in whom medical or behavioural weight reduction therapies are ineffective. Operations include gastric banding, gastric bypass, biliopancreatic diversion, liposuction and jaw wiring. However, the choice of the optimal therapeutic strategy in these patients depends on a risk/benefit ratio, which needs to be assessed individually. It can achieve long-term

weight reduction and is increasingly being used in management of the severely obese. Economic and practical issues and significant morbidity limit it to the most extreme cases. The surgery itself is usually laparoscopic, and leads to less opioid consumption and more rapid recovery and mobilisation.

ANSWERS TO SELF-ASSESSMENT

No. 1

You are asked to assess a 42-year-old woman who requires an emergency extensor tendon repair to her left hand. There is no neurovascular deficit. She is 158cm tall and weighs 102kg. She last ate 2 hours ago. What factors will you especially need to consider in her pre-assessment?

Her calculated BMI is 40.85; therefore she is defined as morbidly obese. She is not adequately starved, and is not an emergency, therefore she should be delayed for at least another 4 hours, if possible overnight. A careful history should be taken, specifically considering symptoms of sleep apnoea, gastro-oesophageal reflux, diabetes, ischaemic chest pain and her normal exercise tolerance should be established. Pre-operative investigations would include a blood sugar, an ECG, pulse oximetry and non-invasive blood pressure with an appropriately sized cuff. Discussion should take place with the patient and surgeon as to the option of a regional technique. If she requires a GA then she will need intubation so a careful assessment of her airway is required additionally considering factors such as breast size to facilitate laryngoscope placement. Pre-medications would ideally include a proton pump inhibitor or H₂ antagonist. Sedation of any sort would ideally be avoided.

No. 2

A 55-year-old man with a BMI of 37 is having an anterior resection for colon cancer. Twenty minutes into the case you notice his oxygen saturations are falling and are now 88% despite FiO₂ 0.5. What actions can you take to improve his oxygenation?

Increase the FiO₂ to 100% immediately with an appropriate increase in volatile agent if previously using nitrous oxide. Check the position of the endotracheal tube and confirm bilateral air entry with auscultation and the presence of a CO₂ trace on the capnograph. Ensure adequate muscle relaxation. Try a recruitment manoeuvre such as increasing the tidal volume with hand ventilation or a sustained increase in airway pressure of 30-40cmH₂O for up to 40 seconds. Beware of cardiovascular compromise. If not already applied, add PEEP to keep any recruited alveoli patent. If the surgery allows, then the reverse Trendelenburg position might help.

No. 3

A 65-year-old woman with a BMI of 41 is 24 hours post an elective total knee replacement. She has been given intramuscular morphine 2 hourly overnight. She is hypoxic with a SpO₂ of 87% on room air. Her respiratory rate is 8 breaths per minute. What is your diagnosis and action plan?

She has respiratory depression from excess opioid. There is a high chance that this lady suffers sleep apnoea and is particularly sensitive to the effects of opioids.

She is in imminent danger of respiratory arrest. Give 100% oxygen and assist ventilation with a bag-valve-mask. Give IV naloxone 100-200mcg initially and up to 400mcg if required. Given naloxone has

a shorter half-life than morphine; close monitoring of respiratory rate, sedation score and oxygen saturation is vital for the subsequent 2 hours. It is highly likely the lady will require a further bolus or possibly an infusion of naloxone.

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ATRIAL FIBRILLATION AND ANAESTHESIA

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Atrial fibrillation (AF) is one of the commonest arrhythmias. It may be paroxysmal (sudden episodes), persistent or permanent. Atrial depolarization is very rapid, irregular and disorganized. This causes irregular and rapid ventricular conduction. AF may be seen in patients presenting for anaesthesia or may occur during anaesthesia.¹

Haemodynamic deterioration occurs due to the loss of atrial mechanical function, irregular ventricular response and a rapid heart rate. The loss of atrial contraction decreases cardiac output by up to 30%, particularly in patients with impaired ventricular diastolic filling. This is of importance in patients with hypertension, left ventricular hypertrophy, mitral stenosis and hypertrophic and restrictive cardiomyopathy.² The ventricular response rate depends on electrophysiological factors in the atrioventricular (AV) node, drugs and sympathetic and vagal tone. A rapid ventricular response results in a reduced cardiac output due to inadequate time for passive filling of the ventricles.³ A persistent rapid ventricular response may result in a dilated ventricular cardiomyopathy.²

Decreased blood flow in the left atrium (LA) and left atrial appendage (LAA) is associated with thrombus formation. Embolism from the LA may result in a stroke or other arterial occlusion. The pathogenesis of thromboembolism is complex and affected by other factors including intrinsic cerebrovascular disease, hypertension, atheroma in the proximal aorta and carotid artery stenosis.²

Pre-operative assessment and atrial fibrillation

Ask about the **first detected episode**. AF is recurrent after 2 or more attacks. Distinguish between paroxysmal, persistent and permanent AF.

Paroxysmal AF is self terminating. The patient may have no symptoms and be unaware of the episode(s) of atrial fibrillation. Symptoms include palpitations, chest pain, dyspnoea, fatigue, light-headedness and syncope. Symptoms may vary depending on the duration, the ventricular rate and the functional status of the patient.²

Persistent AF is sustained and requires electrical or chemical cardioversion to establish sinus rhythm. Inquire about modes of termination and drugs used on a regular or as needed basis: the "Pill-in-the-Pocket" approach.⁴

Permanent AF is long-standing persistent AF where cardioversion was not successful or has not been attempted.²

Although atrial fibrillation may occur without associated disease in younger patients, it may be associated with underlying disease. Treatment of the associated conditions while managing the AF normally resolves the arrhythmia.²

Examination

Expect a completely irregular pulse and jugular venous pulsation. The loudness of the first heart sound may be variable. A rate of between 60 and 80bpm at rest and between 90 and 115bpm during

Associated cardiovascular disease	Non-cardiac associations
<ul style="list-style-type: none"> • Hypertension • Coronary artery disease • Cardiomyopathy • Valvular disease (mitral) • Cardiac surgery • Myocarditis • Pericarditis • Other supraventricular arrhythmia(s) and • Wolff-Parkinson-White syndrome (WPW) 	<ul style="list-style-type: none"> • Alcohol • Hyperthyroidism • Pulmonary disorders • Pulmonary embolism • Obstructive sleep apnoea • Thoracic or oesophageal surgery • Sepsis • Vagal and sympathetic mechanisms.⁵

exercise is considered controlled and minimises the haemodynamic consequences of AF. Associated valvular disease may be diagnosed on auscultation and signs of heart failure should be looked for.²

Investigations

An **ECG** should be done to confirm AF. In AF the p-waves are replaced by fibrillatory waves that rapidly oscillate and are variable in time, size and shape. The ventricular response (QRS complex) is irregular. The ECG should also be studied for LV hypertrophy, pre-excitation (Wolff-Parkinson-White syndrome), bundle branch block, Q waves (previous MI's) and other arrhythmias. Measure the RR, QRS and QT intervals if the patient is on anti-arrhythmic medication.²

A **CXR** evaluates the lungs, and the heart size and shape.

Preoperative **blood analysis** will identify acid base, anaemia and electrolyte abnormalities. AF is more common with hypokalaemia or hypomagnesaemia.

Drugs used for AF

This can be divided into attempted rhythm control,

rate control and anticoagulation for thromboembolic prophylaxis.

Rhythm Control: The aim is to maintain sinus rhythm and prevent the adverse symptoms the patient experiences in AF. Embolism and cardiomyopathy will also be avoided if the patient remains in sinus rhythm.²

Drugs commonly used for rhythm control include amiodarone, sotalol, verapamil and flecainide.

When drugs in class 1c are used the QRS duration should not exceed 150% of the pre-treatment QRS duration. The upper limit for the QT interval for drugs in class Ia and III is 520ms.²

Rate Control: AF is accepted and the aim is to control the ventricular rate during rest and exercise. Drugs used include beta-blockers, calcium channel blockers and digoxin. These agents depress conduction across the AV node and may cause bradycardia or heart block, which requires permanent pacing in order to continue treatment.²

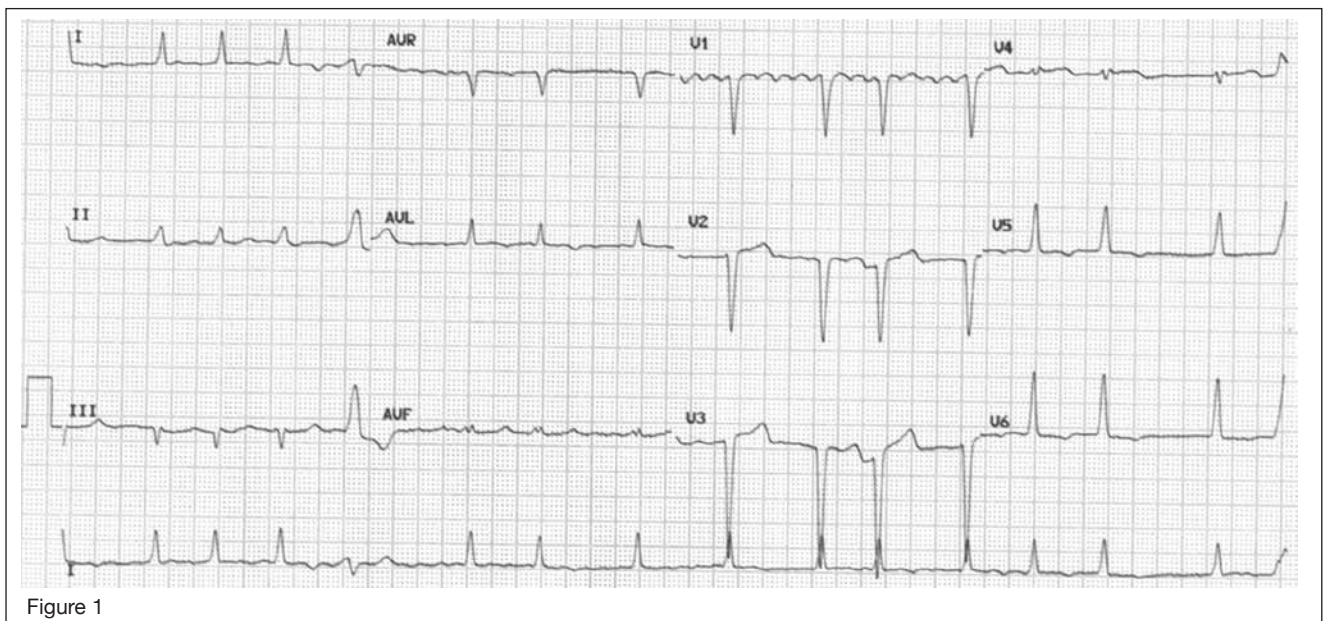


Figure 1

Class	Action	Drugs
Ia	Membrane-stabilising	Procainamide Quinidine Disopyramide
Ic	Membrane-stabilising	Flecainide Propafenone
II	β-adrenoceptor blockers	Esmolol Propranolol
III	Action potential prolongation	Amiodarone Sotalol
IV	Calcium channel antagonist	Verapamil Diltiazem
Others	Cardiac Glycosides	Digoxin ¹

Anticoagulation: Current evidence indicates that patients in paroxysmal, persistent and permanent AF have a similar risk for stroke. The duration of episodes and the time spent in AF has not been shown to determine the risk for stroke. Patients with the greatest risk are the elderly and those with a history of thromboembolism, diabetes mellitus, coronary artery disease, hypertension, heart failure and thyrotoxicosis.⁵

Oral anticoagulation is effective for primary and secondary prevention of stroke in AF with a reduction of more than 60% compared to placebo. Maximum protection occurs with an INR of between 2 and 3. Bleeding is an obvious complication. Balance the risk

of stroke to major bleeding. The protection against stroke with the use of aspirin is modest.²

Oral anticoagulation for a patient in AF, with no mechanical valve, can be discontinued for up to 1 week without the need for additional anticoagulation. If oral anticoagulation needs to be discontinued for a period greater than 1 week, unfractionated heparin or low-molecular-weight heparin can be used.²

Pre-operation medication

In patients undergoing cardiac surgery an oral beta-blocker can prevent postoperative AF. Sotalol or amiodarone may also be given prophylactically in patients with an increased risk of developing AF.²

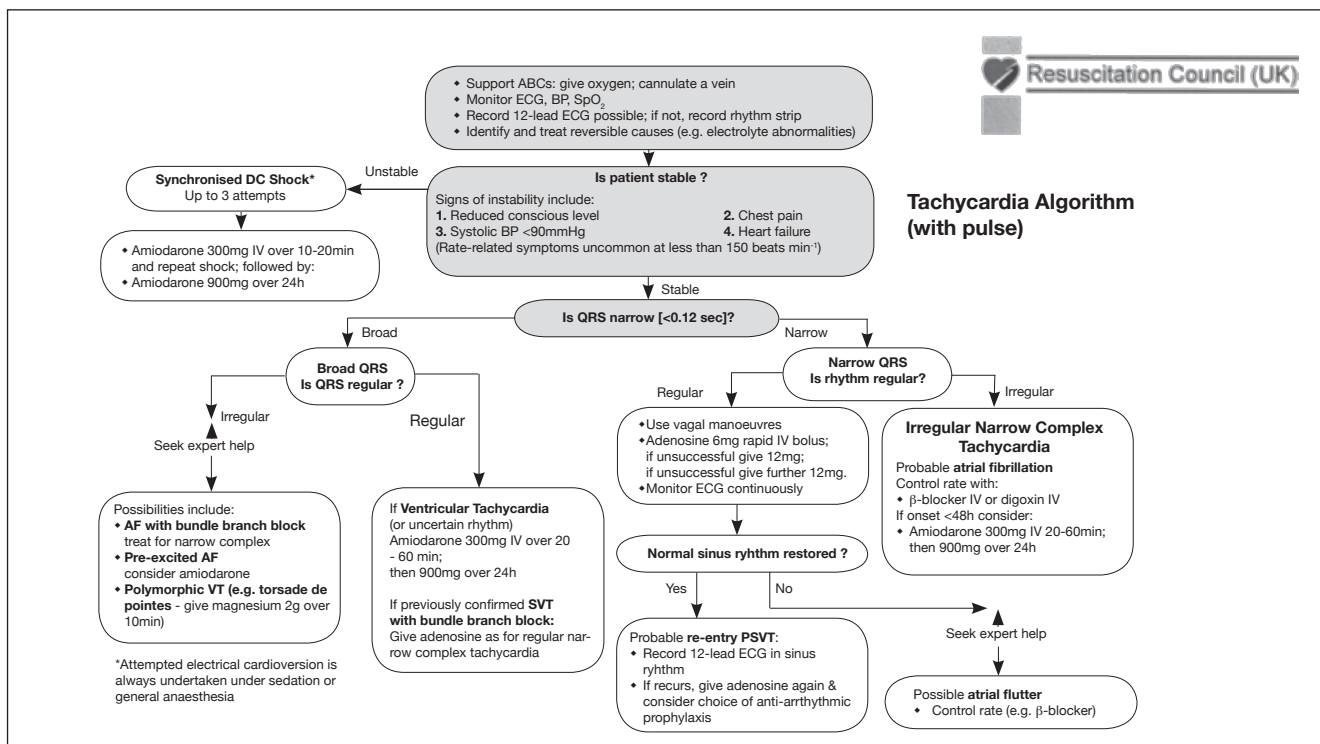


Table 2: Recommended antithrombotic therapy for AF	
Aspirin 325mg od	<ul style="list-style-type: none"> • < 60years, no heart disease. • < 60years, with heart disease, no other risk factors. • 60-75years with no risk factors. • If warfarin is recommended but contraindicated or refused.
Warfarin to INR of 2	<ul style="list-style-type: none"> • > 75years, especially women.
Warfarin to INR between 2 and 3	<ul style="list-style-type: none"> • > 60years with diabetes or coronary artery disease (aspirin is optional). • Heart failure with an ejection fraction less than 35%, thyrotoxicosis or hypertension.
Warfarin to INR between 2.5 and 3.5	Rheumatic heart disease (mitral stenosis), prosthetic valve, previous thromboembolism and current atrial thrombus. ⁵

Peri-operative atrial fibrillation

If possible establish the diagnosis of AF with a 12 lead ECG. Most, if not all anaesthetized patients will have oxygen and IV access in place. Further treatment will depend upon the clinical condition of the patient.⁶ (See figure 2).

Unstable patients

Examine for adverse signs and clinical evidence of low cardiac output. Pallor, sweating, cold and clammy extremities are secondary to sympathetic activity. Hypotension may develop. If awake, observe for decreasing level of consciousness. A very high ventricular response rate (>150) can reduce coronary blood flow and cause myocardial ischemia with chest pain. Look for signs of heart failure: pulmonary oedema (left sided failure) raised JVP and hepatic engorgement (right sided failure).⁶

Electrical cardioversion is the preferred method of treatment. Synchronized direct-current cardioversion (DCCV) should be attempted as soon as possible. When using a biphasic defibrillator, shocks should start between 120-150J and at 200J with a monophasic defibrillator. Increase in increments during the initial 3 attempts.⁶

If the patient remains in AF and unstable, 300mg amiodarone should be given intravenously over 10-20 minutes (ideally through a central line) before electrical cardioversion is tried again. A further 900mg amiodarone may be given intravenously over 24 hrs.⁶

Look for precipitating and reversible factors:

- Central venous catheters
- Electrolyte and acid base abnormalities (especially hypokalaemia or hypomagnesaemia)
- Hypertension
- Hypovolaemia
- Hypoxia
- Myocardial ischemia
- Pre-excitation syndromes (WPW)
- Pulmonary embolism

- Sepsis, especially pneumonia

Surgery may also play part in the development of AF:

- Atrial and pericardial manipulation
- Cardiac surgery
- Electroconvulsive therapy
- Oesophagectomy
- Pneumonectomy¹

The stable patient

If there are no adverse cardiovascular signs, treatment options include:

- Rate control
- Chemical cardioversion
- Electrical cardioversion
- Prevention of complications with anticoagulation

Control rate with an IV beta-blocker, digoxin, magnesium or combinations of these 3 agents. If the onset of AF is less than 48hrs, amiodarone (may result in chemical cardioversion) may be given as 300mg over 20-60 min followed by 900mg over 23hours.⁶ Digoxin as the sole agent for rate control in persistent AF is commonly used, but is thought to be less effective. Digoxin has no benefit in preventing episodes of paroxysmal AF.²

Other drugs which may be used for rate control in the emergency setting:

- Diltiazem 0.25mg/kg IV over 2 min with a maintenance of 5-15mg/hr
- Esmolol 0.5mg/kg IV over 1 min, maintenance 0.05-0.2mg/kg/min
- Metoprolol 2.5-5mg IV over 2min up to 3 times
- Propranolol 0.15mg/kg IV
- Verapamil 0.075-0.15mg/kg IV over 2 min
- Digoxin 0.25mg IV every 2 hrs up to 1.5mg²

It is vital never to use beta blockers and calcium channel blockers together as the combination may prove fatal.

Broad complex (QRS > 0.12 sec) irregular tachycardia in a stable patient may be AF with aberrant conduction, pre-excited AF or polymorphic VT. Compare the pre-operative ECG with a new 12 lead ECG. Look on the initial ECG for bundle branch block or a delta wave as in Wolff-Parkinson-White syndrome (WPW). Seek expert advice if available. AF with bundle branch block may be treated as above. Amiodarone could be considered in WPW with AF, but avoid adenosine, diltiazem, verapamil and digoxin.⁶

Wolff-Parkinson-White syndrome (WPW): this group of patients have an accessory pathway connecting the atria and the ventricles. In AF the accessory pathway can conduct rapidly leading to a very rapid ventricular response, hypotension and arrest. Digoxin, calcium channel blockers and beta-blockers do not block the accessory pathway and can enhance conduction through the accessory pathway. They should therefore be avoided. If the patient is haemodynamically unstable, electrical cardioversion is indicated. If not under a Cardiologist, this group of patients should be transferred for possible ablation therapy.²

Chemical cardioversion takes longer to work than DCCV and is not as reliable. It tends to be reserved for stable patients and it is therefore advisable to seek the help of an expert.⁶

Reversible precipitants should be identified and dealt with before the administration of anti-arrhythmic drugs.²

In a patient with uncomplicated AF a beta-blocker could be tried, but flecainide and sotalol are very effective.²

In **adrenergically associated** AF the first choice is a beta blocker followed by sotalol or amiodarone.²

Congestive cardiac failure: Patients are prone to the pro-arrhythmic effect of anti-arrhythmic drugs. Most agents are negatively inotropic. Amiodarone is recommended.²

Coronary artery disease: Beta-blockers may be considered first. Sotalol has good beta-blocking activity and can be the initial agent. Amiodarone is associated with long-term toxicity. Flecainide is not recommended.²

Hypertensive heart disease: Left ventricular hypertrophy causes early post-depolarization with increased risk of 'torsade de pointes' VT. Drugs which do not increase the QT interval are the best option. If the patient is free from coronary artery disease, flecainide is a reasonable choice. Although amiodarone lengthens the QT interval the risk of it being pro-arrhythmic is low.²

WPW syndrome: Radiofrequency ablation is the preferred management option.²

Combinations of a beta-blocker, sotalol or amiodarone with a class Ic agent may be tried if a single agent fails.²

Some of these drugs may become pro-arrhythmic if used with other drugs that prolong the QT interval. Check <http://www.torsades.org.com> for further details about drugs which prolong the QT interval. Deterioration in renal function could lead to accumulation of anti arrhythmic drugs and should be monitored along with K⁺ and Mg⁺⁺ levels. Patients should be warned about symptoms such as dyspnoea, angina and syncope.²

A large proportion of patients with new AF will spontaneously cardiovert within 1-2 days.²

DCCV is still an option in the stable patient with AF for less than 48hrs and this is more effective than drugs in restoring sinus rhythm.⁶

The recovery phase and atrial fibrillation

If a patient develops AF postoperatively in recovery:

- Control the patients rate with AV nodal blocking agents.
- DCCV may be attempted.
- If the AF is recurrent or refractory give anti arrhythmic drugs as for a patient with coronary artery disease.
- Anticoagulation is recommended as for non surgical patients.²

In a patient with newly diagnosed AF there is a suggested "minimal evaluation":

- 12 lead ECG.
- CXR.
- Transthoracic echo to look at valve function, chamber size, peak right ventricular pressure, hypertrophy and pericardial disease.
- Thyroid function tests.

Additional investigations may be indicated:

- Exercise tolerance test.
- 24 hour cardiac monitoring.
- Transoesophageal echocardiogram and
- Electrophysiological studies.⁵

Consider referring the patient to a specialist. It may not be possible to start anticoagulation immediately, but if indicated it should not be omitted.

Anaesthesia for DC Cardioversion

It is not in the best interest of all patients to attempt electrical cardioversion. In a patient with recurrent persistent AF who has had at least one attempt of electrical cardioversion, it may be reasonable to accept the progression of persistent AF to permanent AF and to focus on anticoagulation and rate control.²

Anaesthesia technique

Elective cardioversion is a day case procedure and should be performed on a fasted patient. Adequate anaesthesia must be obtained by using short acting anaesthetic agents enabling rapid recovery (e.g. propofol).²

In the emergency setting the patient may not be starved and airway management must then be as for the non-starved patient with rapid sequence induction.

The anterior-posterior paddle position with one paddle on the sternum and the other on the left scapula seems to be superior to the anterior-lateral position where one paddle is on the ventricular apex and the other inferior to the right clavicle.²

Implanted permanent pacemakers (PPM) or defibrillators (AICD) should be interrogated just before and after electrical cardioversion to establish good working order. Anterior-posterior paddle position is the preferred position since the paddles should be as far away from the device as possible.²

The anaesthetic position of the patient could be improved by using hands free paddles.

The risks of electrical cardioversion mainly relate to arrhythmias and thromboembolism. Transient ST-segment elevation may appear and cardiac enzymes may be elevated without obvious myocardial damage. A variety of arrhythmias are possible:

- Ventricular and supraventricular premature beats
- Bradycardia (may indicate a conduction defect in the absence of AV nodal blocking agents)
- Sinus arrest
- VT and VF (with hypokalemia and digoxin toxicity).²

Anticoagulation

If the duration of AF is more than 48hrs (or unknown) the patient should be anticoagulated for 3 to 4 weeks before cardioversion (electrical or chemically). The patient should also be anticoagulated for 3-4 weeks after successful cardioversion. The left atrium and left atrial appendage (LA/LAA) may take several weeks after cardioversion to recover from mechanical “stunning” and during this recovery the patient remains at risk of thrombus formation.²

Alternatively, the patient could be screened for a LA/LAA thrombus with transoesophageal echo. If thrombus has been identified the patient should be anticoagulated for 3-4 weeks prior to attempted cardioversion. If there is no thrombus heparin should be given before cardioversion, as a bolus followed by an infusion, aiming for an activated partial thromboplastin time (APTT) of 1.5-2 times the control time. Successful cardioversion should be followed by oral anticoagulation for 3 – 4 weeks.²

In the acute setting with haemodynamic instability where DCCV is urgent, unfractionated or low-molecular-weight fractionated heparin should be used. Protection against late embolism may require further oral anticoagulation, but this will depend on the risk of recurrence and the patient’s intrinsic risk for thromboembolism.²

Recurrent and refractory AF

Some patients have resistant AF and DCCV is entirely unsuccessful. Others convert back to AF 1-2 minutes after cardioversion. In a further group AF will recur from 1 day up to 2 weeks after successful cardioversion. The first 2 groups account for 25% of patients and the last group for a further 25%.²

Drugs which increase the DC cardioversion success rate and decrease early recurrence are most appropriate in patients who have previously failed to convert to sinus rhythm and those with immediate or subacute recurrence of AF.²

Aim to obtain therapeutic plasma levels before and for a few weeks after cardioversion with one of the following agents:

- Amiodarone
- Flecainide
- Quinidine
- Sotalol²

Patients receiving drugs which increase the QT interval should be observed in hospital for 24 to 48 hours after cardioversion.²

Possible risks involved include:

- Paradoxical increase in defibrillation threshold (flecainide)
- Accelerated ventricular rate in the absence of AV nodal blocking (Ia and Ic) and
- Ventricular pro-arrhythmic effect.²

Summary

Management of AF is divided into rhythm control, rate control and anticoagulation. In the unstable patient DCCV is indicated. If the patient is stable, cardioversion may be attempted electrically or chemically. An asymptomatic patient may only require rate control. Anticoagulation reduces the risk of thromboembolic complications. Several factors need to be kept in mind when prescribing or administering drugs for patients in AF.

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AN INFANT WITH A DIFFICULT AIRWAY

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An 8 month old baby girl was referred to our plastic surgery unit for neck contracture release and skin grafting. The child had sustained third degree burns on the left side of the face and the neck at the age of 6 months after she fell over a glowing lamp whilst crawling. Over the next few months she developed severe contractures to the neck (Figure 1).



Figure 1: 8 month old baby girl with neck contractures

The child was referred for preoperative assessment for anaesthesia. She was active but underweight at 7kg. On examination, her mouth opening was severely restricted (Mallampatti class IV) and almost no neck movements were possible. The rest of the examination and baseline investigations were all within normal limits. Difficulty with laryngoscopy & intubation was anticipated. The hospital did not have a fibre-optic bronchoscope suitable for infants so a technique utilizing available equipment was planned and the child was scheduled for surgery.

- On the day of surgery the child was allowed a breast milk feed 4 hours prior to theatre.
- Anaesthesia was induced with intramuscular ketamine 10mg/kg with atropine 20mcg/kg. Oxygen was administered via facemask using the Jackson Rees modification of the Ayres T-piece and monitors applied: ECG, pulse oximeter and NIBP.

- A 22G intravenous cannula was inserted and an infusion of Hartmann's solution 20ml/kg commenced.

- Anaesthesia was deepened with halothane in oxygen and a size 1 LMA was introduced. Anaesthesia was maintained with halothane in oxygen and nitrous oxide.

- The surgeon performed immediate release of the contracture (Figures 2 and 3) following which neck movements were possible.

- The LMA was removed and the child was intubated with

a 3.5mm uncuffed ET tube under deep halothane anaesthesia (grade 1 laryngoscopy), and then allowed to breathe spontaneously (Figure 4).



Figure 2: Surgical release of contracture to give movement (LMA in place)

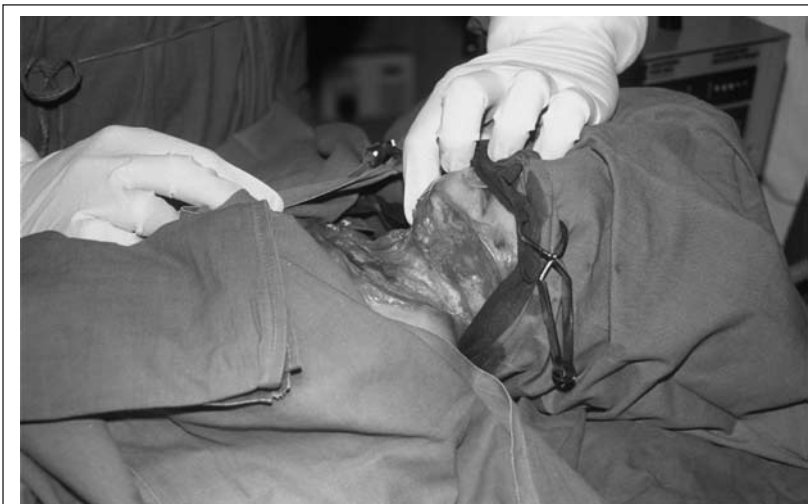


Figure 3: Release of contracture



Figure 4: Intubation

This child presented with what was very obviously a difficult airway due to burns contractures. The procedure required careful planning and discussion in advance between the anaesthesia and surgical teams. There are many acceptable ways of managing this situation safely, but the described technique was chosen, as it did not depend on any special equipment (none was available).

This staged procedure whereby the surgical team released the contracture immediately after induction of anaesthesia with ketamine resulted in immediate improvement of the airway. An impossible intubation was converted to a grade 1 laryngoscopy.

We felt that the use of the LMA allowed an additional degree of airway stability during the contracture release, although we could have used a simple 'chin lift/jaw thrust' to maintain the airway (no LMA).

We felt that after contracture release the tracheal tube allowed greater protection to the airway than performing the whole procedure using the LMA.

We did not think that laryngoscopy under deep halothane anaesthesia prior to contracture release would have had anything to add.

Consent was given for publication of these images

- The child was extubated fully awake following the skin grafting procedure (Figure 5) and recovered uneventfully with regular paracetamol and ibuprofen for analgesia.

Discussion

Respiratory complications of burns injuries may be due to:

- acute airway obstruction resulting from oedema of the airway due to inhaling hot gases, or secondary to facial oedema in burns of the head and neck.
- effects of inhalation of toxic substances.
- chronic airway obstruction due to the development of burns contractures.



Figure 5: After skin graft procedure

LOCAL ANAESTHETIC PHARMACOLOGY

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Introduction

Local anaesthetic drugs are used widely for the provision of anaesthesia and analgesia both intra- and post-operatively. Understanding the pharmacology of these agents as a group, as well as the differences between specific drugs, enables the anaesthetist to use them safely to maximum effect. This article focuses on the basic structure and function of local anaesthetics. Learning will be improved by trying to answer the questions posed in the text before moving on. More detail can be found in the "Further reading" section at the end.

Definition of a local anaesthetic

A local anaesthetic can be defined as a drug which reversibly prevents transmission of the nerve impulse in the region to which it is applied, without affecting consciousness. There are many drugs which exert local anaesthetic activity in addition to their main clinical uses, but this article will focus on those drugs which are principally used for their local anaesthetic properties.

The structural classification of local anaesthetics

Local anaesthetics generally have a lipid-soluble, hydrophobic aromatic group and a charged, hydrophilic amide group. The bond between these two groups determines the class of the drug, and may be amide or ester. Examples of amides include lignocaine, bupivacaine and prilocaine. Examples of esters include cocaine and amethocaine.

The clinically significant differences between esters and amides

The ester linkage is more easily broken than the amide bond so the ester drugs are less stable in solution and cannot be stored for as long as amides. Amide anaesthetics are also heat-stable and can therefore be autoclaved; esters cannot.

The metabolism of most esters results in the production of para-aminobenzoate (PABA) which is associated with allergic reactions. Amides, in contrast, very rarely cause allergic phenomena. For these reasons amides are now more commonly used than esters.

Local anaesthetics as isomers

Local anaesthetics may also be considered in terms of their stereoisomerism. This term describes the existence of molecules with the same molecular and structural formula, but different spatial orientation around a particular atom, the chiral centre. This is analogous the right and left foot being mirror images of each other. Stereoisomerism occurs in the case of bupivacaine which has two stereoisomers,

known as R and S forms, and also in the case of prilocaine. The combination of equal amounts of the two stereoisomers of a particular drug is known as a racemic mixture.

Why might this isomerism be important?

The different arrangements of the R and S forms of bupivacaine are thought to be associated with differences in potency and side-effect profile. This is easy to understand if you were to try and put your right foot in your left shoe – it doesn't work as well and causes side effects (pain)! This is the reason why more drugs are being prepared as a single stereoisomer such as levobupivacaine. Another familiar example of this is ketamine.

In contrast amethocaine (an ester) and lignocaine are achiral, ie they have no stereoisomers.

The mechanism of action of local anaesthetics (Figure 1)

Local anaesthetics disrupt ion channel function within the neurone cell membrane preventing the transmission of the neuronal action potential. This is thought to occur via specific binding of the local anaesthetic molecules (in their ionised form) to sodium channels, holding them in an inactive state so that no further depolarisation can occur. This effect is mediated from within the cell; therefore the local anaesthetic must cross the cell membrane before it can exert its effect. A second mechanism is also thought to operate, involving the disruption of ion channel function by the incorporation of local anaesthetic molecules into the cell membrane (the membrane expansion theory). This is thought to be mediated mainly by the unionised form acting from outside the neuron. Nerve fibres differ in their sensitivity to local anaesthetics. Small nerve fibres are more sensitive than large nerve

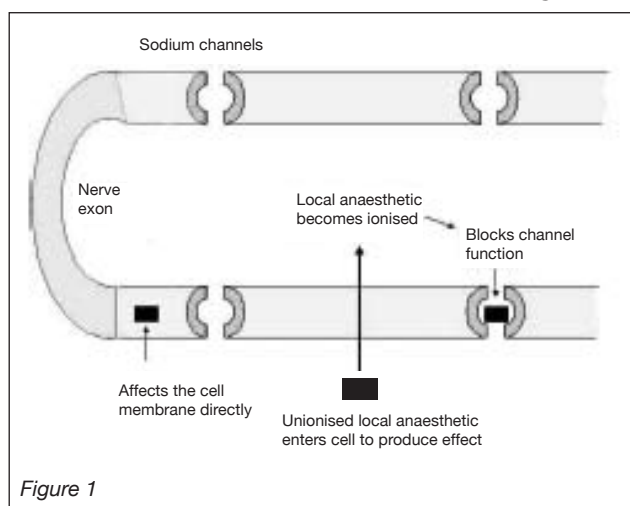


Figure 1

fibres while myelinated fibres are blocked before non-myelinated fibres of the same diameter. Thus the loss of nerve function proceeds as loss of pain, temperature, touch, proprioception, and then skeletal muscle tone. This is why people may still feel touch but not pain when using local anaesthesia.

The importance of the pKa of a local anaesthetic drug.

All local anaesthetic agents are weak bases, meaning that they exist in two forms: unionised (B) and ionised (BH⁺). The pKa of a weak base defines the pH at which both forms exist in equal amounts. As the pH of the tissues differs from the pKa of the specific drug, more of the drug exists either in its charged or uncharged form. This is expressed in the Henderson-Hasselbalch equation:

$$\text{pKa} - \text{pH} = \log [\text{BH}^+] / [\text{B}]$$

where [B] is the concentration of unionised and [BH⁺] the concentration of ionised drug.

How may the pKa of a local anaesthetic influence its speed of onset?

The pKa of a local anaesthetic determines the amount which exists in an ionised form at any given pH. At physiological pH (7.4) all local anaesthetics are more ionised than unionised (as all the pKa values are greater than 7.4). However the proportions vary between the drugs: lignocaine has a pKa of 7.9 and is approximately 25% unionised at pH 7.4. Bupivacaine has a pKa of 8.1 and hence less of the drug is unionised at pH 7.4 (about 15%).

As the drug must enter the cell in order to have its effect it must pass through the lipid cell membrane. Unionised drug will do this more readily than ionised drug. Therefore the drug which is more unionised at physiological pH will reach its target site more quickly than the drug which is less so. This explains why lignocaine has a faster onset of action than bupivacaine.

Can this theory explain why local anaesthetics often don't work in infected tissue?

The relevant feature of infected tissue is that it tends to be a more acidic environment than usual. As the pH is reduced the fraction of unionised local anaesthetic is reduced and consequently the effect is delayed and reduced. Infected tissue may also have an increased blood supply and hence more anaesthetic may be removed from the area before it can affect the neurone.

How else may the physicochemical characteristics of a local anaesthetic affect its function?

Physicochemical features such as the aromatic ring structure and hydrocarbon chain length of a particular local anaesthetic determine the lipid solubility of the drug and hence its potency. This makes sense since the more lipid soluble drug penetrates the cell membrane more easily to exert its effect. The more

potent the drug, the smaller the amount required to produce a given effect. Thus bupivacaine – which is highly lipid soluble – is approximately four times more potent than lignocaine. This is reflected in the different preparations available of these two drugs; bupivacaine being more potent is prepared as a 0.1–0.5% solution. Lignocaine conversely is commonly presented as a 1% or 2% solution.

The duration of action of the drug is also related to its structure, primarily to the length of the intermediate chain joining the aromatic and amine groups. However it should be noted that protein binding is probably at least as important a determinant of duration of action. Clearly the molecular structure of the drug also affects protein binding ability and therefore all local anaesthetics differ in the extent to which they are protein-bound. So, for example, lignocaine is approximately 65% protein bound whereas bupivacaine is 95% protein bound. Therefore one can predict that bupivacaine will have a longer duration of action than lignocaine – which is in fact the case. Procaine (an ester), in contrast, is only 6% protein bound and has a very short duration of action. Differences in protein binding also result in differing duration of unwanted side effects and is one of the reasons that bupivacaine is considered more toxic than lignocaine.

Pharmacokinetics of local anaesthetics

Absorption and distribution

Local anaesthetic drugs are administered to the areas around the nerves to be blocked – which include skin, subcutaneous tissues, intrathecal and epidural spaces. Some of the drug will be absorbed into the systemic circulation: how much will depend on the vascularity of the area to which the drug has been applied and intrinsic effects of the drug or its additives on vessel diameter. Some local anaesthetics have vasodilatory effects at low concentrations, increasing their systemic absorption. This is countered in some preparations which include a vasoconstrictor such as adrenaline or felypressin. Cocaine, in contrast, has a vasoconstrictive effect.

The distribution of the drug is influenced by the degree of tissue and plasma protein binding of the drug. As discussed above, the more protein bound the agent, the longer the duration of action as free drug is more slowly made available for metabolism.

Metabolism and excretion

Ester and amide anaesthetics differ in their metabolism. Esters (except cocaine) are broken down rapidly by plasma esterases to inactive compounds and consequently have a short half life. Cocaine is hydrolysed in the liver. Ester metabolite excretion is renal.

Amides are metabolised hepatically by amidases. This is a slower process, hence their half-life is longer and they can accumulate if given in repeated doses

or by infusion. Prilocaine is also metabolised extra-hepatically.

Which local anaesthetic drugs are more likely to affect the foetus when given in pregnancy and why? How does the situation change if the foetus is compromised?

The esters are metabolised sufficiently rapidly to have minimal effects on the foetus so little remains in the maternal circulation to cross the placenta. Amide local anaesthetics are more likely to cross the placenta. Of these, placental transfer is greater in those which are less protein-bound (such as lignocaine).

If the foetus is compromised it may become acidotic. In this situation more of the foetal local anaesthetic will be ionised and hence unable to return to the maternal circulation. This phenomenon is known as ion trapping and can result in foetal toxicity.

These effects are not likely to be important when small amounts of drug are used during spinal anaesthesia, but may become so when larger amounts are used for epidural anaesthesia or other nerve blocks around the time of delivery.

Clinical uses of local anaesthetics

Preparations

Local anaesthetics are available as solutions for injection, sprays, creams and gels. They are prepared as the hydrochloride salt to enable them to be dissolved in water (resulting in an acidic solution). Of note, due to new legislation, some of the newer local anaesthetics are described in terms of the quantity of free base present alone, in contrast to the older drugs which are described in terms of the quantity of total hydrochloride salt present. This is why, for example, 10ml of 0.5% bupivacaine (a racemic mixture) contains fewer local anaesthetic molecules than 10ml of 0.5% levobupivacaine. Most local anaesthetic preparations contain a preservative agent such as 0.1% sodium metabisulphite, with or without a fungicide. Multidose vials contain 1mg/ml of the preservative methyl parahydroxybenzoate. The drug may also be combined (by the manufacturer or in some cases the clinician) with other local anaesthetics (e.g. EMLA cream - eutectic mixture of local anaesthetics) or additives designed to enhance their effects. These include adrenaline 1/200,000, bicarbonate (eg 0.15ml of 8.4% solution added to 10ml 0.5% bupivacaine) or glucose (usually 80mg/ml).

How might adrenaline, bicarbonate and glucose variously affect the action of local anaesthetics?

Adrenaline acts as a vasoconstrictor. The result is to minimise the vasodilator effect of (for example) lignocaine and decrease the rate at which drug is removed from the site of action by absorption into the systemic circulation. It also reduces traumatic (surgical) blood loss from the site by the same mechanism.

Bicarbonate added to a local anaesthetic increases the pH of the environment when administered. Consequently more drug is present in its unionised form and speed of onset of anaesthesia is increased. Too much bicarbonate however may result in precipitation of the local anaesthetic as the unionised form is much less soluble in water than the hydrochloride salt.

Glucose is added to bupivacaine in order to increase the baricity of the solution to greater than that of CSF. When administered as a spinal anaesthetic this results in more controlled spread of solution within the intrathecal space.

What harmful effects of local anaesthetics do you know?

Potential problems

Local anaesthetics may be toxic if sufficient amounts are absorbed into the systemic circulation. Of these bupivacaine appears to be the most dangerous although all can be harmful. Clinical toxicity appears to relate to the effects of the drug on other excitable membranes in the CNS and cardiovascular systems. CNS effects may include tingling of the lips, slurred speech, reduced level of consciousness and seizures. Cardiac effects on a variety of ion channels may cause arrhythmias and reduced myocardial contractility. In the case of bupivacaine the cardiac effects are particularly difficult to treat since its strong protein binding makes it difficult to displace from the myocardium. In contrast lignocaine may be used clinically for its cardiac effects as an antiarrhythmic.

Unexpected local anaesthetic toxicity can occur where the pharmacokinetics of the drug are altered by co-morbidity such as cardiac or hepatic failure (reducing metabolism of the drug), alterations in plasma protein binding, or interactions with other drugs.

Other clinical problems are more specific to particular drugs. The incidence of allergy to PABA, a metabolite of many esters has been mentioned. Prilocaine is metabolised to O-toluidine which can cause methaemoglobinaemia in susceptible individuals. Cocaine is a potent vasoconstrictor and may cause problems in patients already on vasoconstricting drugs such as monoamine oxidase inhibitors.

Summary

Understanding the pharmacology of local anaesthetics enables the anaesthetist to predict the potency, speed of onset, duration of action and safety of a specific drug in a given clinical situation. This maximises the opportunity for safe and effective use of local anaesthesia in a wide variety of contexts.

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ONE-LUNG VENTILATION

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Self Assessment

Complete these questions before reading the tutorial.

1. What are the indications for inserting a double lumen tube?
2. Describe insertion and checking position of a right-sided double lumen tube.
3. Describe changes in ventilation & perfusion in an anaesthetised compared with an awake patient.
4. A patient desaturates to 85% during one lung anaesthesia for a lobectomy. Describe your management.

The answers can be found in the following text and text boxes.

One lung ventilation (OLV) is the term used in thoracic anaesthesia to describe the ability to ventilate one of a patient's lungs, allowing the other one to collapse. This article will describe indications for OLV, techniques used to achieve OLV, the physiological changes associated with OLV and ways that oxygenation can be improved during OLV.

Indications for OLV

There are 3 indications for OLV:

Improving surgical access. It is much easier for a surgeon to carry out lung surgery, or oesophageal surgery, if a lung is collapsed. Adequate surgical access can be achieved for most lung resections and oesophago-gastrectomies without collapsing a lung simply by ventilating the patient with smaller tidal volumes and the surgeon using a retractor. However, if the surgeon is not used to operating with the lung inflated, or if the tumour is technically difficult to resect, OLV will be required. It is important to discuss with the surgeon any difficulties or specific requirements that he anticipates, and to be aware exactly what he intends to do intraoperatively, since both surgeon and anaesthetist are influencing the organ that is oxygenating the body, lack of communication can be disastrous.

Some surgery definitely needs OLV. Thoracoscopic surgery is impossible without collapsing a lung. A thoracoscopic procedure involves insufflating one side of the chest with carbon dioxide and introducing a camera and instruments through ports in the chest wall, similar to a laparoscopy in the abdomen. This technique is known as video-assisted thoracoscopic surgery (VATS). It can be used to carry out procedures such as stapling of bullae, pleurodesis, lung biopsy, thoracic sympathectomy, inspection of lesions to decide operability, and even lung resection.

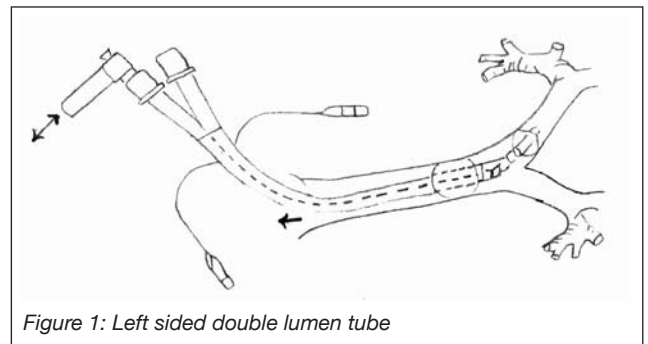
Lung protection. OLV is indicated to protect the other lung from becoming contaminated by blood or pus in the diseased lung during surgery. An anaesthetised patient will lose the ability to cough and therefore the ability to prevent infected material/blood entering the normal lung.

Intensive care ventilation. If a patient has disease of one lung, it may be desirable to ventilate the lungs independently using 2 ventilators so that the normal lung is not subjected to high pressure required to ventilate an abnormal lung. An example of this is after a single lung transplant.

Techniques for OLV

There are 3 devices that can be inserted to achieve one lung ventilation: a double lumen tube, a bronchial blocker, or a single lumen tube inserted beyond the carina.

Double lumen tubes are tubes with one lumen opening just above the carina and the other inserted into a main bronchus. (Figure 1).



By clamping one lumen, this occludes ventilation to the lung on that side. If one lumen is opened to the atmosphere, the lung can deflate and ventilation continued through the other lumen. Tubes come in sizes 26 to 41 French gauge - 37-39 is the usual size for a female and 39-41 for a male.

There are right and left sided tubes. A left-sided tube has the endobronchial part down the left main bronchus; a right-sided tube down the right main bronchus.

Either tube can be used to ventilate either lung depending on which lumen is clamped, however a left-sided tube is usually used as it is easier to position. This is due to the anatomy of the right main bronchus. The right upper lobe comes off the right main bronchus at a variable distance from the carina in different people. It may also be anterior, lateral or posterior as you look down the bronchus. A right-sided DLT has a small hole towards the end of the

endobronchial part called a Murphy eye. This has to be aligned with the entrance to the right upper lobe, or the lobe will not be ventilated. Of the currently available DLTs, the Rusch tube has a larger and more elongated Murphy eye compared to the Mallinkrodt (Figure 2), allowing for more variability in anatomy. Changing tube size may also compensate for variable anatomy.



Figure 2: Murphy eyes of Mallinkrodt & Rusch tubes

A left sided tube can be used for most operations. In surgery involving the left main bronchus such as a pneumonectomy with tumour involvement very near the carina, it may be preferable to use a right-sided tube, but it is perfectly possible to use a left sided tube and just withdraw it when the surgeon is about to staple the bronchus or clamp it ready to suture.

To insert a double lumen tube (DLT) the tip of the tube is inserted just through the vocal cords and then immediately rotated 90 degrees in the direction of the bronchus you are aiming to intubate. The tubes are bulky and can be awkward to place, particularly in dentulous patients. One lumen is clamped at a time and the chest auscultated to make sure that each lung can be collapsed. If possible, the tube position should be checked with a bronchoscope. It is possible that the tube is achieving the desired clinical effect, but with a tiny movement becomes malpositioned. The tubes, usually made of plastic, become softer as they warm to the patient's body temperature, and, combined with the fact that the patient may need to be moved to a lateral position and the surgeon may manipulate the mediastinal structures during surgery, the tube often becomes dislodged. Using the bronchoscope habitually will make it easier to recognise the anatomy and therefore fix problems when they arise. All that is necessary is a check to see that the tracheal lumen is above the carina, the bronchial lumen is in the correct bronchus and that its cuff is not blocking the other (tracheal) lumen by herniating over it, and that the bronchial lumen is clear and not abutting an airway wall. If right sided, the right upper lobe entrance needs to be seen through the Murphy eye.

Inserting DLT without a bronchoscope

1. Insert tip of tube through cords and immediately rotate 90 degrees in direction of bronchus you are aiming to intubate.
2. Advance tube until comes to a halt. (No excess force needed).
3. Inflate tracheal cuff until air leak disappears & check both lungs ventilate (just as you would a single lumen tube).
4. Clamp tracheal lumen & check that only opposite side of chest moves and has air entry. Remember to open cap on clamped side so air can escape and lung collapse. You should feel a 'whoosh' of air as lung collapses. Make sure your clamp is proximal to the open cap or you will have trapped the air in the lung.
5. Inflate bronchial cuff until no leak is heard via tracheal lumen. Need about 2ml air for this.
6. Repeat 4, but clamping bronchial lumen instead of tracheal.
7. Switch on ventilator and collapse lung to be operated on. Check you can achieve a reasonable tidal volume without excessive pressure and that the capnograph trace has not changed compared to 2-lung ventilation.

Tip: It is easier to check tube position while manually ventilating patient as you have to time auscultation with inspiration, and also you will need to compensate for large air leaks as you open caps and inflate cuffs.

Checking DLT position with a bronchoscope

1. Insert scope into tracheal lumen. Check carina is visible. The carina has the appearance of a sharp line. Other airway divisions have a blunter, gentle curve between them. The tube should not be up against carina. This causes airway irritation/obstruction.
2. With scope still down tracheal lumen, look at bronchial portion. Check it inserts into correct side. It is possible to over rotate the tube and end up in wrong side. You should just see the top of the bronchial cuff. It should not be bulging out of the bronchus or impinging on the tracheal lumen (herniation).
3. Withdraw scope and now insert into bronchial lumen. Check that end of tube is not abutting against airway wall and that the end of the lumen is therefore patent.
4. If the tube is right-sided, look for the Murphy eye in the bronchial lumen. This should open into the RUL lumen. It is often hard to see. Because the bronchoscope only flexes in an anterior to posterior direction, it may be easier to insert the scope while standing facing the patient's left side. This avoids the need to twist scope or self.

A bronchial blocker (figure 3) is a device that is inserted into a conventionally placed single lumen tube. It is useful when it is not possible to place a DLT or in situations where the patient has already been intubated with a single lumen tube. It has the appearance of a hollow bougie with a cuff. There is a type that has a steerable tip (Cohen by Cook) as well as the basic type that cannot be steered (Arndt). The blocker has a guidewire in its lumen, the end of which can be hooked over a bronchoscope so the blocker can be inserted under direct vision into the lung that is to be collapsed. This guidewire needs to be removed before air can be withdrawn from the blocker and hence collapse the lung. A disadvantage is that once the guidewire on the device has been withdrawn, it cannot be reinserted so the blocker cannot be reused or repositioned in the patient. Also, because a bronchoscope needs to be used both to guide the blocker into place and to verify its position, this means that if there is blood or secretions in the airway, this technique may not be possible.

The third way of achieving OLV is by use of a single lumen tube intentionally inserted 'too far' into a bronchus. This may be a good option in an emergency such as a left-sided chest stabbing if you fail to insert a DLT, and blood in the airway makes it impossible to use a bronchoscope.

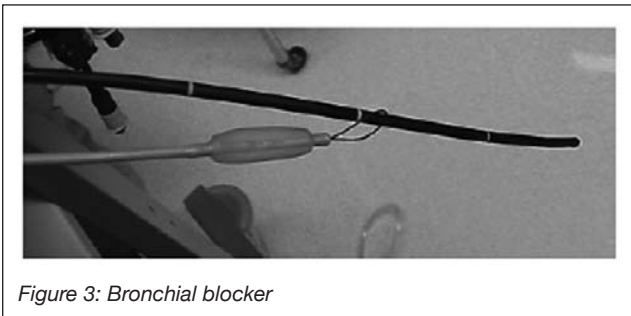


Figure 3: Bronchial blocker

Physiology of OLV

As a simple view of lung physiology, when a patient is awake, the dependent part of a lung (regardless of the patient's position) has a greater blood supply than the non-dependant part due to gravity. The dependent part is also preferentially ventilated compared with the non-dependent lung due to it being slightly more compressed than the non-dependant lung and therefore having a greater compliance once the atelectatic airways at the base have been opened. This can be thought of like blowing up a balloon. Initially, the pressure required is large to start blowing up the balloon (atelectatic bits), it then becomes easier and a small change in pressure will give a big change in volume (dependent lung). As the balloon gets bigger and the material gets more stretched, a larger pressure is needed to give a change in volume (the non-dependent lung). Ventilation (V) and perfusion (Q) are relatively well matched and shunt (lung that is perfused but not ventilated) is only 1-2% in a healthy person.

Simply anaesthetising a patient alters lung physiology before you even consider the effect of collapsing a lung. The functional residual capacity (FRC) decreases as the diaphragm and chest muscles are paralysed. Mediastinal weight becomes unsupported by the surrounding structures becoming relaxed. Figure 4 shows the compliance of the lungs in both the awake and the anaesthetised patient.

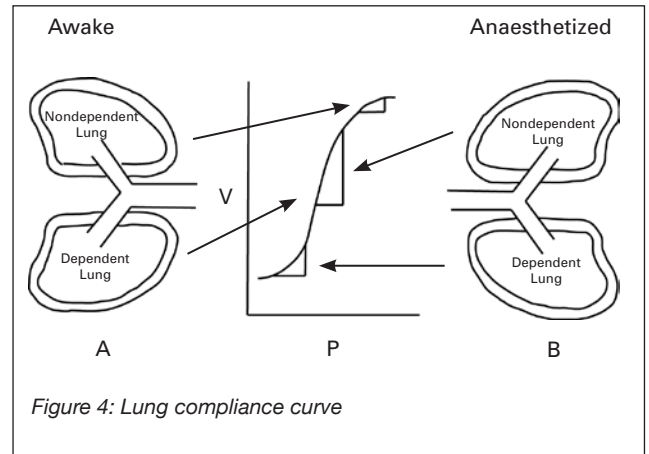


Figure 4: Lung compliance curve

When the patient is anaesthetised, the upper lung moves to the position where the lower lung sits on the curve in the awake patient, and the lower lung moves down the curve past the inflection point. The lungs have shifted down the compliance curve (Figure 4) and the non-dependent lung becomes easier to ventilate than the dependent lung. When the chest is opened, the top lung becomes even easier to ventilate as there is no restriction by the chest wall. Blood supply is still determined greatly by gravity. V/Q mismatch now occurs. This is even worse when the top lung is collapsed as there is then no ventilation to that lung, but there is still perfusion.

By simple maths, you would expect the shunt to now be 50%, however this is not the case. Mechanical collapse of the lung diverts the blood flow towards the ventilated lung. Lack of ventilation and therefore hypoxia in the collapsed lung causes a phenomenon called hypoxic pulmonary vasoconstriction (HPV), which further diverts blood flow away from the collapsed lung. This protective mechanism, which occurs when alveolar pO_2 levels are 4-8kPa, is inhibited to some extent by vasodilators, including all anaesthetic gases and induction agents. There was a vogue for using propofol total intravenous anaesthesia in preference to volatile agents in an attempt to maintain HPV, however it has been shown that HPV is not inhibited by MAC values less than 1%. 1 MAC of isoflurane only inhibits HPV by 20% so it is not clinically a big problem and there is no reason to avoid volatile agents.

The disease itself may have altered the lung physiology. A large tumour may already be obstructing ventilation and so collapse of this lung may not alter the patient's oxygenation.

You will have been taught that a patient needs a tidal volume of 7-10mls/kg during ventilation. During one lung anaesthesia, a balance has to be struck between having enough tidal volume for gas exchange and not too high a peak inspiratory pressure i.e. greater than about 30cm H₂O to avoid barotrauma. A higher than normal level of carbon dioxide, known as 'permissive hypercapnia' may need to be tolerated.

Overcoming hypoxia during OLV

Because of the above changes in lung physiology, it is not uncommon for a patient to desaturate during OLV. If this happens, tell the surgeon early rather than waiting for the saturations to plummet. It may be that you have to reinflate the lung temporarily, and the surgeon may have to, for example, finish tying off a blood vessel before his vision is obscured. Turn the inspired oxygen up to 100%. Make sure that the patient's blood pressure has not dropped as this may be the cause of desaturation. Sometimes hypotension is mechanical due to pressure on the mediastinum by the surgeon.

Tube patency and position should be checked. Secretions may be blocking the tube lumen. Look at the capnograph trace. If it has changed, as a general rule the tube has moved. Even if you have carefully tied it in place, movement may occur from within the chest during manipulation of the mediastinum. Bronchoscopy will confirm this and allow the tube to be repositioned.

Now that you have confirmed the tube is patent and in the correct position, and that the patient has a normal cardiac output, there are other actions that can improve oxygenation. Sometimes switching from machine ventilation to manual ventilation can be helpful. By giving the patient a larger breath by hand with sustained pressure at the end of the breath, you may recruit collapsed alveoli. If this works, then applying positive end expiratory pressure (PEEP) to the ventilated lung, in the form of a valve attached to the expiratory limb of the breathing circuit, may help

to prevent these small airways from closing. Usually 5cm H₂O is enough to keep the saturation up without pushing the peak inspiratory pressure too high (above about 30cm H₂O) and causing barotrauma. Also, if PEEP is too high, blood is diverted to the non-ventilated lung and shunt is increased, worsening the hypoxia.

Oxygen can be insufflated down the collapsed lung by using a small suction catheter attached to an oxygen flowmeter. The catheter needs to be small enough not to occlude the tube lumen or the lung will merely inflate. Similarly, the flow of oxygen must be low, in the region of 2litres/minute, or the lung will inflate. The theory is that this oxygen will diffuse into blood vessels that have not collapsed due to hypoxic pulmonary vasoconstriction. In practice, it is not terribly effective.

Application of continuous positive pressure (CPAP) to the non-ventilated lung may help to reduce shunt by diverting blood to the ventilated lung. Purpose made valves exist for this.

It may be that you have to compromise and settle for saturations in the low 90s.

If these methods all fail, the collapsed lung must be reinflated and the patient ventilated with 100% oxygen. If a pneumonectomy is being carried out, the surgeon may decide at this point to clamp the pulmonary artery. This will improve shunting when the lung is recollapsed as the lung will have no blood supply. It may be that surgery has to be abandoned as the patient will not tolerate one lung anaesthesia.

Further reading

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CARBON DIOXIDE TRANSPORT

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Carbon dioxide is produced by cell metabolism in the mitochondria. The amount produced depends on the rate of metabolism and the relative amounts of carbohydrate, fat and protein metabolized. The amount is about 200ml/min when at rest and eating a mixed diet; this utilises 80% of the oxygen consumed, giving a respiratory quotient of 0.8 (respiratory quotient = rate of carbon dioxide production divided by rate of oxygen consumption). A carbohydrate diet gives a quotient of 1 and a fat diet 0.7.

Carbon dioxide transport in the blood

Carbon dioxide is transported in the blood from the tissue to the lungs in three ways: (i) dissolved in solution; (ii) buffered with water as carbonic acid; (iii) bound to proteins, particularly haemoglobin.

Approximately 75% of carbon dioxide is transported in the red blood cell and 25% in the plasma. The relatively small amount in plasma is attributable to a lack of carbonic anhydrase in plasma, so association with water is slow; plasma plays little role in buffering and combination with plasma proteins is poor.

There is a difference between the percentage of the total carbon dioxide carried in each form and the percentage exhaled from them. For example, 5% of the total is in solution but 10% of exhaled carbon dioxide comes from this source; 10% is protein bound, particularly with haemoglobin, but this supplies 30% of the exhaled amount.

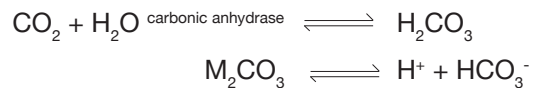
Dissolved carbon dioxide

Carbon dioxide is 20 times more soluble than oxygen; it obeys Henry's law, which states that the number of molecules in solution is proportional to the partial pressure of the gas at the liquid surface. The carbon dioxide solubility coefficient is 0.0308mmol/litre/mmHg or 0.231mmol/litre/kPa at 37°C. Solubility increases as the temperature falls. This corresponds to 0.5ml/kPa carbon dioxide in 100 ml blood at 37°C. The partial pressure of carbon dioxide is 5.3kPa in arterial blood and 6.1kPa in mixed venous blood; therefore, arterial blood will contain about 2.5 ml per 100ml of dissolved carbon dioxide and venous blood 3ml per 100ml. A cardiac output of 5 litre/min will carry 150ml of dissolved carbon dioxide to the lung, of which 25ml will be exhaled. Because of this high solubility and diffusion capacity, the partial pressure of carbon dioxide in alveolar and pulmonary end-capillary blood are virtually the same. Even a large shunt of 50% will only cause a

end-pulmonary capillary/arterial carbon dioxide gradient of about 0.4 kPa.

Carbonic acid

Carbon dioxide combines with water to form carbonic acid, a reaction accelerated by carbonic anhydrase. The carbonic acid then freely dissociates (equation 1).



The enzyme carbonic anhydrase is present in a number of organs of the body including the eye, kidney and brain; however, for this purpose, it is the red blood cell carbonic anhydrase that is important. Once carbonic acid is formed it dissociates easily so that the ratio of H_2CO_3 to HCO_3^- is 1:20 (Equation 2).

$$\frac{\text{CO}_2}{\text{H}_2\text{CO}_3} = \frac{1000}{1}$$
$$\frac{\text{H}_2\text{CO}_3}{\text{HCO}_3^-} = \frac{1}{20}$$

Carbon dioxide and water diffuse freely into the red blood cell and are converted to carbonic acid, which dissociates into hydrogen and bicarbonate ions. Hydrogen ions do not pass through cell membranes but carbon dioxide passes readily. This situation cannot be sustained as the intracellular hydrogen ion and bicarbonate ion concentration, osmolarity and cell size will rise and rupture the cell. The bicarbonate ion diffuses out to the plasma to be exchanged for chloride ions. This is known as the **chloride shift** (Gibbs–Donnan equilibrium or Hamburger effect). An ion exchange transporter protein in the cell membrane called Band 3 for Cl^- and HCO_3^- facilitates chloride shift.

A build up of hydrogen ion in the red blood cell would also prevent further conversion and production of bicarbonate ion.

However, hydrogen ions bind easily to reduced haemoglobin, which is made available when oxygen is released; therefore, free hydrogen ions are removed from solution. Reduced haemoglobin is less acidic than oxygenated haemoglobin. This is another way of stating the **Haldane effect**, which explains that, at any given PCO_2 , the carbon dioxide content of

deoxygenated blood is greater than that of oxygenated blood.

As a result of the shift of chloride ions into the red cell and the buffering of hydrogen ions onto reduced haemoglobin, the intercellular osmolarity increases slightly and water enters causing the cell to swell. This can be measured as an increase in mean corpuscular volume (MCV). The reverse process occurs as the red blood cell passes through the lung.

Key points

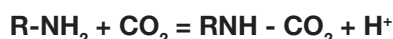
Carbon dioxide is transported in the blood in three ways:

- (i) dissolved in solution;
- (ii) buffered with water as carbonic acid;
- (iii) bound to proteins, particularly haemoglobin.

At a haemoglobin concentration of 15g/dl, and a mixed venous PCO_2 of 6.1kPa, venous blood contains 52ml/dl of carbon dioxide; arterial blood with a PCO_2 of 5.3kPa contains 48ml/dl. The effects of carbon dioxide production in the tissues include: increased plasma Cl^- ; increased red blood cell mean corpuscular volume; and haemoglobin becoming less acidotic than oxygenated haemoglobin.

Bound to haemoglobin and other proteins

Carbon dioxide combines rapidly to the terminal uncharged amino groups ($R-NH_2$) to form carbamino compounds (equation 3).



In most proteins, it is only the terminal amino acid group that combines with carbon dioxide. Haemoglobin is different when forming carbaminohaemoglobin. Reduced haemoglobin is the only effective protein buffer of hydrogen ion at physiological pH because of its high content of the amino acid histidine. Hydrogen ions attach to the imidazole group of the histidine. About 30% of exhaled carbon dioxide was transported combined with haemoglobin protein.

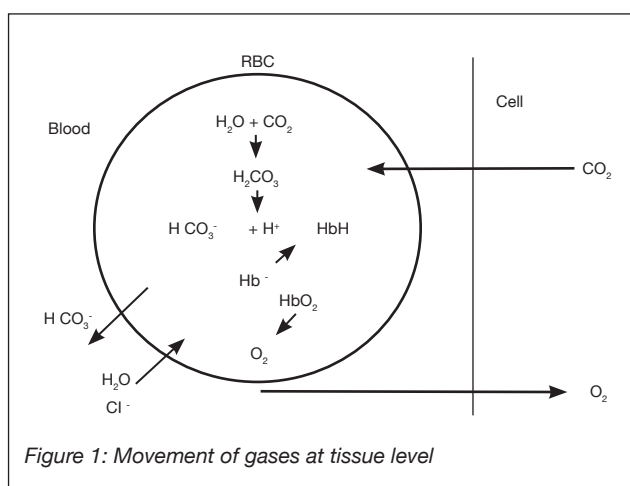
The amount of carbon dioxide held in blood in the carbamino form is small but it accounts a third of the difference between venous and arterial carbon dioxide content. The Haldane effect reflects the difference in carbon dioxide content between oxygenated and reduced haemoglobin at the same PCO_2 . This effect is partly attributable to the ability of haemoglobin to buffer hydrogen ions and partly due to the fact that reduced haemoglobin is 3.5 times more effective in combining with carbon dioxide than oxyhaemoglobin.

Different haemoglobins vary in their affinity for carbon dioxide, carbon monoxide and oxygen. Carbon

dioxide combines readily with haemoglobin to form a carbamino bond at a lower partial pressure than oxygen, but haemoglobin carries less than a quarter of the amount of carbon dioxide compared with oxygen. By contrast, foetal haemoglobin, owing to the replacement of the β -chain with γ -chains, combines with oxygen at a lower partial pressure. Carbon monoxide has a greater affinity for haemoglobin and so displaces oxygen.

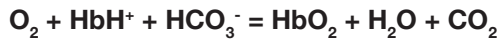
Carbon dioxide transport in the tissues

Carbon dioxide transport in the tissue is summarized in Figure 1. It combines with water to form carbonic acid. This reaction is very slow in plasma but fast within the red blood cell owing to the presence of the enzyme carbonic anhydrase. Carbonic acid (H_2CO_3) dissociates into Hb and HCO_3^- ions; therefore, the concentration of both Hb and HCO_3^- is increased in the red blood cell. HCO_3^- can diffuse out of the red blood cell into plasma whereas Hb cannot. In order to maintain electrical neutrality, chloride ions diffuse into the red blood cell from the plasma as HCO_3^- diffuses out. Hydrogen ions are taken up by reduced haemoglobin. The imidazole group of the amino acid histidine gives haemoglobin a very significant buffering capacity, not present in other amino acids. This buffering capacity is made possible by the fact that each tetramer of haemoglobin contains 38 histidine residues and the dissociation constant of the imidazole groups of the four histidine residues, to which the haem groups are attached, is affected by the state of oxygenation of the haem. In the acidic state, the oxygen bond is weakened, while reduction of haemoglobin causes the imidazole group to become more basic. In the tissues, the acidic form of the imidazole group weakens the strength of the oxygen bond at the same time as hydrogen ions are being buffered by the more basic haemoglobin.



Carbon dioxide transport in the lungs

The combination of oxygen with haemoglobin is facilitated by the histidine group becoming more basic, which increases the affinity of the haem group for oxygen as the carbon dioxide is lost (equation 4). This is one reason for the **Bohr effect**.



Release of Hb shifts the equilibrium in favour of carbon dioxide formation and elimination. HCO_3^- concentration decreases as carbon dioxide is formed and eliminated (Figure 2).

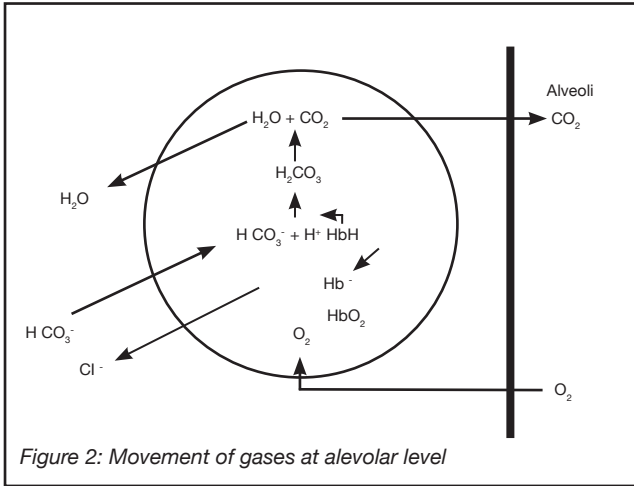


Figure 2: Movement of gases at alveolar level

Carbon dioxide dissociation curves

Carbon dioxide dissociation curves relate PaCO_2 (kPa or mmHg) to the amount of carbon dioxide (ml) carried in blood (Figure 3). The amount of dissolved carbon dioxide and bicarbonate vary with PCO_2 , but are little affected by the state of haemoglobin. However, the amount of carbamino haemoglobin is much affected by the state of oxygenation of haemoglobin, less so by the PCO_2 .

In mixed venous blood, PCO_2 is 6.1kPa (46mmHg) and in arterial blood PCO_2 is 5.3kPa (40mmHg). Total carbon dioxide in venous blood is 52ml per 100ml and in arterial blood 48ml per 100ml. Consequently, the curve is more linear than the O_2Hb dissociation curve.

Figure 4 illustrates the difference between the content in blood of oxygen and carbon dioxide with change in partial pressure. It emphasizes that the carbon dioxide content rises throughout the increase in partial pressure. Oxygen content rises more steeply until a point at which the haemoglobin is fully saturated.

After that, the increase is small because of the small increased amount in solution.

Differences between venous and arterial blood

The differences between arterial and venous blood are summarized in Figure 5 and Table 1. The high content of carbon dioxide in venous capillary blood reduces the affinity of haemoglobin for oxygen leading to release of oxygen to the tissues.¹ The oxygen dissociation curve shifts to the right (**Bohr effect**). Deoxygenated haemoglobin takes up more carbon dioxide than oxygenated haemoglobin (**Haldane effect**). Removal of oxygen from haemoglobin in the tissue capillaries causes the haemoglobin molecule to behave more

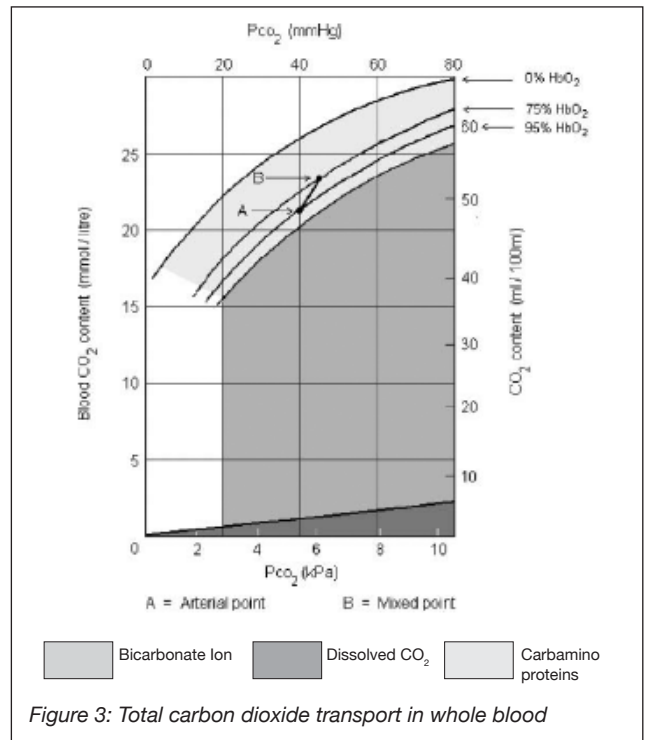


Figure 3: Total carbon dioxide transport in whole blood

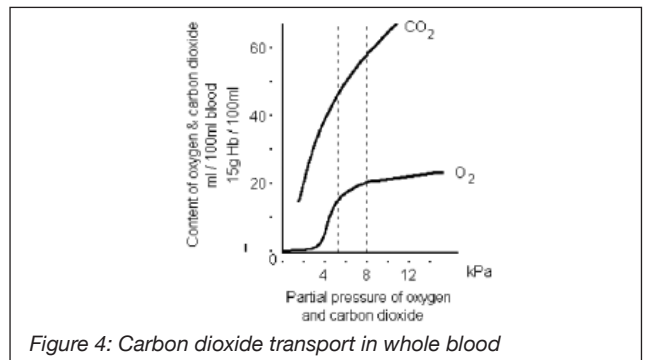


Figure 4: Carbon dioxide transport in whole blood

like a base (better proton acceptor). Therefore, haemoglobin increases the amount of carbon dioxide that is carried in venous blood (equation 4)



Each carbon dioxide molecule added to the red blood cell increases the intracellular osmotic pressure by an increase in either HCO_3^- or Cl^- ions. Therefore, the red blood cell increases in size and the haematocrit of venous blood is some 3% more than arterial blood. The plasma concentration of chloride ions is lower but bicarbonate ion concentration is greater.

pH of red blood cells

The total reduction of all haemoglobin would result in a rise in blood pH by 0.03. At 25% desaturation, the pH increases by 0.007 (at constant PCO_2). If the PCO_2 rises by 0.8kPa (6mmHg) i.e. the difference between mixed venous and arterial blood, the pH will reduce by 0.04. The net effect is a fall in pH of 0.033 from 7.4 to 7.36.

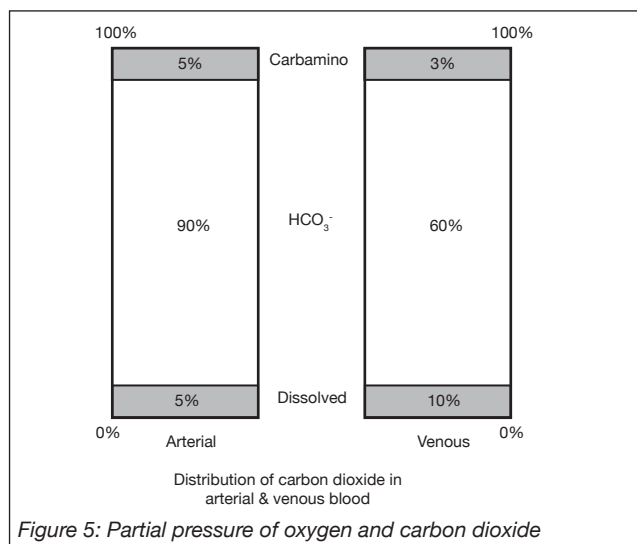


Figure 5: Partial pressure of oxygen and carbon dioxide

Changes in red blood cells during passage through the lungs

In pulmonary capillary blood, the red blood cell releases carbon dioxide and the haemoglobin affinity for oxygen is increased.

The oxygenated haemoglobin binds fewer hydrogen ions making it more acidic but the fall in PCO₂, and the shift in chloride and bicarbonate ions, makes the red blood cell less acidic. The outward shift of water gives a smaller MCV and reduced haematocrit. The oxygen dissociation curve will shift to the left (Bohr effect). The plasma concentration of chloride ion is higher in arterial compared with venous blood; bicarbonate concentration is lower.

The role of carbon dioxide in acid elimination

Every minute, 200ml of carbon dioxide is exhaled; this is the equivalent to 12–13mol of hydrogen ions in 24h.² Urine pH varies from 4.5 to 8.0. A pH of 4.0 represents 10⁻⁴mol/litre of hydrogen ions. Therefore, the passage of 3 litres of urine accounts for a relatively small amount of hydrogen ion elimination in 24h; however, this includes the phosphate and sulphate ions that cannot be converted to carbon dioxide.

Effect of apnoea

The total body content of carbon dioxide including bicarbonate ion is 120 litres or 100 times that of oxygen. If there is apnoea and all the carbon dioxide is retained in the body, PCO₂ will rise by 0.4 to 0.8kPa min⁻¹ (3–6mmHg). Alveolar gas will rapidly equate with venous blood, giving an alveolar PCO₂ rise from 5.3 to 6.1kPa and a PO₂ fall from 14 to 5.3kPa in 1min. Therefore, the patient becomes rapidly hypoxaemic. If the patient is pre-oxygenated with oxygen 100%, the arterial oxygen tension will remain above 13kPa and 100% saturation is maintained for several minutes as 250ml min⁻¹ of oxygen is used from a high partial pressure in the lung. However, PaCO₂ will steadily rise; after 5 min, it will be approaching 10kPa with an associated fall in pH.

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Table 1: Summary of normal values for pH and carbon dioxide carried in arterial and venous blood (1mmol = 22.32 ml)³

	Arterial blood		Mixed venous blood		Arterial/venous difference	
Whole blood						
pH	7.4		7.36		-0.033	
PCO ₂ kPa	5.3		6.1		+0.8	
mmHg	40		46		+6.0	
Total CO ₂ mmol/litre	21.5		23.3		+1.8	
ml/dl	48		52		+4.0	
Plasma	mmol/litre	ml/dl	mmol/litre	ml/dl	mmol/litre	ml/dl
Dissolved carbon dioxide	1.2	2.5	1.4	3.0	+0.2	+0.5
Carbonic acid	0.0017		0.002		+0.0003	
Bicarbonate ion	24.4		26.2		+1.8	
Carbamino carbon dioxide	negligible		negligible		negligible	
Total	25.6		27.6		+2.0	
Erythrocyte fraction						
Dissolved carbon dioxide	0.44	1.0	0.51	1.2	+0.07	
Bicarbonate ion	5.88	13.0	5.92	3.2	+0.04	
Carbamino carbon dioxide	1.10	2.5	1.70	3.8	+0.6	+1.3
Plasma fraction						
Dissolves carbon dioxide	0.66	1.5	0.76	1.8	0.1	+0.3
Bicarbonate ion	13.42	30.0	14.41	32.0	0.99	+2.0
Total carbon dioxide in 1 litre of blood (mmol litre ⁻¹)	21.5	48	23.30	52	+1.8	+4.0

PHARMACOLOGICAL MANAGEMENT OF ECLAMPSIA AND PRE-ECLAMPSIA

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MANAGEMENT OF PRE-ECLAMPSIA (PET)

Definition

Pre-eclampsia is a complex multi-system disorder that may sometimes precede eclampsia. There are several definitions of pre-eclampsia, which generally involve hypertension occurring after 20 weeks gestation (blood pressure above 140/90 or a rise of 30 systolic or 15 diastolic above baseline BP), with the involvement of at least one other organ system, for example headache or epigastric pain. The classical diagnostic triad for pre-eclampsia of hypertension, proteinuria and oedema is no longer considered useful.

Features of severe pre-eclampsia (in addition to hypertension and proteinuria) include:

- sustained severe hypertension ($\geq 160/110$)
- severe proteinuria, oliguria (urine output $< 500\text{ml}/24$ hours), raised creatinine
- neurological symptoms and signs including headache, visual disturbance, confusion, papilloedema and clonus
- platelet count falling to below $100 \times 10^9/\text{l}$
- epigastric pain and/or right upper quadrant (liver) tenderness
- abnormal liver enzymes (ALT or AST rising to above 70 IU/l)
- HELLP syndrome (haemolysis, elevated liver enzymes and low platelet count)

Goals of management

- Prevent convulsions (progression to eclampsia).
- Control blood pressure (BP). The goal is to stabilise the diastolic BP between 90 and 100mmHg.
- Anticipate and prevent complications.
- Prevent damage to the foetus.

Initial assessment and management

Use 'ABC'

A – Airway:

- Usually no problems.

B – Breathing:

- Increased respiratory rate can be an early sign of pulmonary oedema.
- Auscultate chest to exclude pulmonary oedema.

C – Circulation:

- Measure BP, pulse, oxygen saturation.
- Left lateral tilt.
- Insert IV cannula - at least 18G (green).
- Take blood for Hb, platelets, clotting, blood group.
- If platelets low ($< 100 \times 10^9/\text{l}$) check liver function tests.
- Insert urinary catheter, dip for protein, monitor urine output hourly.
- Record strict fluid balance and administer maintenance fluids (Hartmann's or 0.9% saline), initially at 1000ml per 12 hours. There is a delicate balance between two potential complications; renal failure exacerbated by hypovolaemia and fluid overload causing cerebral and/or pulmonary oedema. Awareness of this balance is crucial to successful treatment of patients with pre-eclampsia and eclampsia.
- If oliguric (urine output $< 30\text{ml}/\text{h}$ average over 4 hours) consider a modest fluid challenge (250ml 0.9% saline).
- Look for oedema.

D – Disability:

- ask specifically about headache, blurring of vision or fits
- assess reflexes, looking for clonus and perform fundoscopy

Record vital signs on a flow sheet or critical care chart.

Further management of pre-eclampsia

The main aims are:

1. To prevent convulsions:

- If severe PET (BP $\geq 160/110$) and/or symptoms of CNS irritability, suggesting risk of progression to eclampsia (headache, blurred vision), start magnesium sulphate (MgSO_4). Administer as described below.

2. To control BP

- Re-assess BP after loading dose of MgSO_4 as it will reduce BP.
- Institute further treatment if BP $\geq 160/110\text{mmHg}$.
- Aim to slowly reduce BP to 130-140/90-100mmHg.

Prevention of convulsions - administration of MgSO₄

The Magnesium Sulphate for Prevention of Eclampsia (MAGPIE) Trial found that women with pre-eclampsia taking magnesium sulphate had a 58% lower risk of eclampsia and a lower mortality rate compared to women in the placebo group. The magnesium sulphate group had a 27% lower relative risk of placental abruption. The trial did not detect a difference in neonatal mortality between the two groups.

Indications

Severe PET with signs of increased irritability of central nervous system:

- headache
- visual disturbances
- hyperreflexia

Administration

MgSO₄ can be diluted in 5% glucose or 0.9% saline.

Two regimens are described.

A. Combined intramuscular/intravenous administration of MgSO₄

Loading dose:

Add 8ml 50% MgSO₄ (**4g**) in 100ml 0.9% saline or 5% glucose: administer IV over 20 min.

(Alternatively, if you have a syringe-driver pump: add 8ml 50% MgSO₄ (**4g**) to 12ml 0.9% saline or 5% glucose and infuse over 20 min - 60ml/hour).

and

Give **2.5g** MgSO₄ IM into each buttock.
(Total initial dose 4g IV + 2x 2.5g IM = 9g).

If the convulsions do not stop:

Administer a further 2g MgSO₄: draw 4ml (2g) of 50% MgSO₄ into a 10ml syringe and add 6ml of 0.9% saline or 5% glucose; inject over 2 min (5ml/min).

Do not exceed 8g total IV dose of MgSO₄ during the first hour

If convulsions still continue consult medical staff and consider diazepam 5mg or 1mg lorazepam. Be aware of risk of respiratory depression.

Maintenance:

2.5g MgSO₄ IM 4 hourly using alternate buttocks if there are no signs of MgSO₄ overdose.

Check reflexes before giving MgSO₄.

Continue for 24 hours after the last convulsion or delivery.

B. Intravenous administration of MgSO₄

Loading dose:

Fill a paediatric infusion burette set with 22ml 5% glucose.

Add 8ml 50% MgSO₄ (4g).

Infuse at 60 drops/min (60 ml/hr); the total of 30ml will run over 30 min.

If the convulsions do not stop:

As above.

Maintenance:

Fill a paediatric infusion burette with 112ml 5% glucose.

Add 8ml 50% MgSO₄ (4g).

Infuse at 30 drops/min (30 ml/hr); the total of 120ml will run over 4 hours = 1g/hour.

Repeat the same management every 4 hours for at least 24 hours after the last convulsion or delivery.

For recurrent seizures:

Administer a second loading dose or increase the infusion to 1.5 or 2g/hour (45 or 60 drops per minute)

Adverse effects of MgSO₄

- hypotension, arrhythmias.
- respiratory depression.
- flushing, nausea/vomiting.
- drowsiness, slurred speech, double vision.

Monitoring

Measure hourly:

- Urine output: aim for urine output > 120ml over 4 hours (average 30ml/hour). If low, assess for symptoms or signs of MgSO₄ toxicity.
- Respiratory system: stop infusion if RR less than 10/min and/or general condition deteriorates (drowsiness, difficulty speaking).
- Check patellar reflex (knee-jerk) every 2-4 hours. If knee-jerk depressed, stop infusion.
- Blood pressure: if diastolic blood pressure (DBP) is more than 110mmHg start antihypertensive therapy (see below).
- Continuous CTG (cardiotocograph) monitoring of foetus if available.
- If available, monitor serum Mg²⁺ levels 4-6 hourly.
- After delivery: check uterus is contracted and whether there is any vaginal bleeding.

If any sign of overdose:

- Stop MgSO₄ infusion.
- Call for help.
- Assess and resuscitate guided by 'ABC'.
- Calcium gluconate should be available to treat

magnesium toxicity: administer 10ml 10% calcium gluconate (1g) IV over 2-3 minutes.

Duration of treatment

- If magnesium sulphate is given, it should be continued for 24 hours following delivery or 24 hours after the last seizure, whichever is the later, unless there is a clinical reason to continue longer.

Blood pressure control in pre-eclampsia

Indications

- Diastolic BP over 110mmHg or systolic BP over 160 mmHg. For women with other markers of potentially severe disease, treatment can be considered at lower degrees of hypertension.

When measuring the blood pressure, the woman should be rested and sitting at a 45-degree angle. The blood pressure cuff should be of the appropriate size and should be placed at the level of the heart. Multiple readings should be used to confirm the diagnosis. Korotkoff phase 5 (the last sound heard) is the appropriate measurement of diastolic blood pressure. The method used should be consistent and documented.

Automated methods need to be used with caution, as they may give inaccurate blood pressure readings.

Agents to consider are: nifedipine (oral or sublingual), labetalol (oral or IV), and IV hydralazine.

Atenolol, angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor-blocking drugs and diuretics should be avoided.

Nifedipine

Mode of action

- Peripherally acting calcium antagonist.

Administration

- Use orally or sublingually.
- Give 10mg nifedipine, repeating dose after 30 minutes if required.
- Maintenance dose is given 8 hourly, with a maximum dose of 20mg.

Adverse effects

- Sublingual use may cause a rapid profound BP drop and impair uteroplacental perfusion if other agents are also in use.
- Use cautiously with MgSO₄ (both antagonise calcium).

Labetalol

Mode of action

Combined α - and β -adrenergic blocker.

Administration

- Give 5-20mg boluses slowly IV at 10 minute intervals to a maximum of 50mg.
- Alternatively, start IV infusion at 20 mg/hour. Double infusion rate every 30 minutes as needed to a maximum of 160 mg/hour.
- May be given orally (dose: 100-200mg PO hourly, until BP controlled - maintenance dose is given 12 hourly). Absorption may be reduced in labour.

Contraindications

- Asthma and cardiac failure.

Intravenous hydralazine infusion

Mode of action

Direct acting arterial vasodilator.

Administration

- Never infuse hydralazine via the same cannula as magnesium sulphate – preferably avoid using the same arm.
- Dilute 80mg (4 vials) of hydralazine in 500ml of 0.9% saline or Hartmann's solution (not in 5% glucose).

Infuse hydralazine at 2mg/hour (= 12.5ml/hour). The correct number of drops per minute can be calculated from information on the packets of the IV giving set.

- If you have a syringe-driver pump, use 40mg hydralazine in 40ml and start at 2 ml/hour (= 2mg/hour)
- If diastolic blood pressure (DBP) is still over 100, increase rate by 1mg/hour and check BP in next 30 min (maximum of 5 mg/hour).
- If DBP is between 90-100 keep same rate and continue to monitor BP every 30 min.
- If DBP is less than 90, reduce hydralazine infusion by 1mg/hour.

Monitoring

- Record BP results and rate of infusion on a monitoring sheet.

Adverse effects

- Hypotension. If DBP decreases suddenly below 90mmHg stop the infusion and administer a 250ml fluid bolus over 1 hour.
- Maternal tachycardia is often a limiting side effect of hydralazine.

MANAGEMENT OF ECLAMPSIA

Definition

The occurrence of seizures in a parturient who may have no underlying pathology.

Goals of management

- Cessation of seizures.
- Stabilisation of airway, breathing and circulation.

- Prevention of further seizures.
- Prevention of damage to and safe delivery of the foetus.

Initial assessment and management

Use ABC as for any life threatening emergency.

A – Airway:

- Maintain the airway, using airway adjuncts (e.g. Guedel airway) as necessary, position patient on the left side, give oxygen via face mask (15 l/min).

B – Breathing:

- Ensure patient is breathing. Be aware of influence of administered drugs on respiration (e.g. diazepam).

C – Circulation:

- Insert 2 IV cannulas (18G at least), take blood investigations as for PET.
- Look for pulmonary oedema - a major cause of maternal mortality in eclampsia.
- Restrict fluids unless indicated by blood loss.

D – Disability:

- Assess consciousness level using Glasgow Coma Score chart.
- Protect from injuries (falling from bed).

Further management of eclampsia

The main aims are:

1. To terminate convulsions:

- Start magnesium sulphate (MgSO₄) (see above) and continue for 24 hours after delivery or last fit.

2. To control BP

- As described for PET, above.

3. To deliver the baby

- Start steroids if gestation <36 weeks.
- Plan delivery when patient is stable.
- Regional anaesthesia is preferred if coagulation and platelet count is adequate.
- Avoid ketamine and ergometrine.

Don't forget that:

- The ultimate treatment of pre-eclampsia or eclampsia is delivery of the baby.
- Eclampsia can happen 48 hours or longer after delivery.

Further reading

1. Guidelines of the Royal College of Obstetricians and Gynaecologists (UK), available at: www.rcog.org.uk/resources/Public/pdf/management_pre_eclampsia_mar06.pdf
2. The Magpie Trial Collaborative Group. Do women with preeclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomized, placebo-controlled trial. *Lancet* (2002); 359: 1877-90

Thanks to Dr Matt Rucklidge for helping edit this article.

BOOK REVIEW: THE YEAR IN ANAESTHESIA AND CRITICAL CARE

Hunter JM, Cook TM, Priebe H-J, Struys MMRF, Clinical Publishing, Oxford, UK, 2005. £60

This 430 page book is the first volume of a series providing up to date review articles covering a wide range of issues. The book's contents are arranged into four sections - Perioperative Care, Clinical Pharmacology, Monitoring and Equipment, and Critical Care.

The reviews are written by experts in their fields and provide an enjoyable read of an up to date account of a variety of issues. This is very practical for the busy clinician who would value a summary of the evidence about a particular topic without the need to review the literature personally.

The topics chosen for review are broad in nature ranging from Perioperative Fluid Therapy to New

Airway equipment. Most are clinically based and practically written.

The layout of each section looks at the latest major publications in each topic, describes the findings and then provides a critical analysis on what the publication adds to the knowledge of the topic. This is an engaging way of both learning about the subject itself, but I also found it instructive in learning how to interpret the literature in a meaningful way.

Altogether a good book for anyone wishing to know the latest literature on a particular area – check out the website for more details – highly recommended! www.clinicalpublishing.co.uk



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