UPDATE IN ANAESTHESIA

WFSA's

Update in Anaesthesia

Number 23, 2007

Editor: Bruce McCormick

ISSN 1353-4882

Editorial

Welcome to Update 23!

This edition of Update contains a number of articles relevant to Obstetric Anaesthesia in developing countries, an area of huge demand where maintenance of ongoing education and professional development is needed to continue improving obstetric morbidity and mortality. Thanks to Drs Matt Rucklidge and Emma Hartsilver for their help in editing the obstetric articles.

The majority of patients admitted to intensive care units in all countries of the world suffer an episode of sepsis at some point in their admission and the contribution of sepsis to ICU mortality, particularly in the developing world, is significant. The article on Management of sepsis aims to unravel the recent developments in this field and identify which therapies can be adapted or extrapolated for use in settings where limited resources cannot allow full-scale implementation of such extensive 'bundles' of treatments. Knowledge of this field is essential for all anaesthetists, as management of septic patients often begins as the surgical team ask for the patient to be anaesthetised for life-saving surgery.

I have re-introduced old favourites from Update, such as From the journals, where we have tried to select articles that may change an anaesthetist's practice, or describe simple, novel and practical solutions to common problems encountered in theatre or the ICU.

Please email me at Bruce.McCormick@rdeft.nhs.uk with requests for future articles or if you identify any past Update articles that you feel could be brought up to date. I shall attempt to commission writers for any appropriate topics that our readers request.

Update 23 should reach you with a tougher more durable cover, hopefully improving its longevity on your bookshelf. If you or any of your colleagues wish to subscribe to receive the printed version of future editions of Update please email Carol Wilson at worldanaesthesia@mac.com. If your postal address has changed, please let Carol know as soon as possible.

Thank you to Isabeau Walker for editing the articles on Anaesthesia for neurosurgery and Invasive blood pressure monitoring. Thank you, as always, to the World Federation of Societies of Anaesthesiologists for funding Update, to Angie Frost of Sumographics for type-setting the journal and to Priscilla Ang at COS in Singapore for organising the printing and distribution.

Bruce McCormick

Editor

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RECENT DEVELOPMENTS IN ANAESTHESIA FOR CAESAREAN SECTION

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Introduction
This article reviews current best practice for delivery of safe anaesthesia for obstetric services. Many of the recommendations are based on standards set within the UK, and the vast majority of these are relevant to practice in any country around the world. Resource limitations may make adherence to some suggested practices impossible, but these are included for educational value.

United Kingdom practice
Over the last ten years the rising caesarean section rate in the developed world has stimulated discussion of best anaesthetic and obstetric practice. Much of the impetus for improving obstetric care in the UK has been driven by the findings of the Confidential Enquiry into Maternal and Child Health (CEMACH),[1] formerly the Confidential Enquiry into Maternal Death (CEMD). Over a three year period, CEMACH reports the deaths of UK women while pregnant or within 42 days of the end of pregnancy. An extensive audit of the management of caesarean sections in the UK was reported in 2001.[2] These findings contributed to the development of guidelines by the National Institute for Health and Clinical Excellence (NICE), an independent agency set up by the Department of Health with the responsibility of advising on best clinical practice. NICE published guidance on caesarean section in 2004 and made recommendations that, for UK practice, form a standard of care on obstetric and anaesthetic aspects of management.[3]

Worldwide practice
The World Health Organisation (WHO) recommends an optimum caesarean section rate of 5-15% to ensure best outcome for mother and neonate.[4] Rates in Sub-Saharan Africa are a lot lower than this, possibly as low as 1%.[5] This is a reflection of availability of resources and distance from medical facilities and trained staff. This low rate contributes to a high maternal and neonatal morbidity and mortality. Maternal mortality has been estimated to be over 1% in West Africa and severe maternal morbidity as high as 9%.[6] These mortality and morbidity rates are over 30 times those of the developed world.

It has been suggested that, as a minimum standard, a health service should aim to provide caesarean section for all maternal indications, if not neonatal. The main maternal indications are obstructed labour, placental abruption, previous caesarean section, eclampsia, placenta praevia and malpresentation.[5] In areas where HIV is prevalent, caesarean section may increasingly be indicated to reduce risk of transmission from mother to child.[2]

The rate of caesarean section in developing countries is increasing. Where facilities exist this is performed under spinal anaesthesia.

Caesarean section itself is associated with a significant mortality and morbidity and improvements in surgical and anaesthetic management can reduce this. In a prospective study conducted in Latin America, which investigated more than 105,000 deliveries, mothers delivered by caesarean section were over two times more likely to suffer from severe maternal morbidity compared with vaginal delivery. Neonatal mortality was also increased by over 1.7 times. In breech presentation caesarean section was found to be protective.[7]

Important issues that are influencing current practice in obstetric anaesthesia for caesarean section in the UK are outlined below. Many of these are also relevant to practice around the world.

Categorisation of urgency of caesarean section
The traditional categorisation of elective and emergency caesarean section has limitations both for optimal communication in the clinical setting and for post-delivery audit. A four tier classification, shown in table 1, has been proposed and broadly accepted.[8]

The suggested standard for a category 1 caesarean section is delivery within 30 minutes of the time of decision. It is debatable whether there is evidence linking this time period with neonatal outcome[9] and

Table 1: Categorization of urgency of caesarean section

Grade	Definition
Category 1	Immediate threat to life of woman or fetus
Category 2	Maternal or fetal compromise, not immediately life threatening
Category 3	Needing early delivery but no maternal or fetal compromise
Category 4	At a time to suit the woman and maternity team

for some category 1 caesareans, delivery may need to be well within the 30 minute threshold.

General anaesthesia for caesarean section

As a result of the increased mortality and morbidity associated with general anaesthesia, 84% of caesarean sections in the UK are performed under neuraxial anaesthesia (i.e. spinal, epidural or combined spinal/epidural).[2] Of concern is the fact that CEMACH/CEMD has reported an increase in maternal deaths from general anaesthesia over the last three enquiries. General anaesthesia is now only indicated if the woman refuses a regional technique, if there is a specific medical condition which precludes neuraxial blockade (e.g. coagulopathy) or when it is felt there is not enough time available to provide a regional anaesthetic. In many poor resource settings availability of appropriate equipment, such as spinal needles, local anaesthetic and vasopressor drugs will strongly influence the proportion conducted under neuraxial blockade.

Rapid sequence induction

It is widely accepted that rapid sequence induction is required for general anaesthesia for caesarean section however there is debate as to the best choice of agents to allow effective and safe control of the airway. The traditional practice of cricoid pressure, thiopentone, suxamethonium and avoidance of opiates remains the most common approach by obstetric anaesthetists in the UK; however the emergence of new agents and techniques may challenge this accepted technique in the future.

Induction agent

There is vast experience of thiopentone in this setting and it is currently the induction agent of choice for caesarean section. A dose of 4mg/kg (up to 500mg) has been suggested to avoid awareness, minimize maternal hypertension and prevent delayed waking in the event of failed intubation. Propofol is an alternative agent for caesarean section however in one study it has been associated with more maternal hypotension, possibly increased risk of maternal awareness and worse Apgar scores in the neonate when compared with thiopentone.[10] Other studies however have shown no difference. No studies have shown superiority of propofol. Ketamine has a place in the management of the hypovolaemic obstetric patient requiring caesarean section and experience and confidence with this drug is likely to be far greater in many under-resourced areas than in the UK.

Muscle relaxant

Suxamethonium is currently the muscle relaxant of choice. It produces excellent intubating conditions quickly and reliably and in the event of a failed intubation there is rapid offset. Where available rocuronium (an aminosteroid) is becoming increasingly popular with obstetric anaesthetists in place of suxamethonium.[10] A disadvantage is the need for prolonged ventilation in the event of failed intubation; however rocuronium avoids many of the potential side effects and complications of suxamethonium and produces equivalent intubating conditions although the onset may be slower.

The imminent arrival on the market of a specific reversal agent for rocuronium (Sugammadex) will likely reduce the use of suxamethonium for caesarean section in more affluent health systems. Expense and availability may potentially be restrictive in the short term.

Depth of anaesthesia monitoring

General anaesthesia for obstetric patients is associated with a higher incidence of awareness compared with the general population and this has led to consideration of depth of anaesthesia monitoring for this patient group.[11] There are several commercially available devices, most based on technology that processes EEG (electroencephalogram) waves and presents them in a readily interpretable manner e.g. Bispectral Index (BIS) monitoring. Although depth of anaesthesia monitoring in caesarean section is not routinely practiced in the UK, its use may potentially increase in the future.

Regional anaesthesia for caesarean section

Management of hypotension

There has been a shift from the long held belief that vasoconstrictors should be avoided following subarachnoid block, because of a possible detrimental effect on uterine blood flow. Studies on sheep had previously shown this and as a result ephedrine was felt to be the vasopressor of choice. There is now a growing body of evidence that alpha-adrenergic agonists (e.g. phenylephrine and metaraminol) prevent spinal induced hypotension more effectively and result in improved umbilical artery pH.[12] Ephedrine appears to contribute to fetal acidosis by crossing the placenta and increasing fetal metabolic activity. The alpha-adrenergic agonists are now preferred, if available, and should be given pre-emptively and titrated to maintain maternal blood pressure near to baseline levels. Maternal bradycardia can be anticipated as a result of activation of the baroreceptor reflex.

Another technique that may reduce hypotension and vasopressor requirements following spinal anaesthesia is through combination of a reduced spinal dose of local anaesthetic with epidural volume extension (EVE), using a combined spinal epidural (CSE) technique.[13] A volume of either local anaesthetic or saline is instilled into the epidural space shortly after the spinal injection to manipulate the desired spread of intrathecal local anaesthetic. The epidural injection is believed to compress the spinal space resulting in a tailored increased spread. EVE may be beneficial for patients at risk of cardiovascular instability e.g. pre-eclampsia or maternal cardiac disease; however the technique may be associated with undesirable effects, including increased risk of intra-operative pain and reduced duration of action.

Testing of adequacy of block
(See also 'Assessment of spinal anaesthetic block' in Update 22).
Spread of subarachnoid and epidural local anaesthetic varies between patients and may be influenced by the volume of anaesthetic used, patient positioning and local anaesthetic baricity. It is essential to test the adequacy of sensory block prior to commencement of surgery to prevent pain during caesarean section.

Sensory modalities of light touch, temperature (cold) and pinprick are transmitted by different nerve fibres and are frequently found to be at inconsistent levels relative to each other following spinal local anaesthetic injection. Traditionally cold, as it is transmitted with pain in the spinothalamic tracts, has been used to document block adequacy, however there is evidence that the sensation of pain returns prior to a clinically detectable return of cold at any given level. Over the last decade light touch has been increasingly regarded as the modality that confers the best indication of pain free surgery with a block to T5 considered the acceptable target.[14] Both the most accurate method of assessing touch sensation and also the exact location of the T5 dermatome, remain unclear.[15]

General issues
Use of oxytocic drugs
Bolus administration of syntocinon (oxytocin) following caesarean delivery reduces the risk of post-partum haemorrhage (PPH). In addition, many obstetric units now routinely give an infusion in the immediate postoperative period (e.g. 10 IU syntocinon/hour for 4 hours). Syntocinon causes vasodilation and tachycardia and bolus injection has been associated with catastrophic collapse in vulnerable parturients. In light of these cases a reduction in dose from 10 IU to 5 IU, given slowly following caesarean delivery, has been recommended.[1] In women at very high risk, for example women with significant cardiac disease, syntocinon should be avoided, or, if clearly indicated, given in a dilute infusion over 10 to 15 minutes.

Major obstetric haemorrhage
(See also 'Obstetric haemorrhage' in Update 21).
This was highlighted by CEMACH as a significant cause of maternal mortality, especially given the rising caesarean section rate. Previous caesarean section increases the incidence of low lying placenta and the chance of placenta accreta.

There have been several advances in management of major obstetric haemorrhage:

Drugs to improve uterine tone

- Further syntocinon (oxytocin) - given slowly IV.
- Ergometrine (IM) - acts on smooth muscle (causes vasoconstriction / hypertension).
- Carboprost (e.g. hemabate) IM or directly into myometrium – a prostaglandin (avoid in asthmatics, risk of bronchospasm / hypertension) .

Interventional radiology

- Use of arterial balloons or embolisation to prevent or control PPH.
- Balloons can be placed electively prior to high risk cases (e.g. suspected placenta accreta) or used in an emergency to reduce the need for hysterectomy, requirement for blood products and ICU admission.[16]

Intraoperative cell salvage

- This is a technique that collects and washes the patient's own red blood cells. The cells are then processed in a suspension, filtered and returned to the patient. This reduces the requirement for transfused blood.
- Concerns over amniotic fluid embolus appear unproven.

Use of recombinant activated Factor VIIa (rFVIIa / Novoseven ®)

- There is a growing number of reports of rFVIIa being successfully used to treat coagulopathy associated with massive obstetric haemorrhage, but to date there are no randomised controlled trials.
- rFVIIa binds to tissue factor at the site of endothelial damage initiating localised haemostasis.[17]
- There is an unsubstantiated concern that it may lead to an increased incidence of systemic thrombotic events.
- The cost of a standard single 90mcg/kg dose in the UK is about £4000.

Thromboelastography (TEG)

- Many patients with obstetric haemorrhage develop an associated coagulopathy. TEG is a near-patient testing device that provides dynamic information on all aspects of coagulation and can help guide appropriate replacement of blood products.

Blood transfusion

- In the obstetric setting there is a decreasing trend in use of blood transfusion outside the setting of major haemorrhage.
- This follows the TRICC study, a large trial in critically ill (non-obstetric) patients, proving the outcome of patients treated with a restrictive transfusion strategy (only transfusing at a haemoglobin level of less that 7g/dl) was at least as good as those treated with a liberal strategy.[18] This reduces exposure to the risk of transfusion in otherwise healthy individuals.

Fetal monitoring

Cardiotocography (CTG) consists of an external transducer that continuously records fetal heart rate and uterine contractions. It is commonly used in higher risk labours although it has a relatively low specificity and sensitivity for identifying fetal distress. The diagnosis of fetal compromise from CTG is one factor felt to contribute to the increased rate of emergency caesarean sections. Methods of improving sensitivity, such as combining CTG with fetal electrocardiography (fetal ST segment analysis, STAN®) or increased use of fetal blood sampling to detect fetal acidosis (pH<7.2) as supporting evidence for diagnosis of fetal distress, have been suggested.

Postoperative analgesia

Single shot spinals are the most frequently used technique for both elective and emergency caesarean sections in the UK.[19] The practice of adding preservative free opiates (e.g. morphine, diamorphine) extends postoperative analgesia and is now common practice in the UK. Maternal side effects include pruritus, sedation and delayed respiratory depression, particularly if other opiates are co-administered.

Following general anaesthesia for caesarean section, regional techniques such as bilateral ilioinguinal, rectus sheath blocks or transversus abdominus plane (TAP) blocks may be useful to improve postoperative analgesia.[20]

Post-caesarean pain relief should be multimodal using simple analgesics including regular paracetamol and non-steroidal anti-inflammatory drugs to help reduce opiate requirements. Effective analgesia is important for early mobilisation and prevention of thromboembolic events.

Thromboprophylaxis

Thromboembolic disease (TED) consistently represents the leading cause of direct maternal death in the UK. Its prevention and a low threshold for investigation and treatment of suspected cases are essential. The Royal College of Obstetricians has recommended thromboprophylaxis guidelines based on risk stratification of obstetric patients.[2] Rising rates of obesity in the UK are contributing to the increasing obstetric risk of TED. Caesarean section is an independent risk factor for TED with a relative risk of 3.8.[2] Simple measures such as graduated thromboelastic stockings, adequate hydration and early mobilisation should be considered for all patients. Prophylactic, once-daily low molecular weight heparin is routinely given in the UK. Timing of this relative to neuraxial anaesthesia and removal of epidural catheters must be considered.

Issues in training

With the reduced number of caesarean sections performed under general anaesthesia and the increased rate of failed intubation in this population, it is essential that failed intubation drills are regularly practiced and there is immediate availability and familiarity with alternative emergency airway equipment.

The experience of the aviation industry in using high-fidelity simulation to train and demonstrate competency is increasingly used in anaesthesia training in the UK.[22] This may have a role in practising anaesthetic management of uncommon events including failed obstetric intubation and obstetric collapse.

Conclusion

With the rate of caesarean section increasing in the developed world it is likely that the absolute number of complications from obstetric surgery and anaesthesia will increase. Best practice must be constantly debated, adopted and audited to reduce morbidity and mortality.

The issues and advances above are relevant to obstetric anaesthesia throughout the world though, for now, limitations in availability of equipment and resources may preclude their full implementation. Africa accounts for 47% of global maternal mortality;[23] this can be reduced with systematic improvement in education, training, funding and resources.

Recommended Reading

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FROM THE JOURNALS

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A factorial trial of six interventions for the prevention of post operative nausea and vomiting

Apfel CC, Korttila K, Abdalla M et al (IMPACT investigators). *New England Journal of Medicine* 2004; 350; 2441-51

Patients often rate postoperative nausea and vomiting (PONV) as worse than postoperative pain. Untreated, about one third of patients will suffer postoperative nausea, vomiting or both. PONV often delays discharge from post anaesthesia care units and it is the leading cause of unexpected hospital admission after planned day case surgery.

High (at least 40%) risk of PONV is predicted by presence of 2 of the following risk factors:

- Female sex
- Non-smoker
- Previous PONV
- Previous motion sickness
- Anticipated requirement for postoperative opioid analgesic

In this trial 5199 patients who were at high risk of PONV were enrolled and randomised to receive 1 of 64 possible combinations of six prophylactive interventions. These interventions included ondansteron, dexamethasone, droperidol, propofol or a volatile anaesthetic, nitrogen or nitrous oxide and remifentanil or fentanyl. The primary outcome was nausea and vomiting within 24hrs of surgery, which was evaluated blindly.

Prophylaxis with each of ondansetron, dexamethasone or droperidol alone gave a relative risk reduction for PONV of 26 percent. Propofol reduced the risk (again relative risk reduction) by 19% and nitrogen (i.e. avoiding nitrous oxide) by 12%, thus the risk reduction achieved using total intravenous anaesthesia with propofol was similar to that seen for each of the antiemetics used alone.

In this study the antiemetic interventions employed were all similarly effective, so in a limited resource environment the least expensive should be used first.

- Prophylaxis is rarely warranted in low risk patients.
- Moderate risk patients may benefit from a single intervention.
- Multiple interventions should be reserved for high risk patients.

Manual displacement of the uterus during caesarean section
Kundra P, Khanna S, Habeebullah S and Ravishankar M. *Anaesthesia* 2007; 62: 460-65

Ninety ASA 1 and 2 women with term singleton pregnancies, scheduled for elective or emergency caesarean section under spinal anesthesia, were allocated to receive either manual displacement of the uterus or 15° left lateral tilt. Manual displacement was achieved by maximal leftward push applied by the right hand to the right upper border of the uterus to achieve a displacement of about 1.5 inches from the midline. Following subarachnoid block a median sensory level of T6 was observed in both groups.

The incidence of hypotension was significantly lower in the manual displacement group compared with the lateral tilt group (4.4% vs. 40%). The mean fall in systolic blood pressure was 29mmHg in the lateral tilt group compared with 20mmHg in the MD group.

The authors concluded that manual displacement effectively reduces the incidence of hypotension and ephedrine requirements when compared with left lateral tilt. This is an important finding for settings where access to vasopressor agents or intravenous fluids is unreliable.

Intra-abdominal pressure measurement: validation of intragastric pressure as a measure of intra-abdominal pressure
Turnbull D, Webber S, Hamnegard CH and Mills GH. *British Journal of Anaesthesia* 2007; 98: 628-34

Elevated intra-abdominal pressure and the adverse physiological effects that follow is termed abdominal compartment syndrome. This condition may present in critically ill patients following a variety of insults including sepsis, pancreatitis, retroperitoneal haemorrhage, bowel obstruction and trauma. Intra-abdominal pressures above 30mmHg may result in impaired organ perfusion. Persistent elevation causes bacterial translocation with subsequent multi-organ failure and death. Intravesical pressure measurement (measured via a catheter in the bladder) has been validated and remains the accepted estimate of intra-abdominal pressure for clinical use. Continuous pressure measurement kits are commercially available, however these are unlikely to be available in an environment with poor resources.

In this study 29 female subjects, scheduled for elective gynaecological laparoscopic surgery were recruited. Intra-abdominal pressure was measured via a 13mm laparoscopic trochar. Intra-gastric pressure was measured via an 80cm polyvinyl chloride balloon catheter inserted to a length of 60-70cm.

Measured intra-gastric pressure was always more positive than intra-abdominal pressure. Both showed linear correlation, with an estimated pressure difference between intra-gastric and intra-abdominal of ± 2.5mmHg.

The authors concluded that intra-gastric pressure, measured in this fashion, could be used for continuous intra-abdominal pressure measurement in normal individuals. Follow up studies in critical care patients are necessary to validate the accuracy of intra-gastric pressure measurement.

Which port in a storm? Use of suxamethonium without intravenous access for severe laryngospasm (editorial).
Walker RWM and Sutton RS. *Anaesthesia* 2007; 62: 757-59

This interesting editorial reviews past and present literature regarding the administration of suxamethonium via a route other than intravenous for the treatment of severe laryngospasm. The authors compare and contrast the efficacy of the intramuscular, intralingual and intraosseous routes.

In a previous editorial in 2001 it was suggested that there was no substitute for the intravenous route. This does not, however, offer a solution if intravenous access should fail in an emergency situation.

Intramuscular (IM) suxamethonium was first evaluated in the 1950's, when onset time was found to be predictable but consistently slower than the intravenous route. An IM dose of 3-4mg/kg slightly reduces onset time. Side effects related to intramuscular administration are rare and the authors

suggest that, where IV access is not available, the intramuscular route is the most favourable. It can be employed without leaving the airway, however one must have sufficient drug prepared beforehand to give the recommended dose of 4mg/kg.

The intralingual or submental route provides access to an extremely vascular muscle that retains blood flow to a greater extent when compared to skeletal muscle during times of reduced perfusion. A sublingual dose of 1.1mg/kg, gives an onset time of 75s (compared with 35s for intravenous and 210s for intramuscular), however there is a higher incidence of cardiac side effects. The submental route offers an alternative to this and enables the mask seal to be maintained. The benefits of the submental approach are marginal when compared to the intramuscular.

Despite the intraosseous route being widely accepted as a means of emergency circulatory access, administration of suxamethonium via this route is rarely reported. Two cases of rapid sequence induction in children in whom intraosseous access was established have been reported, with relaxation occurring 30-45s later, but to date there are no reports of its use in severe laryngospasm. Intraosseous access should be attainable within 60 seconds.

The authors conclude that in the absence of intravenous access any of the above routes may be considered as alternative means of suxamethonium administration. Choice of route may be dictated by personal experience and preference.

Successful use of pharyngeal pulse oximetry with the oropharyngeal airway in severely shocked patients
Yu H and Liu B. *Anaesthesia* 2007; 62: 734-6

One of the major drawbacks to standard oximeters is inaccuracy or inadequate signal and/or slow response from peripheral sites due to poor perfusion. The pharynx is highly perfused and lies in close proximity to the carotid artery, with relative preservation of blood flow in hypoperfusion states. Pharyngeal oximetry using the LMA and cuffed oropharyngeal airway (COPA), is possible with a side by side alignment of light emittor and sensor, rather than the opposing arrangement traditionally utilised in finger probes. This has previously been shown to be feasible and accurate in well-oxygenated anaesthetised patients.

The authors present two case reports, one patient with septic shock and one with haemorrhagic shock, where they used pharyngeal oximetry with the oropharyngeal airway (OPA) when conventional finger pulse oximetry had failed. In both cases a paediatric oximeter probe was attached to the superior surface of the OPA using adhesive tape, with care not to obstruct the optical components (see figure 1). Finger oximetry, pharyngeal oximetry and arterial blood gas analysis were compared at 30 minute intervals in both cases.

Pharyngeal oximetry gave a good waveform and oxygen saturation was 0-2% lower than the arterial samples, whereas the finger pulse oximetry was much lower or unobtainable.

The authors conclude that pharyngeal oximetry with an OPA is a simple, feasible and accurate method of assessing oxygen saturation in low perfusion states when finger/ear oximetry becomes unreliable or fails.

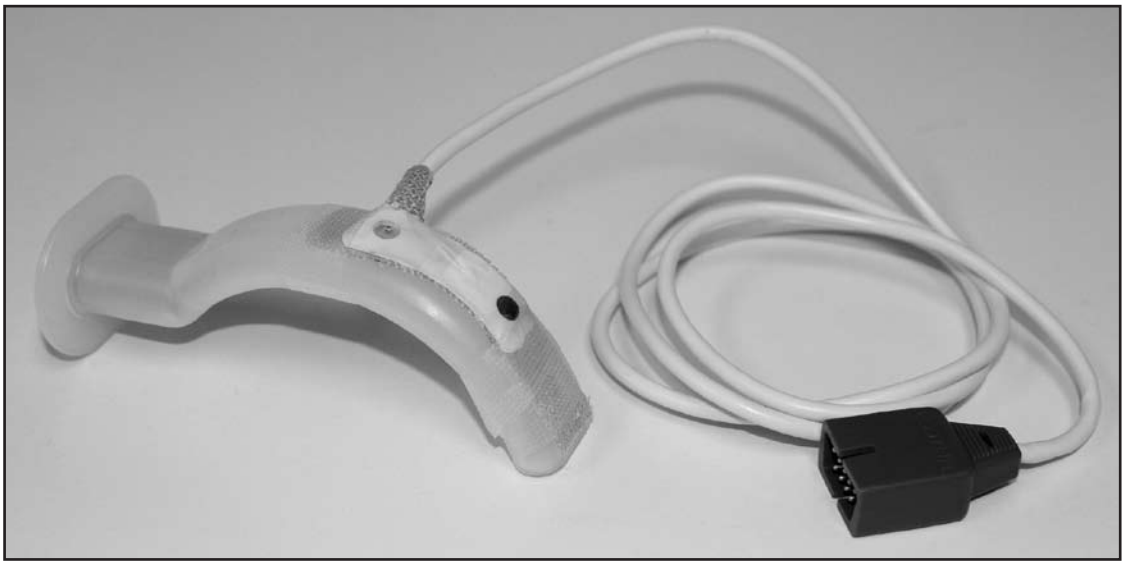

Figure 1: Pharyngeal pulse oximetry in shocked patients, using a paediatric pulse oximetry probe taped to an oropharyngeal (Guidel) airway.

Inflation with air via a facepiece for facilitating insertion of a nasogastric tube: a prospective, randomised, double-blind study
Gupta D, Agarwal A et al. *Anaesthesia* 2007; 62: 127-30

Nasogastric tube insertion in an anaesthetised patient is often straightforward, but at times can be time-consuming, frustrating and difficult. Many techniques to improve the reported success rate (66-68% on first attempt) have been described, and to date neck flexion would appear to be the most successful intervention. However, no technique is universally accepted. Techniques involving lateral and forward flexion of the head and neck may be unsafe in some circumstances. Interventions involving bougies or introducers may cause soft tissue trauma. Endoscopic techniques require expertise and expensive equipment that may not be available.

This paper describes a prospective, randomised study exploring the hypothesis that creation of positive pressure in the oropharynx, (by means of a facemask attached to a self inflating bag) facilitates insertion of a nasogastric tube.

160 consecutive adult patients were recruited and randomised into two groups. All were ASA status 1-2 and scheduled for elective surgery where nasogastric intubation would be required. Patients with anticipated difficult airways, morbid obesity, full stomach, nasal deformity, thyroid disease or history of abnormal bleeding were excluded. Anaesthesia was standardised, and all patients were paralysed and intubated with a tracheal tube.

In the study group, two positive pressure breaths (500-600ml) were delivered over 1-2s each, by means of a facemask attached to a self-inflating bag. This immediately preceded attempted passage of a nasogastric tube, previously placed as far as the oropharynx. In the control group, placement of the tube was attempted with the head in neutral position without inflation. A successful attempt was defined as smooth insertion of the tube without the need to pull it back. A blinded observer confirmed correct placement of the tube.

A success rate of 96% (75/78) was observed in the inflation group compared to 68% (54/80) in the non-inflation group ($p<0.001$).

Fibreoptic endoscopy in a selection of patients confirmed that generation of positive pressure (approx 25mmHg from the self inflating bag) was sufficient to cause opening of the upper oesophageal sphincter.

The authors conclude that facemask inflation is a successful intervention to facilitate insertion of a nasogastric tube, when performed immediately preceding an attempt. No particular expertise or expense is involved, the technique is simple and non-traumatic, and may be suitable to use in cervical trauma.

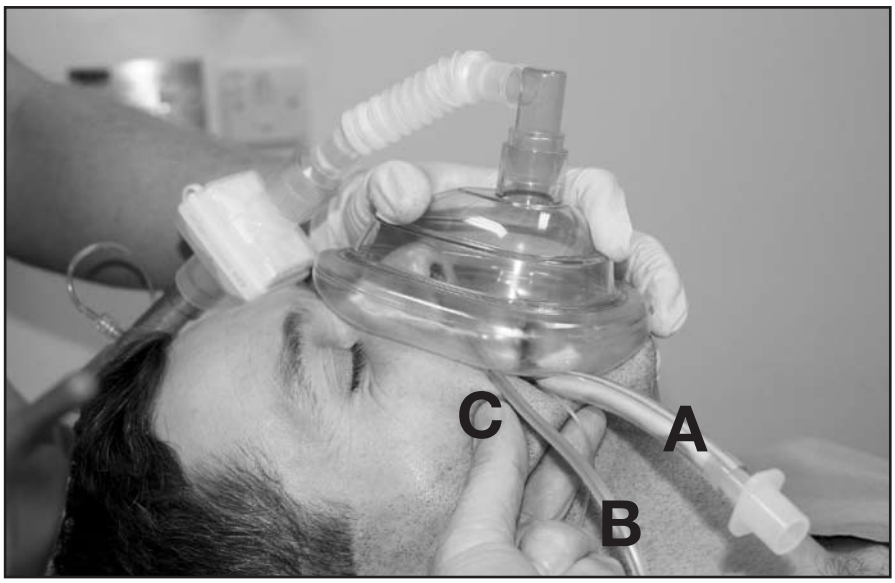

Figure 2: Air inflation via a facemask to facilitate nasogastric tube insertion.

*(**Editor's note:** I have tried this twice and it has been successful on both occasions. Note that patients should be anaesthetised and intubated (reducing the risk that any soiling of the airway will lead to aspiration into the lungs). It can be a technical challenge to obtain a seal with the facemask around the endotracheal (A) and nasogastric (B) tubes. This was more effective using an assistant to manipulate the patient's facial tissues to minimise the leak (C).*

Guidelines for the Management of Severe Local Anaesthetic Toxicity
The Association of Anaesthetists of Great Britain & Ireland 2007

The AAGBI has recently published guidelines for the management of local anaesthetic toxicity, incorporating the use of lipid emulsion ('Intralipid') as an infusion. These are available as a PDF file that can be accessed by the link: http://www.aagbi.org/publications/guidelines/docs/latoxicity07.pdf

MATERNAL COLLAPSE AND PERIMORTEM CAESAREAN SECTION

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Introduction
Maternal collapse is a non-specific description that can be applied to a variety of medical conditions, ranging from a simple faint through to cardiac arrest. The clinical outcome is largely determined by the promptness of management of the collapse. The fetal outcome is directly related to the wellbeing of the mother.

Maternal collapse can occur from direct obstetric complications, indirectly from pre-existing medical conditions exaggerated by the pregnancy, or from conditions unrelated to the pregnancy.

Maternal mortality
The most recent estimate of the overall world maternal mortality ratio (MMR) is 400 per 100,000 live births.[1] This figure is an estimate since accurate data is reliant on reporting of all maternal deaths; this tends to be more accurate in developed than developing countries. The MMR is calculated as the number of direct and indirect maternal deaths per 100,000 live births.

Direct deaths are defined as deaths resulting from obstetric complications of the pregnant state, from interventions, omissions, incorrect treatment or from a chain of events resulting from the above.'[1]

Indirect deaths are defined as 'deaths resulting from previously existing disease, or disease that developed during pregnancy and which was not due to direct obstetric causes, but which was exaggerated by the physiological effects of pregnancy.'[1]

The risk and causes of death occurring during pregnancy, childbirth or unsafe abortion is determined geographically. The average MMR in developing countries is 1 in 65, compared to 1 in 9,000 in the United Kingdom. More than 99% of all maternal deaths occur in developing countries.

Causes of maternal mortality
Beyond the numbers, published by the World Health Organisation in 2004, looked not only at the number of maternal deaths, but at the principle causes.[3] The key message was that preventing many maternal deaths is possible, even where resources are scarce, as long as appropriate programmes are in place. More than 80% of deaths are estimated to be avoidable through affordable and effective actions, possible in even the poorest countries. The WHO is working towards the United Nations Millennium Development Goal to reduce maternal deaths by 75% by 2015.

Globally, 80% of maternal deaths are due to direct obstetric causes and 20% due to indirect causes. The five leading direct causes account for 80% of the direct deaths and are shown in table 2.

Indirect deaths account for 20% of worldwide maternal deaths. In developing countries infections are the commonest cause of indirect deaths with HIV/AIDS the leading cause in most African countries. In areas with endemic malaria, women are at risk from malaria itself and also from malaria related anaemia which contributes to death from haemorrhage.

In contrast, in the UK, the latest Confidential Enquiry into Child and Maternal Health (CEMACH) showed that there are more indirect deaths (55%) than direct deaths (44%) and that the commonest cause of death overall was due to psychiatric disease.[4] The commonest cause of direct death in the UK is thromboembolic disaese.

Management of maternal collapse
The UK Resuscitation Council published guidelines for the management of maternal cardiac arrest in 'Standards for Clinical Practice' in 2004.[5]

Specific management of a collapsed pregnant woman is dependant on the number of weeks of gestation.

Table 1: Maternal mortality estimates by the World Health Organisation and United Nations, 2000.[2]

Region	Number of maternal deaths	Maternal mortality ratio
World total	529,000	400
Developed regions	2,500	20
Developing regions	527,000	440
Africa	251,000	830
Asia	253,000	330
Latin America/Caribbean	22,000	190
Oceania	530	240

Table 2: Estimated incidence of major global causes of direct maternal deaths 2000.[2]

Cause	Number of maternal deaths	% of all direct deaths
Haemorrhage	132,000	28
Sepsis	79,000	16
Preeclampsia/eclampsia	63,000	13
Obstructed labour	42,000	9
Abortion	69,000	15

After 22-24 weeks the physiological and anatomical changes seen in pregnancy become significant and may hinder effective resuscitation.

The most significant effect is aortocaval compression in the supine position, which can reduce maternal cardiac output by up to 25%. For this reason any woman of more than 22 weeks gestation should be managed with a lateral tilt or with a wedge. Even if there is no sign of hypotension in the supine position there may still be some compromise of venous return and cardiac output.

As with any acute medical condition requiring resuscitation, the initial management is that described by the European Resuscitation Council (*see Update 22, 2007*): assess and manage the airway (and apply lateral tilt), breathing, circulation whilst treating the underlying cause. As well as calling for the resuscitation team, the delivery suite must also be informed so that obstetricians and paediatricians can become involved.

Factors affecting resuscitation

A – Airway

- Increased incidence of difficult intubation, with a failed intubation rate of about 1 in 250.[6,7] Can't intubate, can't ventilate occurs in about 1 in 500.
- Anatomically made difficult by oedema or obesity of the neck, large breasts and/or supraglottic oedema.
- Difficult airway equipment should be available.
- Increased risk of aspiration.
  - Increased intragastric pressure from 8 to 16cmH_2O.
  - Reduced oesophageal tone.

B – Breathing

- Less effective pre-oxygenation:
  - 20-30% increased oxygen requirements.
  - 10-15% decreased functional reserve capacity (raised diaphragm).
- Reduced thoracic compliance.

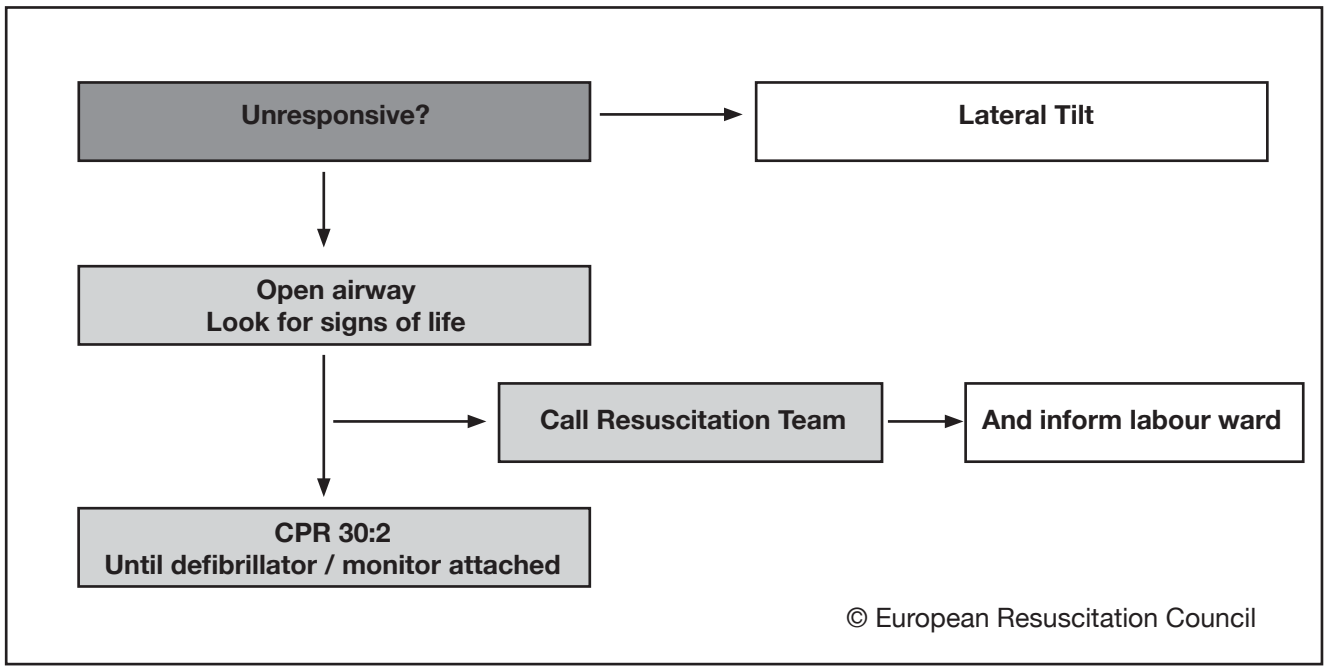

Figure 1: Adult basic life support 2005 with additional considerations (white boxes) for pregnant patients.

C – Circulation

- Lateral tilt to minimise aortocaval compression.
- Chest compression is physically more difficult in the lateral tilt position.
- 2 large bore cannulae.
- Epinephrine should be used despite its effect on fetal circulation.
- Consider **perimortem caesarean section.**

Perimortem caesarian section

The concept was first introduced in 1986 and adopted by the American Heart Association.[8] The recommendation is to perform a caesarean section within four minutes of maternal arrest, when cardiopulmonary resuscitation (CPR) has been unsuccessful. The rationale is that delivery of the fetus makes CPR more effective, aortocaval compression ceases to be a factor and cardiac output increases by as much as 20%. The patient can then be managed in a supine position making resuscitation easier.

Indications for perimortem caesarean section

- Pregnancy more than 22 weeks gestation.
- Personnel with appropriate skills available.
- The mother fails to respond to CPR with return of spontaneous circulation after 4 minutes.
- Appropriate facilities to care for the mother and (ideally) the baby afterwards.

A perimortem caesarean section is potentially a life-saving procedure for both mother and baby, and should be performed even if there is no fetal heart beat and no time should be wasted in assessing the fetus before undertaking the procedure.

The best survival rates are reported when the caesarian section is performed in under 5 minutes, although there are reports of infants surviving after up to 20 minutes of cardiac arrest time. It is clear that the caesarian section greatly improves the chances of survival for the mother.

The practice of perimortem caesarean section was reviewed in 2006, covering the period from 1985 to 2004.[9] This showed that of 38 perimortem caesarian sections, 34 infants survived and 4 survived initially but died several days later. Of the 20 caesarian sections performed on women with potentially reversible causes of cardiac arrest, 13 were discharged from hospital in good condition. In 12 of 18 cases that documented haemodynamic status, delivery brought a return of maternal pulse, and it was also noted that in the other cases the caesarian section did not cause deterioration in maternal condition.

For those women who survive appropriate post-operative care is essential. The long-held belief that pregnant women can endure great haemodynamic fluctuations without longstanding morbidity because of their young age has recently been challenged. New evidence is emerging that a proportion of pregnant patients, suffering collapses and significant haemorrhages, do suffer myocardial damage and, where facilities exist, monitoring of myocardial damage with troponin levels is performed.[10]

Conclusion

Some 80% of all maternal collapses are from a potentially treatable cause. For the outcome to be favourable regular updates and training in resuscitation must be provided for all staff on delivery units. There must be clear protocols for the management of all obstetric emergencies in an effort to prevent collapse, but, in the event of maternal cardiac arrest, perimortem caesarean section must be considered at an early stage.

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PARACETAMOL - A REVIEW OF THREE ROUTES OF ADMINISTRATION

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Paracetamol is used extensively in the treatment of both acute and chronic pain. Previously only manufactured for oral and rectal use, an IV formulation is now available. This article provides a short review of paracetamol as an analgesic and discusses the benefits of each route in the perioperative period.

Mechanism of Action

Although paracetamol was found to be an effective analgesic more than a century ago, its mechanism of action remains unclear and is the subject of continuing research. Unlike non-steroidal anti-inflammatory drugs (NSAIDs), whose analgesic and anti-inflammatory effects are thought to relate to their inhibition of the cyclooxygenase enzymes (COX-1 and COX-2), paracetamol is a weak anti-inflammatory agent with an abscence of COX-related adverse effects. Experimental studies show that paracetamol can inhibit both COX-1 and COX-2 in an environment where the ambient concentrations of arachidonic acid and peroxides are kept low. However, where extracellular concentrations of these two chemicals are high, in inflammatory conditions such as rheumatoid arthritis, paracetamol shows limited in vivo suppression of inflammation and platelet activity.[1]

It has been demonstrated that paracetamol may exert its analgesic effect via molecular targets distinct from COX. In the brain and spinal cord paracetamol is conjugated with arachidonic acid to form N-arachidonoylphenolamine (AM404).[2] AM404 is a known activator of the capsaicin receptor (TRPV1) and the cannabinoid CB1 receptor system both of which confer analgesia in the central nervous system. This pathway may also account for the antipyretic effect of paracetamol, known to be related to inhibition of prostaglandin production in the brain.[3] Cerebrospinal fluid levels of prostaglandin are shown to be high in rats during pyrogen induced fever, and these levels are reduced, along with the fever after paracetamol administration.[4] At this time, however, such a link remains speculative.

Analgesic Efficacy

There is good evidence to show paracetamol as an analgesic is effective and safe. A Cochrane systematic review of oral paracetamol use in acute postoperative pain analysing 47 studies, including 4186 patients, found the *number-needed-to-treat* (NNT) - see box - for at least 50% pain relief, over 4-6 hours was 3.8 (*95% confidence intervals:* 3.4-4.4).[5] There was no significant difference in the frequency of reported adverse effects between paracetamol and *placebo*. Side-effects after paracetamol use are rare, and usually mild and transient. At therapeutic doses paracetamol use is associated with an extremely low rate of liver dysfunction (less than 1 in 500000)[6] and there are only two contra-indications; paracetamol hypersensitivity and severe hepatocellular insufficiency. There are few known drug interactions and breast-feeding women may use paracetamol. Paracetamol has been shown to have a comparable benefit to ibuprofen and diclofenac in general and orthopaedic surgery[7] and can significantly reduce the opiate requirement postoperatively – it has an **opioid-sparing effect**.[8]

Number-needed-to-treat (NNT) – This gives the clinician an indication of the size of the treatment effect described by a clinical trial of a treatment. It tells the reader the number of patients that they would need to treat in order to see an effect in one patient.

95% confidence intervals – These give the reader of a study an indication of the reliability of the result of the study. If you repeated the study 100 times, 95 of the studies would give a result within these two confidence intervals. Larger studies tend to give narrower confidence intervals (i.e. results that more accurately represent reality). 95% (rather than a higher or lower figure) is a generally agreed acceptable level of certainty that a study result reflects a true treatment effect.

A **placebo** is a pharmacologically inert substance that may have a medical effect based solely on the power of suggestion. This is known as the placebo effect. By comparing drugs to a placebo, the pharmacological effects of the study drug are identified.

Route of Administration

Plasma concentrations of paracetamol between 10-20 mcg/ml are known to produce an antipyretic effect, but the concentrations required to provide analgesia are not well defined.[9] One study, in which 120 children were given oral or rectal paracetamol post tonsillectomy, concluded an effect site concentration of 10mcg/ml was needed to achieve pain scores of less than 4/10.[10] However, both higher and lower values than this have been suggested.[11,12] There are significant differences in the absorption of paracetamol, and therefore in the time to reach peak plasma levels, when it is given orally, rectally or intravenously. All three routes are able to achieve adequate plasma concentrations, but intravenous (IV) administration can achieve these levels in a shorter time.

Oral administration
Paracetamol is well absorbed from the gastrointestinal tract with low *first pass metabolism (see box)* in the liver, and *oral bioavailability* is estimated at 63-89%. Two recent trials have compared the administration of oral and intravenous paracetamol. In a study of 35 patients undergoing day-surgery, intravenous propacetamol (the IV *prodrug* of paracetamol) reached therapeutic plasma concentrations more quickly and predictably than oral paracetamol.[11]

Paracetamol plasma concentrations were observed for the first 80 minutes after administration of either 1g or 2g oral paracetamol or 2g intravenous propacetamol. Intravenous paracetamol provided an average concentration within the therapeutic range after 20 minutes. There was a large and unpredictable variability with oral administration; some patients who received 1g orally did not achieve detectable plasma levels within the 80 minute study period, and the average plasma concentration after receiving this dose was subtherapeutic throughout. 2g oral paracetamol achieved a median plasma concentration within the therapeutic range after 40 minutes, suggesting that when paracetamol is given orally, a loading dose can reduce the time needed to achieve therapeutic levels.

Clinically, this difference has been shown to lead to a faster onset of analgesia when paracetamol is given intravenously. Propacetamol infusion provided a significantly faster onset of analgesia than oral paracetomol, after 3rd molar surgery.[13] Intravenous propacetamol had a greatly reduced time until meaningful pain relief (8 minutes for propacetamol compared to 37 minutes for oral paracetamol) and maximal pain relief (15 minutes for propacetamol compared to 1 hour for oral paracetamol).

Rectal administration
Rectal absorption of paracetamol is more unpredictable, with a bioavailability between 24-98%. The variability in the rate and extent of absorption of suppositories is thought to be due to several factors. Regarding the formulation of the suppositories, lipophilic bases provide greater bioavailability than hydrophilic bases, and absorption is affected by the volume of the suppository, the number of suppositories used, and the particle size of the paracetamol.[14] Rectal pH may also influence the absorption of paracetamol, altering the degree of dissociation and therefore the ability of the drug to pass through biological membranes. In children, rectal pH can vary from 7.8-11.4, and in this range the degree of dissociation of paracetamol will vary from 2-99%.[15]

Several studies have shown that the time needed to achieve therapeutic plasma levels with rectal administration is significantly greater than with the oral or intravenous routes. In healthy adult volunteers given doses of 15 mg/kg, 25 mg/kg, 35 mg/kg and 45 mg/kg, only doses of 35 mg/kg and 45 mg/kg provided concentrations above the minimum therapeutic level of 10mcg/ml for a significant period of time (median 5.5 and 6 hours respectively).[16] A minimum duration of 1-2 hours was needed before this level was achieved. 15mg/kg failed to achieve a median plasma concentration above 10 mcg/ml at any time, while 25mg/kg achieved plasma concentrations at the lower end of the therapeutic range. A higher loading dose (45mg/kg) was not associated with a significantly greater risk of overdose, as the highest plasma concentration measured in the study was 25 mcg/ml, substantially less than the accepted toxic concentration of 120mcg/ml.

A study of the pharmacokinetics of paracetamol, after repeated rectal administration of 25mg/kg, 6 hourly, in 23 children following major surgery showed large variations in the absorption and resulting steady state concentrations.[15] The mean time to reach 90% of the steady state concentration was 11.4 hours.

In a randomised study of 48 patients admitted to ICU after cardiac surgery,[17] half received paracetamol as suppositories and half received intravenous injections. Mean plasma concentration peaked at 14.4mcg/ml within 20 minutes after intravenous administration of 1g, while after a 1g suppository, the mean plasma concentration at 80 minutes was 1.2mcg/ml. Stable plasma concentrations within the therapeutic range were not reached until after the 3rd rectal dose. Similarly, a study of oral and rectal paracetamol in 24 women following minor gynaecological laparoscopic surgery found that after the administration of 2g rectally, the mean plasma concentration at 4 hours was below the minimum analgesic level (8.4mcg/ml, range 4.2-16.3).[18]

There is some evidence to show that the delay in reaching therapeutic plasma levels may limit the usefulness of rectal paracetamol as analgesia in the immediate postoperative period. Hein et al performed

First Pass Metabolism – A drug taken orally is absorbed through the intestine wall into the portal vein system and then delivered to the liver. It may therefore be partially metabolised in the liver before reaching its target site. Drugs given sublingually, intramuscularly or intravenously avoid first pass metabolism.

Oral Bioavailability – The fraction of an oral dose of a drug that reaches the systemic circulation, compared to the same dose given intravenously. Drugs given intravenously have 100% bioavailability.

A **prodrug** is the inactive form of a drug that is broken down by a body enzyme into its active form. This can provide a way of administering drugs that would otherwise be toxic if given systemically in the active form.

a randomised controlled, double-blinded trial involving 140 women undergoing elective termination of pregnancy.[19] Following surgery, patients were randomly allocated to receive either 1g paracetamol rectally, or a placebo suppository. There was no difference in postoperative pain scores between the 2 groups, and no difference in the need for additional analgesia or for time to discharge.

Intravenous administration

As well as being available for oral and rectal administration, paracetamol has previously been available for intravenous use in the form of its pro-drug, propacetamol. Used in France since 1985, propacetamol, provided as a powder for reconstitution, is water soluble and rapidly hydrolysed by plasma esterases to form paracetamol and diethylglycine; a dose of 1g propacetamol provides 0.5g paracetamol after hydrolysis.

The analgesic benefit of propacetamol is well recognised. In a double-blinded study of analgesia following gynaecological surgery, 200 women were randomised to receive either 2 intravenous doses of propacetamol 2g, or ketorolac 30mg, alongside morphine via a *patient-controlled analgesia (PCA)* system.[20] Patients were monitored for 12 hours and propacetamol was found to be comparable to ketorolac in terms of pain scores and reduction in morphine consumption. In a study of patients undergoing dental extraction, propacetamol was significantly better than placebo for all measured parameters; pain relief, pain intensity, patient's global evaluation and duration of analgesia.[13] Similarly propacetamol and diclofenac were found to be similarly effective and superior to placebo following total hip arthroplasty.[21] Although an effective analgesic, propacetamol has a relatively high incidence of adverse effects (up to 49% of patients will develop local pain at the injection site)[22] and there have been reports of contact dermatitis in health-care workers administering the drug.

Intravenous paracetamol (Perfalgan, Bristol-Myers Squibb) is formulated as a 10 mg/ml aqueous solution in 50ml and 100ml glass vials, for infusion over 15 minutes. Solubility is achieved through addition of the hydrophillic ingredients mannitol and disodium phosphate, while hydrolysis to 4-aminophenol, a toxic nitrogenous compound, is avoided by the addition of buffers to sustain neutral pH. Containment in glass vials prevents oxidation. Advantages of intravenous paracetamol over propacetamol are that it is available in a preformed solution, and it is not associated with pain on injection or contact dermatitis. Paracetamol is bioequivalent to propacetamol.[23]

A number of trials have shown comparable efficacy between intravenous paracetamol and propacetamol. Recently, two randomised, double-blinded placebo controlled trials of paracetamol analgesia, after major orthopaedic surgery and dental surgery, found no difference between intravenous paracetamol and propacetamol.[6,22] Both interventions were significantly superior to placebo for pain relief, time to morphine rescue, and overall morphine sparing. Both studies showed intravenous paracetamol to have a rate of adverse effects almost identical to that of placebo, and no cases of injection site reaction were reported.

Patient Controlled Analgesia – An infusion pump filled with an opiate is connected to the patient via an intravenous drip. The pump can deliver a pre-set dose of analgesic (e.g. 1mg) on demand when the patient presses the PCA button. A lockout time (usually 5 minutes) is set when the pump is started, and during this period no further doses are given. This prevents the patient inadvertently overdosing.

Bioequivalence describes pharmaceutical compounds that are equal to each other in bioavailability and potency.

Cost[24]

Route of administration	Cost per 1g dose
Oral	£0.02
Intravenous	£1.50
Rectal	£1.98

Summary

The disproportionate cost, slow onset time and wide variation in bioavailability make rectal paracetamol less attractive in the presence of the intravenous formulation. Given the similar cost, intravenous paracetamol should be considered as a more effective alternative to suppositories, when oral dosing is not possible. It may also have a role to play when prompt analgesia is required and oral administration is not appropriate. Oral paracetamol is a simple well-tolerated analgesic; however a more generous loading dose is needed if meaningful early plasma concentrations are to be achieved. Intravenous paracetamol provides a method of achieving rapid therapeutic concentrations of paracetamol that can subsequently be maintained by oral absorption.

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BOOK REVIEW - OXFORD SPECIALIST HANDBOOKS IN ANAESTHESIA: PAEDIATRIC ANAESTHESIA

Edited by Edward Doyle

This small book is surprisingly comprehensive. It covers paediatric physiology, pharmacology and anatomy, the nuts and bolts of paediatric anaesthesia, including a thorough section on equipment, practical procedures and pain management, specific operations and problems. The section on specific procedures is well set out, with practical information on preoperative assessment, highlighting likely problems encountered in each patient population, advice on anaesthetic technique, including likelihood of pain and the postoperative course, with advice on analgesia and oral intake. The chapter on syndromes and conditions gives succinct advice on what is relevant to the anaesthetist, and includes both the common (such as cerebral palsy and diabetes) and the rare. It has useful advice on stabilising a child for transfer, with a handy checklist, and has the latest resuscitation guidelines. The book offers advice on paediatric fluids, but does not include the recent National Patient Safety Agency guidelines (see below), probably due to the lag time between writing and publication. The format of the book means that there is some repetition of information between chapters. However, overall I found this book useful and easy to read. It is relevant to the anaesthetist in district hospitals doing routine paediatric surgery, but also covers specialist surgery confined to specialist centres. It will therefore be useful to trainees undertaking a paediatric anaesthesia module. I suspect I shall end up carrying it around with me.

Further reading
The NPSA alert 22 on paediatric fluid management is available at: http://www.npsa.nhs.uk/patientsafety/alerts-and-directives/alerts/intravenous-infusions/

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MANAGEMENT OF SEPSIS WITH LIMITED RESOURCES

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Why is sepsis important?
Sepsis is common, has a high mortality and its incidence is increasing. Studies in developed countries have shown a hospital mortality for severe sepsis of up to 55%.[1] Sepsis is the most common cause of death in children in the world. Sixty percent of deaths in developing countries occur as a result of communicable disease.[2] Although sepsis is a complex topic, early recognition, resuscitation and basic treatment can significantly improve outcome.

The aim of this review is to explain sepsis, the principles of its management and to describe the major recent advances in this field. Financial limitations make many of the more recent technological developments and expensive interventions impractical in developing countries. These techniques are described briefly for educational value, with an emphasis on how they can be incorporated into practice in a poor-resource setting. The main focus is adults, but the same principles apply to children.

What is Sepsis?
The Systemic Inflammatory Response Syndrome (SIRS) is an immune response to a variety of severe insults including infection, burns, pancreatitis, and trauma. It affects many organ systems.

Sepsis is SIRS in response to infection. Definitions are summarised in Box 1.

Box 1: Definitions of Sepsis[3]

Systemic Inflammatory Response Syndrome (SIRS): Two or more of the following:

- Temperature > 38°C or < 36°C
- Heart rate > 90 beats/minute
- Tachypnoea (respiratory rate > 20 breaths/min) or hyperventilation ($PaCO_2$ < 4.25 kPa)
- White blood count > 12 x 10^9/l, or < 4 x 10^9/l

Sepsis: 2 or more SIRS criteria in response to infection.

Severe Sepsis: Sepsis associated with hypotension or organ dysfunction or organ hypoperfusion (eg oliguria, altered mental status, lactic acidosis).

Septic Shock: Sepsis-induced hypotension (systolic blood pressure < 90mmHg or a reduction ≥ 40mmHg from baseline) despite adequate fluid resuscitation along with signs of hypoperfusion.

Circulatory insufficiency in sepsis results from hypovolaemia, myocardial depression and vasoregulatory abnormalities including vasodilatation and impaired regulation of organ perfusion. This, together with increased metabolic rate, causes an imbalance between tissue oxygen supply and demand, leading to global tissue hypoxia.

The interactions between infecting micro-organisms and the immune, inflammatory and coagulation responses in sepsis are complex. Pro-inflammatory and pro-coagulant responses are amplified by ischaemia and hypoxia, and immunosuppression occurs in severe sepsis.[4]

Recognition of sepsis
Good hygiene practices and hand washing can help prevent healthcare associated infections. Identifying infections early and treating appropriately can prevent the development of sepsis. This includes good wound care and reviewing patients regularly, asking about and examining for signs of infection. Patients with early sepsis may have a significant imbalance between oxygen supply and demand despite normal vital signs. A vigilant clinician with a high index of suspicion may notice subtle signs such as cool peripheries, sweating, altered mental state, reduced urine output as well as tachypnoea and tachycardia.

Signs of SIRS should be picked up on routine observations. These should include temperature, heart rate, respiratory rate, blood pressure, urine output and conscious level. Low blood pressure, persistently low urine output or confusion suggests severe sepsis and a high risk of death. When dealing with children it is important to know the normal values for age, and a delayed capillary refill time (>2 seconds) is a particularly useful sign of shock.

Patients with abnormal vital signs should receive prompt attention - just charting observations is not enough. Nurses need to be trained to recognise abnormal signs, call for help and initiate treatment if possible. Medical Early Warning Scores (MEWS) provide an effective way of streamlining the required chain of events, to direct the appropriate level of medical expertise to sick patients.

Early recognition and treatment of sepsis is important. Rivers' study of early goal-directed therapy in patients with septic shock demonstrated marked improvements in mortality.[5] Several aspects of their protocol including liberal fluid therapy, inotropes and liberal blood transfusion have been studied before in intensive care patients and failed to show benefit. The

difference in this study was that interventions were applied early, during the first 6 hours of admission to the emergency department. Although some of the markers of sepsis and some of the interventions may be unavailable in many countries, the underlying principle of early haemodynamic resuscitation in sepsis is critical.

The key early interventions in sepsis are assessment and management of airway, breathing and circulation to optimise oxygen delivery. Intravenous antibiotics should be started within the first hour.[6]

Initial Management

Airway

- Give oxygen.
- A patient with an obstructed airway should be managed immediately with simple airway manoeuvres and an oro- or nasopharyngeal airway if necessary. Patients with reduced conscious level should be nursed in the recovery position.
- Where facilities exist, immediate intubation and ventilation is indicated for airway obstruction or failure to localise to pain because of a low conscious level. Some of these patients may respond to fluid resuscitation with an improvement in conscious level, and a fluid challenge is a sensible initial step before giving any anaesthetic drugs.

Breathing

All septic patients should be given as much oxygen as possible. Higher concentrations of oxygen can be achieved with two oxygen concentrators connected into to a non-rebreathing mask with a reservoir bag, or one connected to a mask and one to nasal cannulae. Respiratory failure may require intubation and ventilation. Signs of respiratory failure include tachypnoea, dyspnoea, use of accessory muscles, poor chest expansion, poor air entry, cyanosis, low oxygen saturation and hypoxia and/or hypercapnia on arterial blood gases, if these are available.

Breathing may also be helped by sitting the patient up, deep breathing, coughing and chest physiotherapy. If available, some patients may benefit from continuous positive airway pressure (CPAP) or non-invasive ventilation (NIV). In the short term (e.g. while preparing to intubate), assisting breathing with an Ambubag and mask (with a PEEP valve if possible) can be helpful. Remember that unless you are assisting breathing, patients find it difficult to breathe through an Ambu–valve and a simple mask with reservoir bag will achieve more effective oxygenation. A Waters circuit is a suitable alternative (see Figure 1).

Intubating critically ill patients has significant risks. They have little oxygen reserve, and despite full pre-oxygenated will desaturate quickly. Fluid resuscitation should be started while preparing to intubate, but expect the blood pressure to drop significantly and have a vasopressor agent drawn up. Ketamine may cause less hypotension than other induction agents. Patients who are moribund and have a depressed level of consciousness may not tolerate any sort of intravenous agent. Occasionally it is wise to intubate such patients without sedation, using a local anaesthetic agent sprayed through a cannula onto the larynx under direct laryngoscopy.

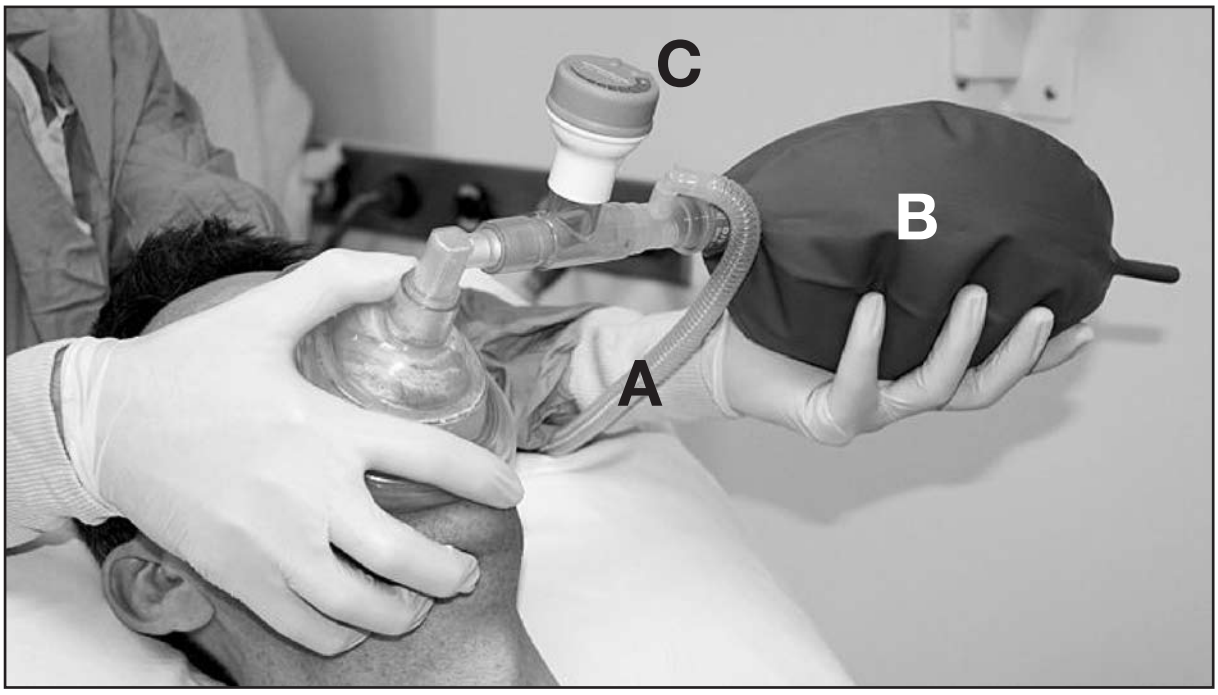

Figure 1: A Waters circuit which has tubing from an oxygen source (A), a reservoir bag (B) and an adjustable pressure limiting (APL) valve (C), is ideal for optimal oxygenation and also gives the facility to deliver a variable level of respiratory support by squeezing the bag, or to apply CPAP by adjusting the APL valve.

Box 2: Intubation checklist for critically ill patients

Monitoring:	As available: SaO_2, ECG, frequent BP, assistant to feel pulses
Assistants:	One or preferably two for cricoid pressure and assistance. Check they know what you expect them to do
Pre-oxygenation:	Deliver as much oxygen as available via facemask and circuit. If using an oxygen concentrator, fill a large bin liner with oxygen and use this source of 100% oxygen to preoxygenate the patient
IV access:	Large drip running freely, fluid resuscitation in progress
Equipment:	2 working laryngoscopes Endotracheal tube of correct size + 1 size smaller, cuffs checked Gum elastic bougie Guedel airway End tidal CO_2 monitor if available, stethoscope to check tube position Suction switched on and within reach Tape to secure ET tube
Intubation drugs:	eg. ketamine & suxamethonium
Resuscitation drugs:	ephedrine 30mg in 10ml (1-3ml boluses) metaraminol 10mg in 20ml (0.5-2ml), epinephrine1mg in 10ml (0.5-1ml), atropine 0.4-0.6mg
Ventilator:	Where available, checked and set up
Other drugs:	To continue sedation and muscle relaxation if necessary

Circulation

Fluid Resuscitation

Septic patients need a lot of fluid. An initial fluid bolus of 20-30ml/kg of crystalloid (e.g. Hartmann's solution) is appropriate - i.e. around 2 litres for a 70kg adult. Further fluid boluses can be given, assessing the response to each. In Rivers' study patients received on average 5 litres of fluid in the first 6 hours and there was no increase in the need for ventilation.[5]

The choice of fluid does not seem to be important. Hartmann's solution has some advantages over 0.9% saline, but either is acceptable. Hartmann's is more similar in composition to extracellular fluid than saline and less likely to cause a hyperchloraemic metabolic acidosis. Dextrose is useless for resuscitation. Colloids theoretically stay in the intravascular space longer than crystalloids, however capillary permeability is increased in sepsis. The SAFE study comparing albumin and saline for resuscitation found no difference in outcome, and showed that only 1.3 times as much saline was needed to produce the same effect as albumin.[7]

Resuscitation goals

Cardiovascular parameters used to guide resuscitation include heart rate, blood pressure, peripheral perfusion (skin temperature, capillary refill), urine output and conscious level. Many clinicians believe that CVP monitoring is not useful, since right atrial pressure correlates poorly with the pressures and volumes of the left side of the heart and use of CVP measurements to guide fluid therapy remains controversial. However, the Rivers paper used a target CVP of 8-12mmHg as part of their 'bundle' of strategies to provide 'early goal-directed therapy', which reduced the mortality from septic shock. It is not possible to say which parts of their protocol were most beneficial and ideally, to replicate the benefits of this study, a clinician should manage his patients exactly as they were managed in the study. This demonstrates the difficulties in implementing the findings of clinical studies into situations where there are insufficient resources to introduce the full package of investigations and interventions.

If a blood gas machine is available, blood taken from a central venous catheter can be analysed to give central venous oxygen saturation ($ScvO_2$). This may be a useful marker of oxygen delivery. A $ScvO_2$ of less than 70% suggests that oxygen extraction is increased due to inadequate oxygen delivery. Oxygen delivery is related to cardiac output, haemoglobin concentration and arterial oxygen saturation. It can be improved by increasing cardiac output with fluid or inotropes, by increasing oxygen carrying capacity with blood transfusion and by supplemental oxygen to increase SaO_2. Oxygen demand may be reduced by intubation, ventilation and sedation.

Some blood gas analysers or labs can measure serum lactate concentration, which is a useful if non-specific

marker of tissue hypoxia. The normal lactate level is < 2.5mmol/l in venous blood and < 1mmol/l in arterial blood. A recent study of patients with an infective diagnosis attending an emergency department, showed that patients with a **venous** lactate level above 4mmol/l on admission were 12.6 times more likely to die than those with normal venous lactate level. The 28-day mortality of patients with a venous lactate above 4mmol/l and a systolic BP below 70mmHg on presentation was 60%.[8]

Several monitors can measure or calculate cardiac output and fluid status (*see Update 21*).[9] This equipment is rarely a priority in regions with limited resources and although the monitors may add useful information, there is little evidence that they improve outcome.[10] In fact a recent trial in patients with acute lung injury (of whom 25% were septic) showed no advantage in using a pulmonary artery catheter to guide haemodynamic management over clinical assessment of circulatory effectiveness (skin colour and temperature, capillary refill, blood pressure and urine output).[11] This emphasises the message that early intervention guided by clinical findings is effective in the management of sepsis.

Vasopressors and Inotropes

Patients with septic shock have low blood pressure and reduced tissue perfusion despite adequate fluid resuscitation. They may be vasodilated, or have a low cardiac output, or both. This high risk group is difficult to diagnose and treat appropriately.

Adequate fluid resuscitation is difficult to determine. A CVP of 8-12mmHg, which goes up and stays up with a fluid challenge suggests adequate filling. Alternatively generous fluid resuscitation with no further improvements in heart rate, blood pressure, or peripheral perfusion with fluid challenges is probably adequate.

Patients who are vasodilated with a high cardiac output have warm peripheries, capillary refill <2 seconds and good volume pulses. If they are hypotensive they may benefit from a vasoconstrictor such as norepinephrine to improve the perfusion pressure to organs such as kidneys and brain, particularly if urine output or conscious level is reduced. Vasoconstrictors used alone can reduce cardiac output and worsen tissue hypoxia, so these patients need to be observed closely with repeat assessments of peripheral perfusion. Where available, a normal lactate and $ScvO_2$ are reassuring. If in doubt, an inotrope such as dobutamine may be added.

Patients with low cardiac output have cool peripheries and slow capillary refill. Their systemic vascular resistance may be high or low. Once adequately fluid resuscitated, they need an inotrope to improve cardiac output. Epinephrine is both an inotrope and vasoconstrictor and is usually very effective. Dobutamine is an inotrope and vasodilator which is more difficult to use and may cause the blood pressure to drop further. It can be used together with noradrenaline but titrating two vasoactive drugs without cardiac output monitoring is not easy. There is some concern over the effects of epinephrine on gut perfusion[11] but a recent Cochrane review concluded that there was not sufficient evidence to recommend one vasopressor over another.[13]

The most common reason why a patient fails to respond to vasopressors / inotropes is that they are under-filled: a fluid challenge is worth trying. Given the difficulty assessing a variable clinical picture, you may not be using the best drug, for example giving norepinephrine to someone who already has a low cardiac output. Intermittent boluses of vasopressor such metaraminol 0.25-1mg, or combined vasopressor and inotrope such as ephedrine 3-9mg or epinephrine 0.05mg may give you an idea of which type of drug the patient responds to. Of course some patients may not respond due to the overwhelming severity of the disease. Recognising this and focusing on comfort can prevent unnecessary suffering.

Blood transfusion

Increasing haemoglobin concentration is one way of improving oxygen delivery, however blood transfusion has risks. The TRICC study showed that in intensive care patients a restrictive transfusion strategy aiming for haemoglobin of 7-9g/dl was at least as effective

Box 3: Resuscitation goals:

Mean Arterial Pressure (MAP) > 65mmHg

Urine Output > 0.5ml/kg/h

Warm peripheries, capillary refill < 2 seconds

Central Venous Pressure (CVP) 8-12mmHg (7.6mmHg = 10cmH_2O)

Central Venous Oxygen Saturation ($ScvO_2$) > 70% where available

Venous serum Lactate < 4mmol/l

Notes: MAP = diastolic BP + (systolic BP-diastolic BP)/3
i.e. MAP 65 compatible with BPs of 85/55, 95/50, 105/45

Box 4: use of inotropes and vasopressors

These are examples only. Use whatever you are familiar with or find easiest to work out. Reliable infusion pumps should be used whenever possible. Use a central line if available, otherwise use a dilute solution via a dedicated reliable cannula in a large proximal vein.

Epinephrine and Norepinephrine

- By infusion pump (via central line if possible):
  - mix 5mg in 50ml (or 4mg in 40ml)
  - start at 1-5ml/hour & titrate according to response
  - for a 50kg person 0.1micrograms/kg/min = 3ml/hour
- If no infusion pumps available:
  - mix 5mg in 500ml. *The infusion rate should be watched continuously.*
  - Paediatric giving sets with 60 drops/ml are helpful, start at 10-50 drops/min
  - Normal 20 drops/ml sets can also be used- divide drops/min by 3
  - For example for a 50kg person:
    - with 60 drops/ml paediatric set 0.1 micrograms/kg/min = 30 drops/min
    - with 20 drops/ml set 0.1 micrograms/kg/min = 10 drops/min.

Dopamine & Dobutamine

- By infusion pump:
  - mix 250mg in 50ml.
  - start around 5 micrograms/kg/min
  - for a 50kg person 5 micrograms/kg/min = 3 ml/hour
- These can also be used without an infusion pump as above.

and possibly superior to a liberal transfusion strategy aiming for Hb 10-12g/dl.[14] However, only 5% of their patients had a primary diagnosis of sepsis, average lactate concentration was less than 2mmol/l, and patients were enrolled up to 72 hours into their ICU stay. This is a different population to that studied in Rivers' trial of early goal directed therapy. The Rivers protocol included transfusion to Hb>10g/dl, if $ScvO_2$ >70% was not achieved by other means. Overall, 68% of patients were transfused in the intervention group (64% before 6h) versus 45% in the control group (19% before 6h). It is not possible to say which parts of their protocol were most beneficial, and transfusion levels in intensive care remain controversial.[15] Crucially, most clinicians working in resource-poor areas will be unable to measure $ScvO_2$ and implement this strategy of treatment. In addition the risks of transfusion are greater, although a WHO initiative is improving blood transfusion services in many countries. Elsewhere screening for blood-borne disease, antibodies and cross-matching may be less thorough and limited resources should be reserved for those with the greatest need and greatest chance of survival.

Antibiotics and source control

Intravenous antibiotics in adequate dosage should be given as early as possible, after taking blood cultures. Giving effective antibiotics within the first hour has been associated with increased survival in septic shock.[15] Lack of appropriate antibiotics in poor resource settings is a major obstacle to providing effective treatment for patients with sepsis. Choice of antibiotics depends on the likely source of infection, should be broad spectrum and take into account local resistant organisms. Even where the choice appears limited a logical approach will provide effective cover; for example long-standing antibiotics such as ampicillin, gentamicin and metronidazole provide excellent cover for abdominal sepsis. Discussion with a microbiologist is helpful. Samples can be sent for gram stain if available rapidly. Further samples including wound swabs, urine, sputum or tracheal aspirate, and CSF should be taken for culture as appropriate, ideally before giving antibiotics.

Detailed history and examination should try to determine the source of infection. Investigations such as chest X-ray, ultrasound and CT scan may be helpful.

Surgeons should be involved at an early stage if surgical drainage or debridement may be required. These patients are high risk for anaesthesia, and a short period of resuscitation is appropriate, but they will die without control of the source of sepsis.

Further Management

Mechanical ventilation

Sepsis may cause acute lung injury (ALI) or acute respiratory distress syndrome (ARDS). This is inflammation of the lungs with increased vascular permeability characterised by bilateral infiltrates on chest X-ray, not caused by cardiac failure. ALI is defined as PaO_2/FiO_2 ratio of 200-300mmHg (26-39KPa). ARDS is more severe with PaO_2/FiO_2 ratio <200mmHg (26KPa).

Box 5: Early Goal-Directed Therapy

Many recommendations in this review and in the Surviving Sepsis Guidelines[6] are based on Rivers' trial of early goal-directed therapy (EGDT) in severe sepsis and septic shock.[5] This was a randomised controlled trial of 263 patients with septic shock, presenting to a US emergency department. The study showed that a protocol of goal-directed therapy during the first 6 hours of admission, aimed at achieving a balance between oxygen delivery and oxygen demand, reduced hospital mortality from 46% in the control group to 30% in the experimental group (p=0.0009, NNT).[7]

Enrolled patients met SIRS criteria (above) and had systolic BP < 90mmHg after 20-30ml/kg of crystalloid, or venous lactate >4mmol/l. The control group received standard therapy to achieve CVP 8-12mmHg, MAP >65mmHg, urine output >0.5ml/kg/h. The experimental group protocol aimed for the same targets plus $ScvO_2$ >70%:

- They were given 500ml crystalloid every 30 mins until CVP 8-12
- If MAP < 65mmHg they received norepinephrine (if MAP >90mmHg vasodilators)
- If $ScvO_2$ <70% they were transfused to Hb>10g/dl
- Then if $ScvO_2$ <70% they received dobutamine (stopped if MAP <65 or HR >120)
- Then if $ScvO_2$ <70% still, they were intubated and ventilated

During the first 6 hours the EGDT group received more fluid (5 litres vs 3.5 litres), more blood transfusion (64% vs 18.5%), and more dobutamine (13.7% vs 0.8%). Use of vasopressors and ventilation was similar between the groups. Volume resuscitation alone was sufficient to correct $ScvO_2$ in 36%, transfusion in an additional 50% and inotropes in 13.7%. During the period 7-72hours after admission the EGDT group required less fluid, less transfusion, less vasopressors and less ventilation. They had lower lactate levels, less acidosis and less severe organ dysfunction.

Mortality at hospital discharge was 29% in the study group compared to 44% in the control group (p=0.006, number needed to treat = 7).

We can conclude that this protocol, applied early, with frequent review, to patients with severe sepsis can reduce mortality. $ScvO_2$ is probably a useful resuscitation goal, however it is not possible to say exactly which aspects of this protocol were most beneficial.

Mechanical ventilation of patients with ALI/ARDS should avoid high airway pressures and high tidal volumes. The ARDSnet study was the largest randomised controlled trial comparing ventilation strategies including 861 patients.[17] Ventilation with tidal volumes of 6ml/kg and plateau pressures of <30cmH_2O compared to ventilation with tidal volumes of 12ml/kg and plateau pressures <50cmH_20 reduced mortality from 40% to 31% and increased ventilator-free days. This study used a protocol based on volume controlled ventilation. However, pressure control ventilation or spontaneous modes are likely to be better tolerated in patients who are not deeply sedated or paralysed. The targets of pressure <30cmH_2O and tidal volume 6ml/kg are probably more important than the ventilation mode.

Permitting modest hypercapnia to allow lower tidal volumes and airway pressures is likely to be safe. However, this is limited if the patient has a metabolic acidosis.[6]

Positive end expiratory pressure (PEEP) prevents lung collapse and can improve oxygenation. A further study comparing high PEEP with low PEEP combined with the ARDSnet ventilatory strategy showed no difference.[18] Increasing PEEP according to FiO_2 as in the original ARDSnet study seems reasonable: minimum PEEP of 5cmH_2O at FiO_2 of 30% up to PEEP of 20cmH_2O or higher with FiO_2 of 100%.

Nursing ventilated patients in the semi-recumbent position (45 degrees) has been shown to reduce the incidence of ventilator-associated pneumonia.[19] Patients may need to be laid flat if hypotensive. Non-invasive ventilation,[20] subglottic drainage and use of heat & moisture exchange filters instead of heated water humidification may also reduce ventilator-associated pneumonia.[21]

A protocol for weaning patients from mechanical ventilation is helpful. Once a patient is improving and meets certain criteria, daily spontaneous breathing trials, breathing through the endotracheal tube with oxygen delivered via a T-piece, reduce the duration of mechanical ventilation.[22]

Activated Protein C

Recombinant activated protein C has been shown to reduce mortality in severe sepsis[23] but not in low risk patients[24] or in children.[25] Its expensive precludes use in many countries.

Steroids in sepsis

Patients on long term steroid therapy or with known adrenocortical insufficiency will require steroid

replacement during critical illness. Many studies have looked at treatment of septic patients with corticosteroids and this remains controversial.

One multicentre randomised controlled trial (RCT) of 229 patients showed an improvement in mortality in patients with septic shock and relative adrenal insufficiency (blood cortisol level failed to rise appropriately in response to a dose of synthetic adrenocorticotropic hormone, ACTH) when they were given hydrocortisone 50mg 6 hourly and fludrocortisone.[26] The only statistically significant difference without adjusting the data was in ICU mortality (70% control group, 58% treatment group – giving a number needed to treat of 8). This effect was only seen in non-responders to the ACTH test, not in the group as a whole, leading to fears that a proportion of septic patients would be treated with steroids inappropriately. Two smaller RCTs showed improvements in shock reversal with low dose hydrocortisone.[6] Two meta-analyses have shown reduction in mortality, but only in studies of low dose, long duration steroid therapy.[27,28] The interpretation of the ACTH stimulation test remains controversial.

The recent CORTICUS trial, a randomized, controlled study of 500 patients comparing hydrocortisone to placebo in septic shock is not yet published but is thought to show no difference in mortality with low dose steroids in septic shock.[29]

Steroid use in sepsis is controversial, but current practice in many ICUs is to give low dose steroids to patients with vasopressor-dependant septic shock, with or without an ACTH test. This may change once the results of CORTICUS are published. Short courses of high dose steroids should not be used.

Nutrition and stress ulcer prophylaxis

Evidence based guidelines recommend that intensive care patients who are not expected to be taking a full oral diet within 3 days should receive enteral nutrition via a feeding tube.[30] There is no difference in the efficacy of jejunal versus gastric feeding, but they recommend jejunal feeding where this is easily carried out (for example placed during laparotomy) and for patients who do not tolerate gastric feeding. Gastric emptying is frequently the rate-determining step so, where available, motility agents such as erythromycin and metoclopramide may be helpful in patients with feed intolerance and high gastric residual volumes. If available and affordable, parenteral nutrition may be considered in patients who cannot be fed sufficient enterally.[30,31] Use of an evidence based algorithm for nutritional support in Canadian intensive care units was associated with more days of enteral nutrition and improved clinical outcomes,[32] and it is advisable that all ICUs use an enteral feeding protocol describing gradual introduction of feed to a pre-determined goal, with regular aspiration of gastric residual volume.

Laparotomy and peritonitis is not a contraindication to enteral feeding and several studies have shown benefits of early nasojejunal feeding in these patients.[33,34] Most studies have used specially designed feeds given by infusion, but these are often not available in developing countries. The above studies used nasojejunal feed prepared in hospital kitchens (and include the recipes). Patients are often given liquidized food, soup, milk etc by nasogastric tube but it is not easy to meet calorific and nutritional requirements without detailed calculations and, ideally, advice from a dietician.

The enteral route can also be useful for electrolyte replacement particularly where IV potassium is not available. Some surgeons will not allow feeding until bowel sounds are present which can take several days and hypokalaemia can worsen ileus. They can often be persuaded to allow oral rehydration solution by mouth or nasogastric tube.

The Surviving Sepsis Guidelines recommend stress ulcer prophylaxis with ranitidine. This is unnecessary once enteral feeding is established.[6]

Blood glucose control

Glucose control in ICU remains controversial. Van Den Berghe's study in 2001 showed improvements in ICU mortality in patients with tight glucose control (4.4-6.1mmol/l versus 10.0-11.1mmol/l).[35] 62% of the patients in this study had undergone cardiac surgery, but despite concerns about the relevance of these results to medical ICU patients, tight glucose control has been widely adopted. The Surviving Sepsis Guidelines recommend keeping blood glucose below 8.3mmol/l (150mg/dl).[6]

Van den Berghe's next study, in medical ICU patients, showed that intensive insulin therapy improved some markers of morbidity but not mortality in the randomised group.[36] 19% of patients in the treatment group developed hypoglycaemia, but with no obvious adverse outcome.[37] The insulin arm of the VISEP trial (Efficacy of Volume Substitution and Insulin Therapy in Severe Sepsis) was stopped due to an unacceptably high incidence of hypoglycaemia in the treatment group (12%).[38]

Septic patients are at risk of both hypo- and hyperglycaemia whether or not they are treated with dextrose and insulin. Blood glucose should be checked in all sick patients, but close monitoring of blood glucose is more difficult in areas with limited resources. Very high blood glucose (>11mmol/l) is likely to be harmful, as is severe hypoglycaemia. Clinicians have to balance the potential benefits of tighter glucose control against the risks of undetected hypoglycaemia. Four to six-hourly subcutaneous insulin, adjusted according to blood glucose is an alternative to intravenous sliding scales where no infusion pumps are available, but still requires frequent blood glucose monitoring.

Analgesia, sedation and neuromuscular blockade
Untreated pain in septic patients increases oxygen demand, by causing tachycardia and distress. The safest way to give analgesia is to titrate doses of intravenous opioid, repeated until pain has improved. Small doses of ketamine (0.2mg/kg) can be a useful co-analgesic, but larger doses may cause disorientation. Regular paracetamol should be given. Nonsteroidal anti-inflammatory drugs (NSAIDs) should be avoided in septic patients – the risks of renal failure and peptic ulceration will be increased.

Sedation of unintubated septic patients is potentially dangerous. Confusion and agitation may be caused by hypoxia, reduced brain perfusion or intracranial pathology, which may be worsened by sedation. Mental state may improve with resuscitation and provides an important marker of organ perfusion. Ketamine is relatively safe, but may worsen confusion and agitation and increase intracranial pressure. Benzodiazepines may cause respiratory depression, particularly if combined with opiates. In patients who are unmanageable and at risk of harming themselves, anaesthesia, intubation, ventilation and continued sedation may be the only safe option.

In ventilated patients sedation may be given by intermittent bolus or by continuous infusion, according to a protocol with sedation goals.[6] Daily lightening of sedation ('a sedation hold') allows assessment of neurological function and reduces the duration of mechanical ventilation and ICU length of stay.[39]

Neuromuscular blockers should be avoided if at all possible due to the risk of prolonged muscle weakness (critical illness polyneuropathy).[6] Use of muscle relaxants without adequate continuous sedation is unacceptable.

Both chemical and physical restraint have risks.[40] In one observational study in European ICUs both prolonged sedation and physical restraint without sedation were associated with post traumatic stress disorder.[41] Physical restraint may be preferable to chemical sedation in some situations, but should be carefully and selectively employed. It should only be used if patients are not competent to make decisions, pain and other causes of agitation have been addressed and it is important to keep trying to communicate with the patient. Restraints must not hurt the patient; for example 'boxing gloves' can be made out of bandages.

Renal support
Septic patients are at high risk of renal failure but renal support is unlikely to be available in resource-poor areas. The risk of renal failure can be reduced by early fluid resuscitation, maintaining renal perfusion pressure and cardiac output (with inotropes if necessary), and avoiding nephrotoxic drugs (e.g. NSAIDs, gentamicin). There is no evidence for using low dose dopamine for renal protection. Treatment of acidosis with sodium bicarbonate does not improve haemodynamics or response to vasopressors.[4] Lactic acidosis should be treated by optimising the circulation.

If available, renal replacement therapy can be with either continuous veno-venous haemofiltration or intermittent haemodialysis.[6] Peritoneal dialysis is appropriate but is contraindicated in the large proportion of patients who have intra-abdominal infection.

Prophylaxis against deep vein thrombosis (DVT)
All ICU patients should receive DVT prophylaxis with either unfractionated or low molecular weight heparin unless contraindicated (thrombocytopaenia, coagulopathy, active bleeding). Graduated compression stockings may be used if heparin is not given.[6,42]

Paediatric considerations [6,43]
To recognise a sick child, it is important to know normal values for vital signs in that age group. Listen to the mother - she will tell you if the child is lethargic, not feeding, not passing urine, hot or generally unwell. Weigh the child if possible: formulas for calculating weight according to age usually overestimate the weight of children in developing countries.

Children have less respiratory reserve than adults. They have a high metabolic rate, higher airway resistance and lower functional residual capacity. Babies breathe using their diaphragm and tire quickly. Signs of respiratory distress include tachypnoea, intercostal and subcostal indrawing, cyanosis and tachycardia. All sick children should receive oxygen, and continuous saturation monitoring if possible. They are more likely to need intubation and ventilation and can decompensate very quickly.

Children have a high cardiac output and cardiovascular reserve; they tend to compensate then deteriorate suddenly and rapidly. They become dehydrated easily and respond to hypovolaemia by an increase in heart rate and vasoconstriction. Capillary refill time is a particularly useful sign in children and should be less than 2 seconds. Hypotension is a late, pre-terminal sign. Aggressive fluid resuscitation is vital in the septic child. 20ml/kg boluses should be given over 5-10 minutes, titrated to heart rate and capillary refill, aiming for a urine output of 1ml/kg/h. 60ml/kg of fluid or more may be required. Venous access may be difficult; intraosseous infusion can be lifesaving and should be undertaking if two attempts at IV cannulation are unsuccessful. Inotropes should only be used after adequate fluid resuscitation and dopamine (or dobutamine) is recommended as first line. Hepatomegaly may indicate fluid overload.

Septic children frequently become hypoglycaemic. It is important to check blood glucose early and treat hypoglycaemia with 5ml/kg 10% glucose.

CASE EXAMPLE: POST-PARTUM SEPSIS [44,45]

A 25-year-old woman is admitted to your district hospital with vomiting, diarrhoea and abdominal pain 4 days after delivering her second child at home. She is apyrexial with a heart rate of 130 and a blood pressure of 140/95. She is seen by a junior surgeon who finds a soft abdomen, diagnoses gastroenteritis and treats her with oral rehydration solution.

Her temperature rises to 39.5° overnight and the next morning she is drowsy and confused and you are asked if she can be admitted to the critical care unit.

How are you going to assess and treat her?
Assess Airway, Breathing and Circulation.
She is responding to voice with confused speech. Her respiratory rate is 35/min, your saturation monitor is not picking up a signal. Her heart rate is 140/min and blood pressure 70/40. She is pale and peripherally cold with a capillary refill time of 5 seconds. The nurses don't know when she last passed urine.

She has septic shock: Give oxygen, fluid resuscitation and IV antibiotics.
You give oxygen 5l/min from an oxygen concentrator, insert two 14G cannulae and start fluid resuscitation with Hartmanns solution as fast as possible, then move her to recovery or the ICU. Further history from her mother reveals that her waters broke 2 days before delivery, but her delivery was uncomplicated with no excessive bleeding and the placenta appeared intact. She has foul-smelling vaginal discharge and a tender uterus. You suspect genital tract sepsis so start amoxycillin 2g 6 hourly, metronidazole 500mg 8 hourly and gentamicin 5mg/kg once (with further doses every 24 hours if renal function normal).

What investigations do you want to do?
Blood cultures should be taken before giving antibiotics, but this is not available in your hospital. You take vaginal swabs for gram stain and culture and send urine for culture as soon as possible, do **a thorough physical examination** looking for other sources of sepsis and take a more complete history. You ask an obstetrician to confirm your diagnosis, do a pelvic ultrasound to look for retained products and to assess whether there is an indication for surgery. You send blood for **full blood count, malaria screen, urea and electrolytes** and check **blood glucose**. **Arterial blood gases, lactate, coagulation screen and CRP** are not available. You would like a **chest X-ray** to look for air under the diaphragm or signs of infection, but this is not available in the evenings.

How are you going to monitor her?
- Frequent nursing observations (minimum hourly): respiratory rate, oxygen saturation, heart rate, blood pressure, ECG, urine output, conscious level, pain score, temperature, blood glucose (4-hourly if stable).
- Frequent medical / anaesthetic review with goal-directed therapy.

After one hour she has had 2 litres of Hartmanns. Observations are: RR 25, SaO_2 100% on 5l/min O_2, HR 130, BP 80/40, capillary refill 2s, drowsy but now orientated and complaining of abdominal pain, a catheter was inserted draining a small amount of dark urine, temperature is 39ºC.

What are you going to do now?
Give more fluid, assessing the response to each bolus.

- You give 250ml of Gelofusine, and paracetamol for pain. HR improves to 120, capillary refill <2s with warm peripheries, BP is unchanged. After another 250ml there is no further change. She passes 15ml of urine in 1 hour. Her pain improves.

Some results come back: Hb 12g/dl, white cell count (WCC) $30x10^9$/l, platelets $90x10^9$/l. Na 150mmol/l, K 4.0mmol/l, Cl 110mmol/l, bicarbonate 15mmol/l, urea 10mmol/l, creatinine 80mcmol/l, glucose 6mmol/l. Gram stain shows gram positive cocci and gram negative bacilli.

What do you think of these results?
The high wcc is consistent with infection (it may also be low in severe sepsis). Low platelets occur in severe sepsis and may indicate disseminated intravascular coagulation. The haemoglobin is relatively high for a woman who has just had a baby, which may reflect dehydration consistent with the slightly raised sodium and urea. The low bicarbonate and raised anion gap suggest a metabolic acidosis, probably lactic acidosis. This may be part of the reason for her tachypnoea. Gram stain shows mixed organisms for which she is on appropriate broad spectrum antibiotics. If culture shows group A streptococcal infection you could consider adding benzylpenicillin. Renal function will have to be watched closely while on gentamicin.

What are you going to do now?

Septic shock unresponsive to fluid: start vasopressor, continue goal-directed therapy.

She has now had 40ml/kg of fluid, and no further improvement with the last bolus. She remains hypotensive with a low urine output. A central venous catheter would be helpful but is not available. You start norepinephrine (epinephrine would be your second choice) 5mg in 500ml through a a paediatric (60 drops/ml) giving set at 30 drops/minute via separate cannula in her antecubital fossa. BP improves to 130/70 and HR to 110, capillary refill <2s. Urine output is 100ml the next hour. You explain to the nurses how to titrate the noradrenaline aiming for a BP>100/50, urine output >30ml/h, capillary refill<2s. You tell them to call you if these goals are not met, heart rate or respiratory rate increase, saturation or conscious level are reduced. You prescribe maintenance fluids at 125ml/h and analgesia.

You have a busy night: frequent fluid boluses are required for decreased urine output, reduced blood pressure or cool peripheries. Oxygen saturations drift down when she is sleeping, but they improve with sitting her up in bed and deep breathing. The next morning, after 5 litres of fluid, she is beginning to improve and the noradrenaline is gradually turned off. You ask for chest physiotherapy, encourage oral fluids and diet, and recheck blood tests.

She continues to improve, IV antibiotics are continued for 48h after the fever settles, and she is eventually discharged home.

How can you improve treatment of sepsis in the future?

Early recognition and management of sepsis on the wards needs to be improved. The diagnosis may not be obvious and patients may not always have a fever, but recognising when a patient is sick is vital. This may include teaching sessions for doctors and nurses, organisational change to allow more frequent observations and improved staffing levels, and resources such as sphygmomanometers and saturation monitors.

You could discuss additional hospital and critical care resources such as blood culture and arterial blood gas analysis, central venous catheters and CVP monitoring. However, early recognition and timely simple interventions are the key to survival.

Children become hypothermic easily, particularly when large volumes of cold fluid are infused. Even in hot climates it is important to prevent heat loss, warm fluids and check the child's temperature.

Summary

Early recognition and treatment of sepsis can significantly reduce mortality. Limitations on resources make implementation of the findings of clinical trials problematic. However, the most important interventions of aggressive fluid resuscitation, oxygen and early antibiotics, with frequent review to adjust treatment, can be achieved in any hospital.

Further Reading

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SPINAL ANAESTHETIC SPREAD

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This article will detail the factors that determine how local anaesthetic spreads within the CSF, therefore determining the extent of the block.

Mechanisms of drug spread

The CSF of the vertebral canal occupies the narrow (2-3mm deep) space surrounding the spinal cord and cauda equina, and is enclosed by the arachnoid mater. As the local anaesthetic solution is injected, it will spread initially by displacement of CSF and as a result of any currents created within the CSF. The next stage may well be the most crucial, and is spread due to the interplay between the densities of both CSF and local anaesthetic solution under the influence of gravity.

Gravity will be 'applied' through patient position (supine, sitting, etc) and, in any horizontal position, by the influence of the curves of the vertebral canal. Many factors are said to affect these mechanisms.

What factors may affect how far the local anaesthetic spreads?

CHARACTERISTICS OF THE INJECTED SOLUTION

Baricity
Volume / Dose / Concentration
Temperature of injectate
Viscosity
Additives

CLINICAL TECHNIQUE

Patient position
Level of injection
Needle type / Alignment
Intrathecal catheters
Fluid currents

PATIENT CHARACTERISTICS

Age
Height
Weight
Sex
Intra-abdominal pressure
Spinal anatomy
Lumbosacral CSF volume
Pregnancy

The key factors are the physical characteristics of CSF and the solution injected, the clinical technique used and the patient's general features. These inter-relate in complex ways. Once bulk spread of the injectate under the influence of the physical forces outlined above is complete, the final stage will be diffusion of drug through the CSF and into the nervous tissue.

The way a local anaesthetic moves in the CSF is determined by its "heaviness". This is variably described in terms of baricity, density and specific gravity? Can you define them?

CSF characteristics

CSF is an isotonic, aqueous medium with a constitution similar to interstitial fluid. The terms density, specific gravity and baricity define its physical characteristics, but are often used inaccurately causing confusion. Precise definitions are:

i) Density: the ratio of the mass of a substance to its volume. It varies with temperature, which must be specified.

ii) Specific gravity: the ratio of the density of a substance to a standard. It is usual to relate local anaesthetic solutions at 20°C to water at 4°C.

iii) Baricity: analogous to specific gravity, but expressed as a ratio of the densities of local anaesthetic and CSF, both at 37°C.

The units of density are weight per unit volume, but the other two, being ratios, have no units. At 37°C the mean density of CSF is 1.0003, with a range of 1.0000-1.0006 (± 2 SD) g/litre. Given the normal variation, it is necessary that solutions which are to be predictably hypobaric or hyperbaric in all patients have baricities below 0.9990 or above 1.0010 respectively. Most glucose-free solutions used intrathecally are slightly hypobaric, but behave in a hyperbaric manner if cooled to 5°C before injection (explained later).

Plain bupivacaine has a baricity of 0.9990, which means that it is only just on the edge of being hypobaric.

CSF density is lower in women than men, in pregnant than non-pregnant women, and in premenopausal women than postmenopausal women and men. Theoretically, these differences could lead to differences in the movement of a particular solution in the various patient groups but the differences between groups are small and probably clinically unimportant.

FACTORS AFFECTING INTRATHECAL SPREAD

Characteristics of the injected solution

Baricity

While various techniques have been used to alter the baricity of local anaesthetics, the addition of glucose is the only one to remain in routine use. The usual choice for the clinician is between a hyperbaric solution and one with a baricity at, or just below, that of CSF. Hyperbaric solutions are more predictable, with greater spread in the direction of gravity and less variability. In contrast, most plain solutions exhibit greater variability in effect and are less predictable, so that the block may either be too low, and inadequate for surgery, or excessively high, and cause side-effects. The greater mean spread of hyperbaric solutions may be associated with an increased incidence of cardiorespiratory side effects, although this is not always the case, and may depend on the concentration of the glucose. Commercially available solutions contain up to glucose 8%, but most of the evidence shows that any concentration in excess of 0.8% will produce a solution that behaves in a hyperbaric manner, but with less spread if the glucose concentration is at the lower end of the range. Hyperbaric solutions can be made by adding 5% dextrose to plain bupivacaine.

Do you think injecting a larger volume will lead to a more extensive block?

Volume / Dose / Concentration injected

Clearly, it is difficult to change one of these factors without changing another. For example, many studies purporting to show an effect of volume fail to change the concentration of local anaesthetic, with a consequent increase in the dose administered.

When the effect of volume (up to 14 ml) is isolated from other factors, most studies suggest there is no significant influence on mean spread although very low volume injections (1.5-2 ml) may reduce mean spread.

Similar basic concerns apply to studies of the effects of different doses: a change in dose will be accompanied by a change in either volume or concentration. Some studies, designed to control for changes in the other factors, have shown that increased dose is associated with increased spread, and others that there is no difference. What really needs to be appreciated is the scale of the effect. If no drug is injected there will be no effect, and a massive overdose (eg accidental intrathecal injection during epidural block) will produce a total spinal, but there is not a straight-line relationship in between. Within the range of doses normally used, a 50% increase in the dose injected will result in an increase of mean spread of only a dermatome or so. Such differences may, on occasion, be statistically significant, but are rarely clinically so, although the increase in duration associated with a larger dose is.

Do you think the temperature of the injectate makes a difference to the spread?

How does temperature affect the density of a solution?

Temperature of the solution

Both CSF and local anesthetics exhibit a curvilinear decrease in density with increasing temperature. Cerebrospinal fluid is at core body temperature whereas local anaesthetic solutions are administered at room temperature. There will be some local decrease in CSF temperature (2–3°C with a 2.7 ml bolus, 6–8°C with a 12ml bolus) immediately after injection but the core figure is restored within 2min, so solution density should be reported at body temperature. The consequences of temperature effects are most relevant with plain solutions, 0.5% bupivacaine, for example, being slightly hyperbaric at 24°C (density 1.0032kg m-3), but slightly hypobaric at 37°C (density 0.9984kg m-3). Even such minor differences in baricity can cause completely opposite distribution patterns, and may also account for the large variability in the spread of plain bupivacaine when injected at 'room' (which may vary considerably) temperature.

Viscosity

This factor has received little attention, but addition of glucose to an aqueous solution affects viscosity as well as density. The more viscous solutions produce significantly greater mean spread than the others. Plain solutions are considerably less viscous than those containing glucose, which may be less miscible with CSF. The injected bolus of hyperbaric solution may thus spread further before mixing fully with CSF, but producing a more 'even' distribution as it does so.

Other drugs can be added to the spinal anaesthetic solution to modify the block. What effect do you think this would have on the spread?

Local anaesthetic drug and additives

The extent of intrathecal spread is not altered by which local anaesthetic is used, as long as the other factors are controlled. Solutions containing vasoconstrictors spread in exactly the same way as those without, although block duration may be prolonged. Addition of other drugs, such as opioids or clonidine, has a dual effect. Density is reduced which could make the mixture behave in a more hypobaric manner, but no effect has been shown in clinical practice, suggesting that the changes in density are small. The second effect is seen with opioids, which increase mean spread and delay regression, presumably due to pharmacological enhancement of sub-clinical block. Alkalinisation of the solution does not increase spread, but does prolong duration.

How do you think patient posture would affect spread?

Clinical Technique

Patient position

The difference between the densities of CSF and the solution injected has a major effect on intrathecal drug spread. This is the result of the action of gravity; hyperbaric solutions 'sinking' and hypobaric ones 'floating', so the degree of caudad or cephalad spread will depend on the interplay between density and patient position. This interplay is the major determinant of the final extent of block with most techniques.

It is widely believed that injection of a hyperbaric solution in a seated patient will result in a more restricted block. However the block, while initially more restricted, eventually extends to a level equivalent to that which would have been obtained had the patient been placed supine immediately after injection. Production of a classical 'saddle block' requires use of relatively small amounts of local anaesthetic in a patient kept in the sitting position for at least 10 minutes. This will restrict the local anaesthetic to the sacral side of the lumbar lordosis when the supine position is resumed. If larger volumes are used, they will still 'spill over' into the higher lumbar and thoracic segments spreading higher up.

Given that most plain solutions are marginally hypobaric, some cephalad extension of block might be expected if patients are kept seated after injection. This will result in an adequate block, but has two disadvantages; delay while the block spreads and the risk of serious hypotension due to venous pooling in the legs as the local anaesthetic reaches and blocks the sympathetic outflow.

When using hyperbaric solutions tilt is sometimes used to influence spread, usually in an attempt to limit the cephalad spread and reduce the risk of hypotension. The maintenance of 10° or so of head-up tilt reduces spread, but also has two potentially adverse effects; the block may not spread far enough for the projected surgery and the risk of peripheral pooling of venous blood causing serious hypotension. In fact, every authority on spinal anaesthesia from the time of Labat has recommended the reverse; a small degree of head down tilt to ensure venous return so as to maintain cardiac output and blood pressure. This manoeuvre does not increase the cephalad spread of a hyperbaric solution; due to the curves of the spine, (see later) particularly the posterior thoracic curve in the supine position. Even a 30° tilt has minimal effect on mean spread, although it does increase variability.

An alternative technique for minimizing sympathetic block is to keep the patient in the lateral position after injection so that only one side of the sympathetic chain is affected. As with 'saddle block', a small volume of local anaesthetic needs to be used and the position maintained for at least 15-20 minutes for any significant effect. Even then, the block will still tend to spread to the other side once the patient is placed supine for surgery.

Placing the patient in the lithotomy position immediately after the injection of a hyperbaric solution might be expected to limit cephalad spread by abolishing the lumbosacral curve, the 'slope' down which the local anaesthetic moves under the influence of gravity. However, this has not been shown to have an effect on spread, perhaps because even the most extreme positioning does not abolish the curve altogether. The cardiovascular effects are less, probably from the beneficial effects of leg elevation on venous return.

In most circumstances, intrathecal local anaesthetic stops spreading about 20-25 minutes after injection. However, marked changes in patient posture, up to 2 hours after injection, can lead to significant changes in extent of the block. The effect is independent of solution baricity, and probably represents bulk movement of CSF still containing significant concentrations of local anaesthetic. All patient movements should be slow and progressive until the block has regressed completely.

Level of injection

Studies with plain solutions of bupivacaine have shown that a higher level of injection results in significantly greater cephalad spread, even when the difference in injection level is only one interspace. Hyperbaric solutions have a more predictable spread, the effect of gravity being the more dominant factor.

Needle type and alignment

Different types of needle bevel impart varying degrees of 'directionality' to the flow of drug solution into the CSF. For instance, fluid leaves the Whitacre needle at an angle of 55° to its plane, and this has been used to promote unilateral block. However, there is conflicting evidence regarding the effect of cephalad orientation of the orifice. With plain solutions, cephalad orientation of the Sprotte needle produces a block of faster onset, but to the same mean level, whereas similar alignment of the Whitacre produces greater spread with less variability. The orientation of the orifice does not seem to influence the spread of hyperbaric solutions. Again this may reflect the over-riding effect of density/gravity with these preparations.

Fluid currents

Currents generated within the CSF by fluid injection are an obvious cause of spread. Many factors might affect the formation of these currents, notably the size, shape and orientation of the bevel and the speed of injection. It is widely thought that barbotage, the intentional creation of such currents by the repeated aspiration and re-injection of CSF and local anaesthetic, increases spread, but evidence does not confirm this. Simply varying the speed of injection has been investigated extensively, but with conflicting

results. In general, faster injections produce greater spread with plain solutions, but the effect is less marked with hyperbaric ones, with some suggestion that slower injection actually produces greater spread. Glass models of the spinal cord are often used to study such factors, but they omit any representation of the cauda equina and spinal cord, which may act as efficient 'baffles' to the generation of fluid currents. Additionally, a fast injection may produce a bulk movement of CSF and pressure changes, which tend to keep the solution near the injection site, whereas a slow injection may allow the solution to spread according to baricity and gravity.

> ***Practical Point:*** The best injection technique depends upon the desired block. In general, it is best to use a slow injection over at least 15 seconds, without barbotage, of a hyperbaric solution which is more controllable and predictable. I usually have the patient sat up as it is easier to identify landmarks, then lie them down immediately after the injection. Testing the block early (5mins and 10mins) can give an idea of how quickly the block is likely to spread. This will often also give an idea of the extent to which it will spread (rapidly spreading block will often reach more segments than a slower spreading block). Head down or head up tilt can then be used to modify the block to a small degree.

Patient characteristics

Although there is significant variation in maximum spread between patients given a standard technique, spinal anaesthesia is very reproducible in the individual patient. Clearly, the variability must be due to patient factors, but it is far from clear which is the most significant.

Age

At the extremes of age there are small, but significant increases in maximum spread, rate of onset of motor block, and cardiovascular instability regardless of the solution used. It is probable that these are secondary to age related changes in spinal anatomy, nerve physiology and cardiovascular reflexes.

Height

No firm correlation between height and spread has been found – this is probably since most of the difference in height between adults is due to the length of the lower limb long bones, not the spine.

Weight

It is often suggested that epidural fat compresses the dural sac, reduces CSF volume and results in the increased spread observed in obese patients. However, these studies used plain solutions, which are known to produce wider variability in block height, and studies with hyperbaric solutions have failed to show a significant relationship. In addition, it is recognized that the level of injection in obese patients is often higher than intended, and this can result in greater cephalad spread. Finally, when an obese patient is lying in the lateral position, the distribution of adipose tissue may alter the alignment of the vertebral canal. There are no data available which have controlled these variables in an attempt to determine if weight per se has any influence on local anaesthetic spread.

Sex

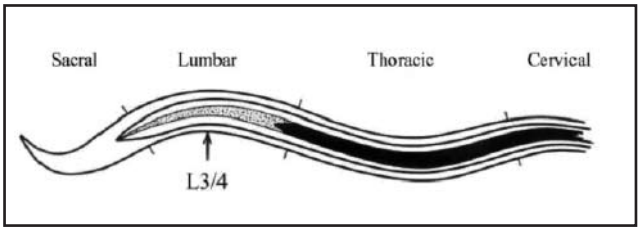
The spread of hyperbaric solutions may be influenced by differences in body shape while the patient is in the lateral position. Males tend to have broader shoulders than hips so that the spinal column has a 'head up' tilt in the lateral position, whereas the reverse is true in females. However, patients are usually turned supine immediately after injection so this effect is likely to be small. Differences in CSF density may be more relevant. This is higher in males, and will reduce the baricity of the local anaesthetic solution, thereby limiting cephalad spread.

Intra-abdominal pressure

It is often said that raised intra-abdominal pressure increases blood flow through the epidural veins, which then distend and compress the theca to decrease CSF volume. However, this theory was not entirely supported by an MRI study which found that increased abdominal pressure decreased CSF volume by displacing tissue into the vertebral canal through the intervertebral foraminae rather than by changing epidural venous volume. A reduction in CSF volume may influence cephalad spread of local anaesthetic, but no study has distinguished this effect from other causes.

Spinal anatomy

Variations in spinal curvature are only of importance when they influence the gravitational spread of local anaesthetic solutions. Consequently, a scoliosis is unlikely to influence spread unless the patient is kept in the lateral position. A kyphosis, or a change in the normal lumbar lordosis (e.g. in pregnancy), is more likely to have an effect because the antero-posterior curves are crucial to the pattern of spread of a hyperbaric solution in the supine patient. Abnormal spinal curvature can be a cause of block failure, particularly if it moves the 'highest' point of the lumbar spine in the supine position from its usual level of L4. The picture shows the curves of the spine in a supine patient.



Lumbosacral CSF volume

Total CSF volume in an average adult is about 150ml, approximately half of which is intracranial. The

remainder lies within the spinal subarachnoid space, and represents the volume through which the injected solution can distribute. While many factors influence CSF volume, and it may have a crucial effect on intrathecal drug spread, detailed study is, unfortunately, inhibited by the difficulties of measuring CSF volume, even with radiological imaging.

Pregnancy

Many physiological changes that occur during pregnancy increase the effect of intrathecal anaesthetic injection. Physical spread of the solution can be increased by changes in the lumbar lordosis, and in the volume and density of the CSF. Cephalad spread may be greater due to a progesterone mediated increase in neuronal sensitivity, The mechanisms which may be involved include direct effects on membrane excitability, indirect actions on neurotransmitters, increased permeability of the neural sheath, potentiation of endogenous opioids, and potentiation of GABA-mediated increases in chloride conductance. These physical and pharmacological factors add up to a considerable increase in the consequences of an intrathecal injection in the full term pregnant patient.

Summary

Many factors affect the intrathecal spread of injected local anaesthetics, however, the influence of most of these is small, unpredictable and outside the clinician's control. The major factors are the baricity of the solution injected and the subsequent posture of the patient. The most predictable effects are produced by the slow injection (into a patient placed supine immediately thereafter) of a small volume of local anaesthetic solution containing glucose. Use of glucose concentrations somewhat lower (about 1%) than are traditional (5-8%), will reduce the risk of excessive spread, but still ensure good quality and extent of block for most surgical procedures for which spinal anaesthesia is appropriate. Manipulation of the factors which affect spread may be used to produce different types of block, as long as the clinician has a clear understanding of what is involved.

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POST DURAL PUNCTURE HEADACHE

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Introduction

Post dural puncture headache (PDPH) was first reported just over one hundred years ago. PDPH has the potential to cause considerable morbidity and is a complication that should not to be treated lightly. PDPH is usually a self-limiting process. If left untreated, 75% resolve within the first week and 88% resolve by 6 weeks. Most treatments are geared towards lessening the pain and symptoms until the hole in the dura can heal, or at least until it can close to the point where the symptoms are tolerable. PDPH continues to be a common morbidity despite several innovations in equipment and techniques used for spinal (subarachnoid) and epidural (extradural) anaesthesia.

Pathophysiology of PDPH

CSF leaking from a dural puncture leads to a loss of cerebrospinal fluid (CSF) pressure around the spinal cord and a loss of buoyancy supporting the brain. When the patient assumes an upright posture, the brain sags and tension on the meninges and other intracranial structures creates the pain seen with PDPH. This explanation is probably overly simplified. Much of the pain in a PDPH may be related to vascular distension - as the body assumes a vertical posture, the hydrostatic gradient across the brain increases forcing more CSF to exit the dural puncture. The body then attempts to compensate for the loss of intracranial volume by vasodilatation. This process is reversed when the patient returns to the supine position.

Prevention of PDPH

Anaesthetists have been active in attempting to reduce the incidence of post-spinal headache by reducing the size of the spinal needle. The quoted incidences are about 40% with a 22G needle, 25% with a 25G needle, 2%–12% with a 26G Quincke needle, and <2% with a 29G needle.[1-4] In 1951, Whitacre and Hart introduced the 'atraumatic' spinal needle . This design offered the handling characteristics of larger needles with a low incidence of post-spinal headache. Needle modifications since that time, such as the Sprotte and Atraucan needles, promise further reductions in post-spinal headache.

In parturients receiving epidural anaesthesia, the incidence of dural puncture is between 0 and 2.6%.[5] The incidence is inversely related to the experience of the anaesthetist and is said to be reduced by orientation of the needle bevel parallel to the dural fibres.[6] Loss of resistance to air confers a higher risk of dural puncture than loss of resistance to fluid.[7] After a dural puncture with a 16G Tuohy needle, up to 70% of subjects will report symptoms related to low CSF pressure.[8]

Onset

Headache and backache are the dominant symptoms that develop after a deliberate or accidental dural puncture. 66% of headaches start within the first 48 hrs and 99% occur within 3 days of the procedure. Headache may present immediately after dural puncture or may rarely develop between 5 and 14 days after the procedure.

Symptoms

Headache is the predominant presenting complaint. The so-called *spinal headache* is usually described as a severe, dull, non-throbbing pain, usually fronto-occipital, which is aggravated in the upright position and diminished in the supine position. It may be accompanied by nausea, vomiting, visual disturbances or auditory disturbances and is exacerbated by head movement. The postural headache is so characteristic that in its absence the diagnosis of post-dural puncture headache should be questioned and other serious intracranial causes for headache must be excluded.

Differential diagnosis

Diagnoses that may masquerade as post dural puncture headache include intracranial tumours, intracranial haematoma, pituitary apoplexy, cerebral venous thrombosis, migraine, chemical or infective meningitis, cerebral malaria and non-specific headache. It has been estimated that 39% of parturients report symptoms of a headache, unrelated to dural puncture, following delivery.

CLINICAL SCENARIO

A 30-year-old primigravida woman had spinal anaesthesia for an elective caesarean section. She had uneventful surgery and had a healthy baby boy. Unfortunately on day 2 post delivery she developed a fronto-occipital headache with postural characteristics. She was bed-bound and had associated nausea, vomiting and photophobia.

How would you manage this patient?

Conservative non-invasive methods

- *Bed rest*

Recent literature provides evidence against this.[9] Bed rest after dural puncture does not reduce the risk of PDPH occurring. Early ambulation after dural puncture is advisable and patients who have already developed PDPH should also be encouraged to ambulate as much as they can tolerate.

- *Position*

If a patient develops a headache, they should be encouraged to lie in a comfortable position. There is no clinical evidence to support the maintenance of the supine position before or after the onset of the headache as a means of treatment. The prone position has been advocated, but it is not a comfortable position for the post-partum patient. The prone position raises the intra-abdominal pressure, which is transmitted to the epidural space and may alleviate the headache. A clinical trial of the prone position following dural puncture failed to demonstrate a reduction in post-dural puncture headache.[10]

- *Hydration status*

There is no evidence to show that over hydration reduces incidence and severity of PDPH, but it is important to maintain hydration in balance.

- *Abdominal binder*

A tight abdominal binder raises the intra-abdominal pressure which is transmitted to the epidural space and may relieve the headache. Unfortunately, tight binders are uncomfortable and are seldom used in current practice.

- *Analgesics*

Paracetamol, non-steroidal anti-inflammatory drugs, opioids, and antiemetics may control the symptoms and so reduce the need for more interventional therapy, but do not provide complete relief.

- *Caffeine*

Caffeine is a central nervous system stimulant that, amongst other properties, produces cerebral vasoconstriction and it has been demonstrated to cause an transient reduction in cerebral blood flow. Sechzer et al evaluated the effects of one or two 0.5g doses of IV caffeine on subjects with established post-dural puncture headache.[11,12] There are some statistical and methodological flaws in his study, but it was concluded that IV caffeine is an effective therapy for PDPH. The dose now recommended for the treatment of PDPH is 300–500mg of oral or intravenous caffeine once or twice daily. One cup of coffee contains about 50–100mg of caffeine, a cup of black tea 60-90mg and soft drinks contain 35–50mg.

Invasive methods

- *Epidural blood patch*

The concept of the epidural blood patch was developed after the observation that 'bloody taps' were associated with a reduced headache rate. The theory is that the blood, introduced into the epidural space, will clot and occlude the perforation, preventing further CSF leak. The high success rate and the low incidence of complications have established the epidural blood patch as the best available treatment of this condition.

Technique

The presence of fever, infection on the back, coagulopathy, or patient refusal are contraindications to the performance of an epidural blood patch. Limited experience with HIV-positive patients suggest that it is acceptable providing no other bacterial or viral illnesses are active.[13]

Under strict sterile conditions, with the patient in the lateral position, the epidural space is located with a Tuohy needle at the level of the dural puncture or an intervertebral space lower. Up to 30ml blood is then taken from the patient's arm and injected slowly through the Tuohy needle. This process may be easiest using two clinicians. There is no consensus as to the most effective volume of blood required. Around 20 ml blood appears most likely to guarantee success, but the injection should be ceased if lower back pain or difficulty to inject occurs. At the conclusion of the procedure, the patient is asked to lie still for 1 or 2hrs, and is then allowed to mobilise.

Risks

Epidural blood patch carries risks of transient paraesthesia, radicular pain, repeated inadvertent dural puncture and epidural infection.

Outcome

The technique has a success rate of 70–98% if carried out more than 24h after the dural puncture.[14] If an epidural blood patch fails to resolve the headache, repeating the blood patch has a similar success rate. However in the presence of persistent severe headache, an alternative cause should be considered. The beneficial effects of earlier studies into this technique may have been overstated.

Conclusion

The evidence base for some therapies used for treatment of PDPH is weak. The benefit of prophylactic blood patching is not so clear but deserves consideration in the parturient with a headache after accidental dural perforation with a Tuohy needle. Epidural blood patch will be ineffective in treating the headache of a certain proportion of patients and it is wise to consider other causes of the headache and use simple conservative measures to alleviate the symptoms, before applying alternative therapeutic options.

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INVASIVE BLOOD PRESSURE MONITORING

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Introduction

Invasive (intra-arterial) blood pressure (IBP) monitoring is a commonly used technique in the Intensive Care Unit (ICU) and is also often used in the operating theatre. The technique involves the insertion of a catheter into a suitable artery and then displaying the measured pressure wave on a monitor. The most common reason for using intra-arterial blood pressure monitoring is to gain a 'beat-to-beat' record of a patient's blood pressure.

Advantages of IBP monitoring

- Continuous 'beat-to-beat' blood pressure monitoring is useful in patients who are likely to display sudden changes in blood pressure (e.g. vascular surgery), in whom close control of blood pressure is required (e.g. head injured patients), or in patients receiving drugs to maintain the blood pressure (e.g. patients receiving inotropes such as epinephrine).
- The technique allows accurate blood pressure readings at low pressures, for example in shocked patients.
- The trauma of repeated cuff inflations is avoided in patients who are likely to need close blood pressure monitoring for a long period of time e.g. ICU patients.
- Intravascular volume status can be estimated from the shape of the arterial pressure trace, either by eye or by waveform analysis by a specific device e.g. a pulse contour analysis system.
- IBP measurement allows accurate assessment of blood pressure in certain patients not suitable for non-invasive blood pressure monitoring, e.g. patients with gross peripheral oedema in ICU or morbidly obese patients.
- The indwelling arterial cannula is convenient for repeated arterial blood sampling, for instance for arterial blood gases. This is not usually the sole reason for insertion of an indwelling arterial catheter.

Disadvantages of IBP monitoring

- The arterial cannula is a potential focus of infection, although arterial lines become infected far less frequently than venous lines, especially central venous lines.
- The arterial catheter can lead to local thrombosis which may result in emboli travelling down the limb or occasionally arterial occlusion – this is rare if the catheter is kept flushed with saline and an appropriate vessel is chosen. The radial, femoral and axillary arteries are commonly used, as are the arteries of the foot, the posterior tibial and dorsalis pedis arteries. Where possible, the brachial artery should be avoided as this is an end artery and has no collateral supply – occlusion of the brachial artery will result in loss of blood supply to the arm.
- Any drug inadvertently administered into the arterial line may form crystals and cause catastrophic ischaemia of the limb. Examples of drugs with which this has been reported are thiopentone and antibiotics. All arterial lines should be clearly labelled and the tubing colour coded (usually with a red stripe) to avoid confusion and drugs should **never** be administered via the arterial line.
- The insertion of an intra-arterial blood pressure monitoring system can be difficult and time consuming, especially in shocked patients. This can potentially distract from other problems that need more urgent attention.
- The monitoring equipment, spare parts and cannulae are expensive when compared to non invasive methods of blood pressure monitoring.
- The arterial monitor requires an electrical supply which will limit its usefulness in some settings.

Components and principles of IBP monitoring

The components of an intra-arterial monitoring system can be considered in three main parts (see Figure 1):

1. the measuring apparatus
2. the transducer
3. the monitor

The measuring apparatus

The measuring apparatus consists of an arterial cannula (20G in adults and 22G in children) connected to tubing containing a continuous column of saline which conducts the pressure wave to the transducer. The arterial line is also connected to a flushing system consisting of a 500ml bag of saline pressurised to 300 mmHg via a flushing device. Formerly 500IU heparin was added to this fluid, but many centres now consider this to be unnecessary. The flush system provides a slow but continual flushing of the system at a rate of approximately 4-5ml per hour. A rapid flush can be delivered by manually opening the flush valve. There is also usually a 3-way tap to allow for arterial blood

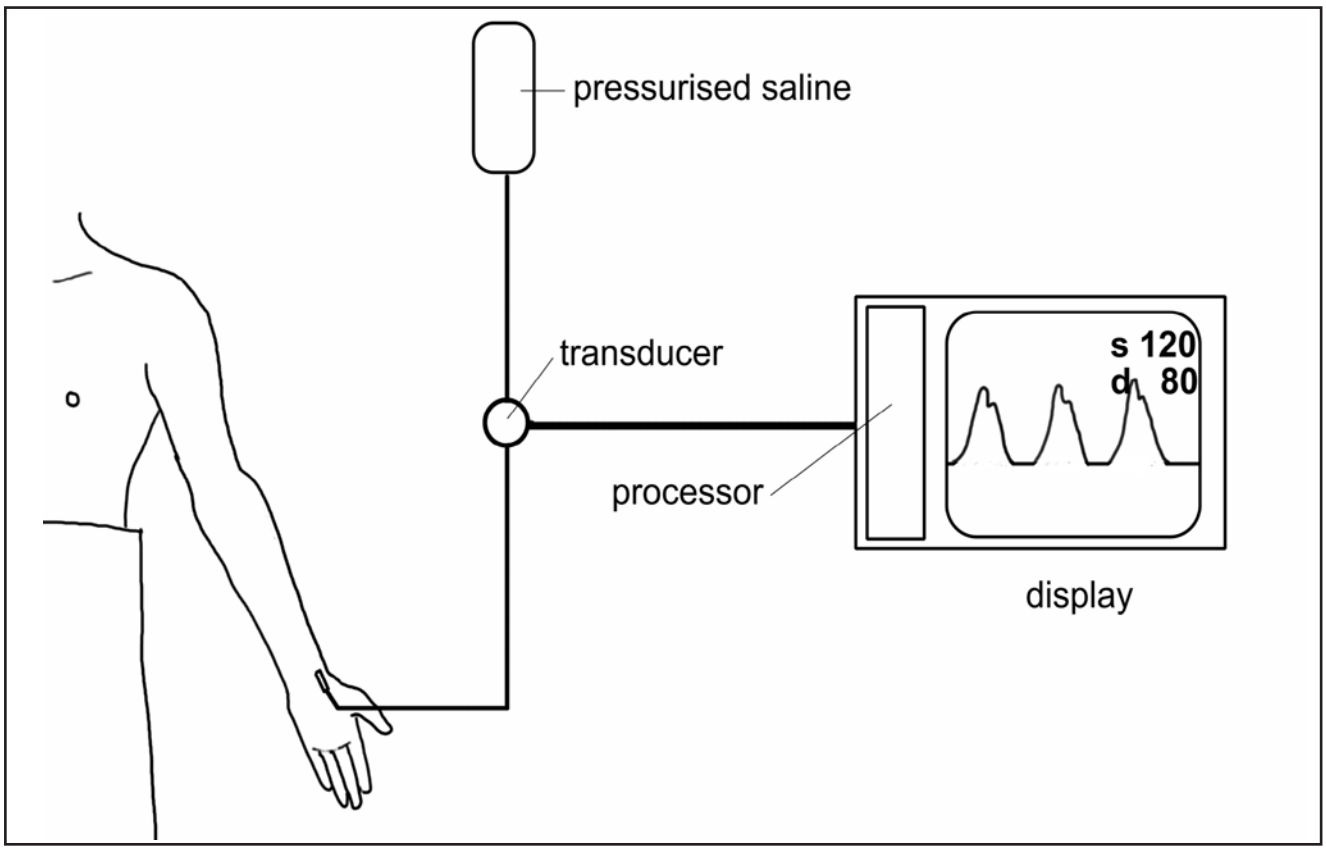


Figure 1: Components of an arterial monitoring system

sampling and the ejection of air from the system if necessary. The three-way tap must also be **clearly labelled** as arterial, to minimise the risk of inadvertent intra-arterial injection of drugs. For small children a smaller volume of flush is administered via a syringe driver, so that it is not possible to over-administer fluid by repeated flushing of the arterial cannula.

The transducer

A transducer is any device that converts one form of energy to another – for example, the larynx is a type of physiological transducer (air flow is converted to sound). The output of transducers is usually in the form of electrical energy. In the case of intra-arterial monitoring the transducer consists of a flexible diaphragm with an electric current applied across it. As pressure is applied to the diaphragm it stretches and its resistance changes, altering the electrical output from the system. The transducers used are differential pressure transducers and so must be calibrated relative to atmospheric pressure before use.

The monitor

It is not necessary for the anaesthetist to have an in-depth understanding of the internal workings of the monitor. Modern monitors **amplify** the input signal; amplification makes the signal stronger. They also **filter** the 'noise' from the signal – unwanted background signal is removed with an electronic filter - and display the arterial waveform in 'real time' on a screen. They also give a digital display of systolic, diastolic and mean blood pressure (see figure 2). Most monitors incorporate various safety features such as high and low mean blood pressure alarms and tachycardia and bradycardia alerts.

Accuracy of IBP monitoring

The accuracy of intra-arterial monitoring is affected by several important physical principles - the *oscillation, natural frequency, damping* and *resonance* of the system

Oscillation

A swinging pendulum is an example of a system that oscillates. When a pendulum is pushed (energy is put into the system), it moves away from its resting position, then returns to it. The resting position for a pendulum is at the bottom of its arc of swing and is dictated by gravity. However, the pendulum doesn't usually just return to the resting position, but tends to overshoot, swinging past the resting point in the opposite direction to the original push. This cycle continues until all the energy put into the system has been dissipated. The tendency of a system to move either side of set point is referred to as its tendency to **oscillate**.

Damping

Imagine you have two identical pendulums. One has recently been well greased at its point of rotation (fulcrum) and the other is stiff from rust. When an equal sized force is applied to each, the well greased one will oscillate freely around the set point but the

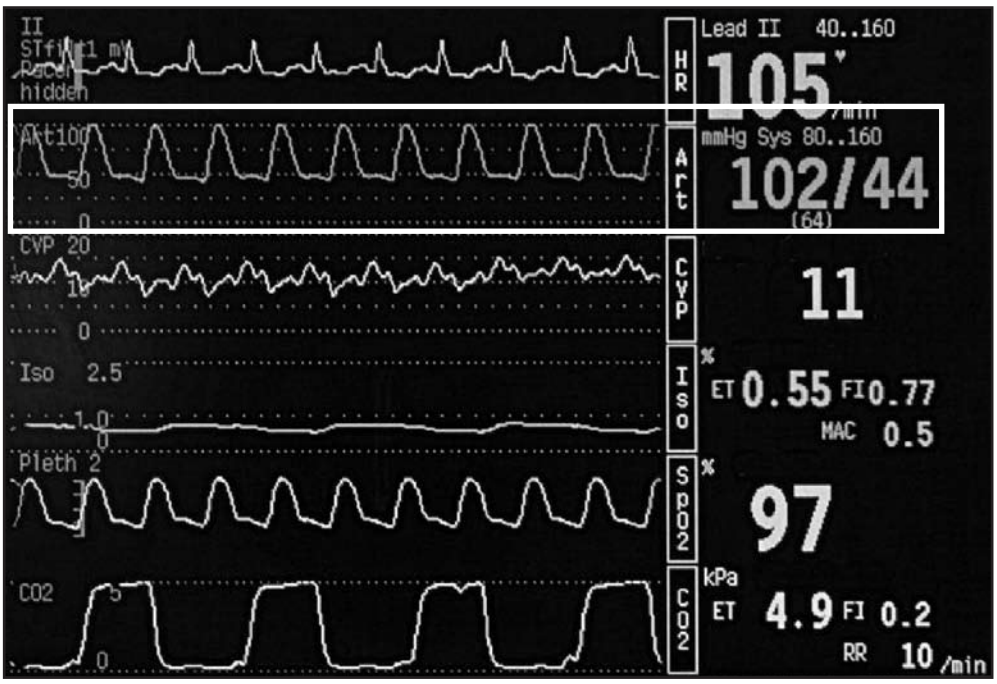


Figure 2: Invasive blood pressure monitoring (boxed). The waveforms are usually colour coded (red for the arterial trace) and the monitor displays the systolic/diastolic BP, with the mean arterial BP in brackets below.

old rusty pendulum may barely move. This is because much of the energy put into the system will be used up or 'damped' in overcoming the frictional force of the rusty axis. The rusty pendulum will tend to oscillate at smaller amplitude (i.e smaller swings) and for a shorter period of time than the well greased one. How freely a system oscillates following an input of energy is dependant on the degree of **damping** in the system.

A 'well damped' system tends not to oscillate freely whereas a 'poorly damped' system may oscillate wildly. The amount of damping inherent in a system can be described by the **damping coefficient (D)** which usually lies between 0 and 1 (but can be greater than 1). A system with a D value greater than 1 describes a system that is over-damped, will not oscillate freely, that takes a long time to initially move away from and to return to its resting point, but does not oscillate (a high friction pendulum). A D value less than 1 and approaching 0 describes a system that is under-damped, that oscillates freely, moving rapidly away from its resting point and back again, but tends to overshoot and then oscillate around the resting point (a low friction pendulum). A D value of exactly 1 is known as **critical damping.**

Oscillations are un-desirable in physiological measuring systems. These systems require accurate measurement of a maximum amplitude (for instance, that caused by the arterial pulsation, the systolic blood pressure), with a rapid response time and rapid return to the set point, ready for the next measurement. The ideal level of damping applied to a measuring system is a compromise between achieving a rapid response time and accurate reflection of maximum amplitude by designing a system with D close to 0, and needing a system that returns to the resting point without excess oscillation (D around 1). In the case of an IBP monitoring system this would represent the difference between using very compliant measuring apparatus (compliant catheters, tubing) i.e. D approaches 0, and very stiff or non-compliant equipment i.e. D is closer to 1. The value of D chosen for physiological measuring systems such as IBP monitoring equipment lies between 0.6 and 0.7 – it is known as **optimal damping** (see Figure 3).

Natural frequency and resonance

A pendulum of set length and with a set weight at the end will always oscillate at exactly the same frequency, no matter what the initial starting point of the oscillation. In other words, whether you give the pendulum a small push or a really hard shove it will make the same number of oscillations per unit time (although the amplitude of the oscillations will differ). This is why pendulums can be used to keep time. Any system such as this will have a frequency at which it 'naturally' oscillates. This frequency is known as the **natural frequency**.

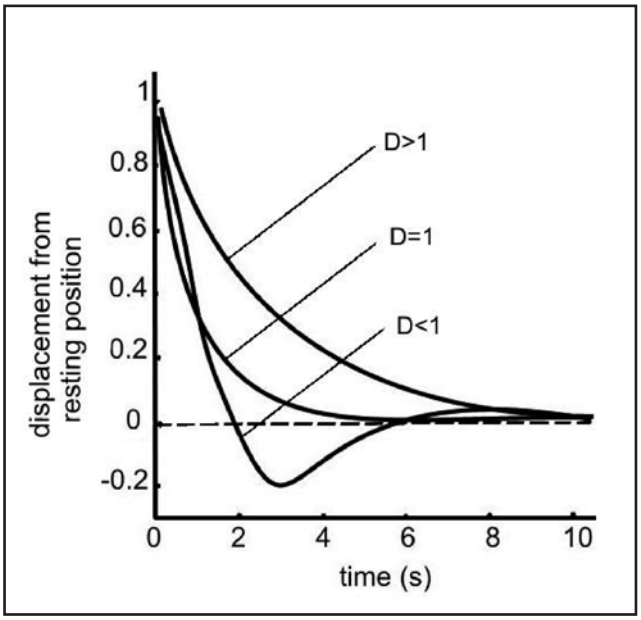


Figure 3: Graph showing the effect of different levels of damping on the oscillation of a measuring system

If the input of energy into a system is occurring at the same frequency (or close to) the natural frequency, a phenomenon called **resonance** occurs and the output amplitude of the oscillations is greatly magnified. In the case of intra-arterial blood pressure monitoring this could lead to over-reading of the systolic blood pressure. Arterial pulsation is a complex sine wave and is composed of many individual sine waves. It is therefore important that the natural frequency of the measuring equipment (the catheter and column of saline etc) does not correspond to any of the component frequencies of the arterial pulsation input. This is achieved by making sure that the natural frequency of the measuring system is raised above any of the component frequencies of the arterial sine waveform.

The characteristics of the measuring equipment that will ensure that the natural frequency of the system is higher than that of the arterial pulsation are:

- Arterial catheter must be short and with the maximum gauge possible
- Column of saline must be as short as possible
- The catheter and tubing must be stiff walled
- The transducer diaphragm must be a rigid as possible

Setting up the arterial line and trouble shooting

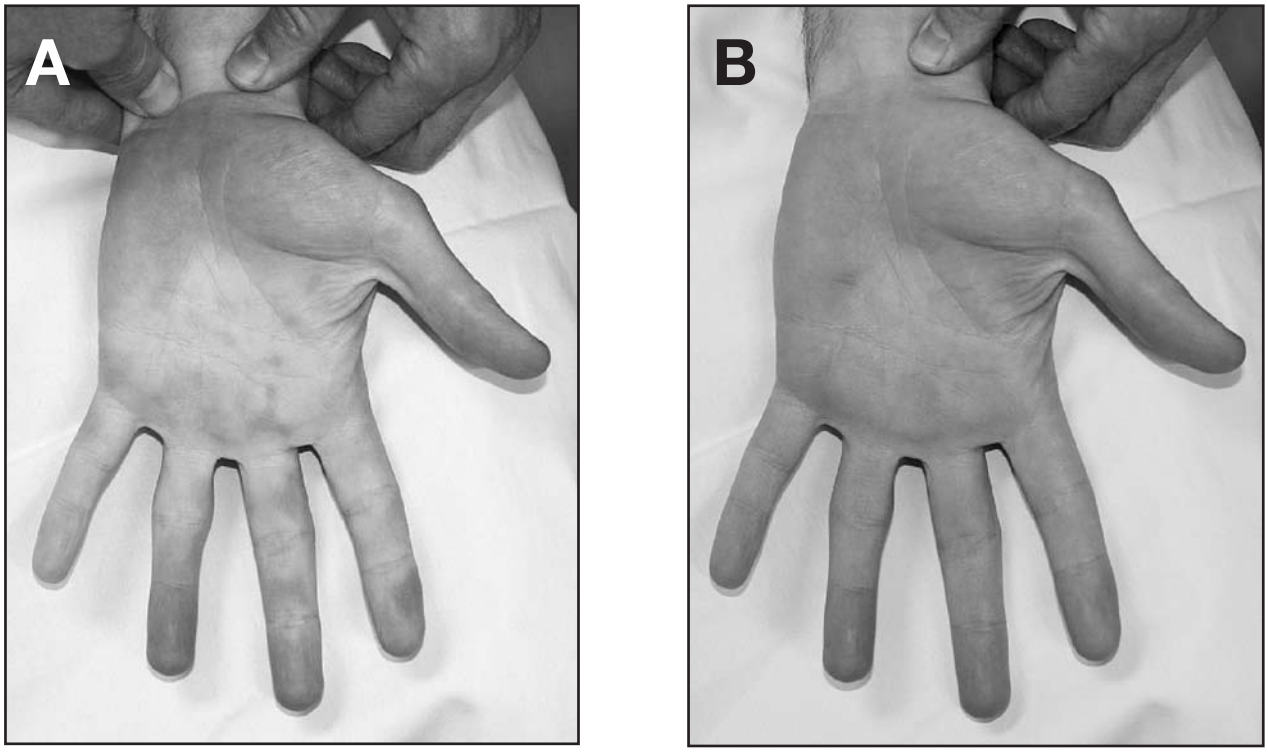
The usual location for insertion of the arterial catheter is the radial artery. The advantage of the radial artery is that it is superficial, easily accessible, and there is a collateral blood supply to the hand from the ulnar artery. It is advisable to perform **Allen's test** to detect adequacy of collateral supply to the hand via the ulnar artery, although the test is not infallible and can only be performed in conscious patients (see figure 4).

The brachial artery should be avoided if at all possible (no collateral supply); the femoral artery, the ulnar artery, arteries of the foot and ankle, and even the axillary artery should be used in preference if necessary. Whichever location of artery is used, the distal limb should be monitored regularly for signs of emboli or distal ischaemia.

Insertion of a radial arterial line

This should be performed as an aseptic technique. The wrist should be cleaned with alcoholic chlorhexidine solution prior to cannulation and in conscious patients the skin should be infiltrated with 1% plain lignocaine. The arm should be abducted in the anatomical position and the wrist should be hyper-extended to aid cannulation (the radial artery is brought closer to the skin surface and the hand moved out of the way). This is most conveniently done by an assistant. If an assistant is not available use tape to secure the patients hand fingers extended over a bag of fluid (see figure 5).

There are various types of stiff, short arterial catheter available. Some feature a simple cannula over needle design similar to an intravenous cannula and some incorporate a guide-wire as part of a Seldinger technique – the needle is inserted, a wire passed through the centre if the needle, the cannula threaded over the wire. The correct cannula to use is the type



Figures 4A and 4B: Allen's test. Ask the patient to make a fist, use your thumbs to occlude the patient's radial and ulnar arteries. Ask the patient to unclench their fist – the palm will remain pale (A), whilst the blood supply is still occluded. When you remove the thumb that is occluding the ulnar artery, the palm will flush red if the ulnar artery is functional (B).

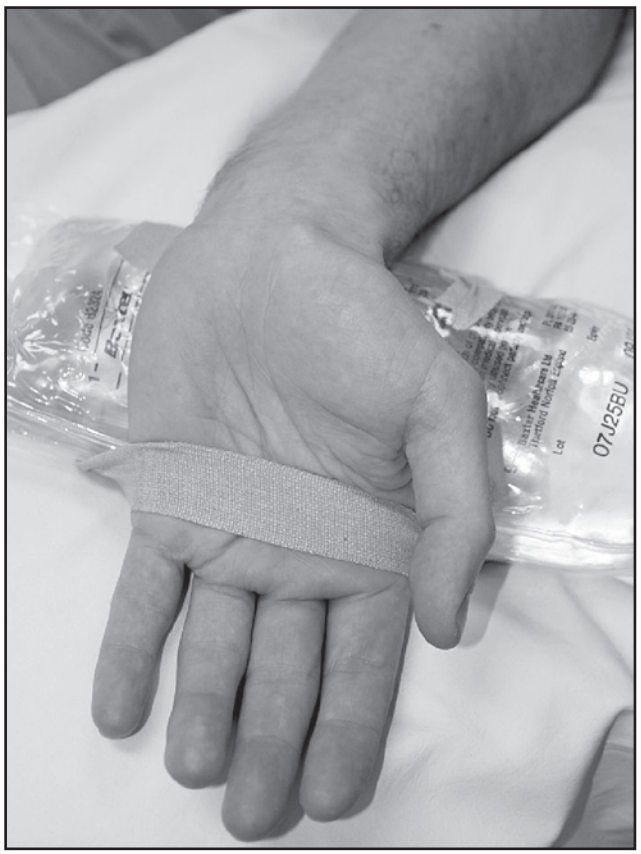


Figure 5: A technique for securing the patient's wrist extended using adhesive tape and a fluid bag.

with which you are most comfortable. Ideally a cannula with injection port should not be used as this may be confused with an intravenous cannula - if such a cannula is used, the injection port should be taped over and the cannula clearly labelled as arterial.

The usual insertion technique is to palpate the artery with the fingers of one hand and locate the artery with the cannula at an angle of about 30 degrees (figure 6A). For practical reasons the catheters are inserted against the flow of blood. Once a 'flashback' has been obtained the cannula should be brought level with the skin and then advanced 2-3mm further (figure 6B). This should ensure that the entire tip of the cannula, rather than just the needle is within the arterial lumen. At this stage either the cannula can be advanced over the needle or the guide-wire introduced. Make sure that you tape the cannula securely in position, and take care not to kink the cannula as you do so. Sometimes it is advisable to suture the arterial line in place.

The arterial catheter should be connected to the tubing, the transducer secured in a position approximately level with the heart and transducer 'zeroed' - that is, closed to the patient and opened to atmosphere to obtain a reading of atmospheric pressure. It is often convenient to tape the transducer to the patient's upper arm to ensure it is level with the heart.

Practical Tips and Trouble Shooting

- The radial artery is very superficial at the wrist. Often when you think you can't find it, you have in fact transfixed it (a technique some people use preferentially). Remove the needle and then slowly withdraw the cannula, aspirating using a 5ml syringe attached to the hub all the time. As the tip of the cannula re-enters the artery, blood will flow into the syringe briskly. From this point slowly advance the cannula whilst rotating the cannula in a twisting motion about its long axis. This technique will salvage the cannulation more often than not.
- If you hit the artery but fail to cannulate it a couple of times, it is often wise to move to the other wrist; the artery will go into spasm following repeated trauma making cannulation progressively more difficult.
- Inserting an arterial catheter in shocked patients is very difficult. Do not waste time making repeated attempts to do so; resuscitation of the patient is more important!

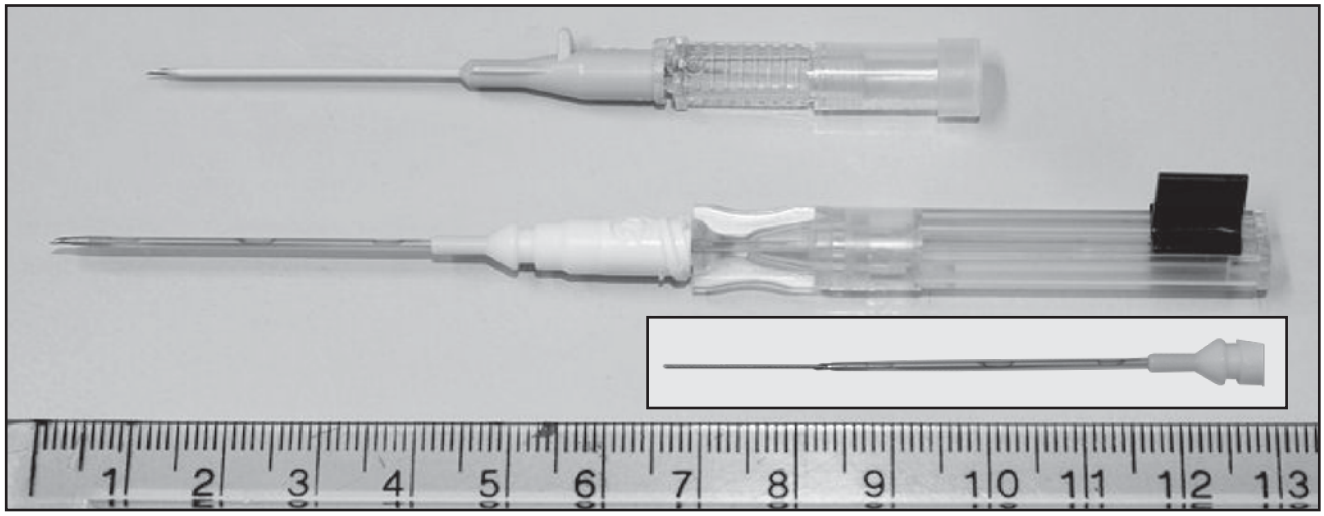
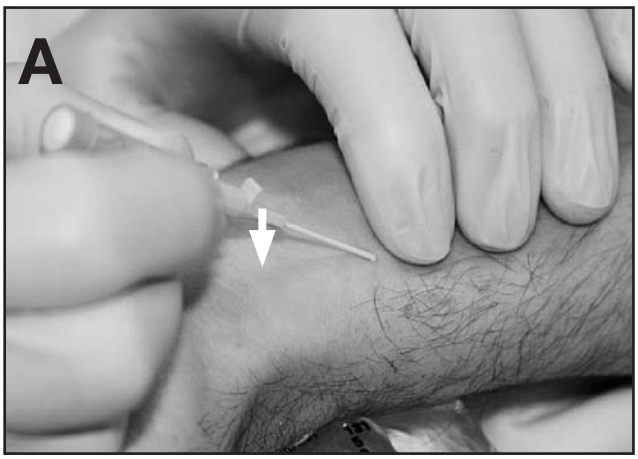
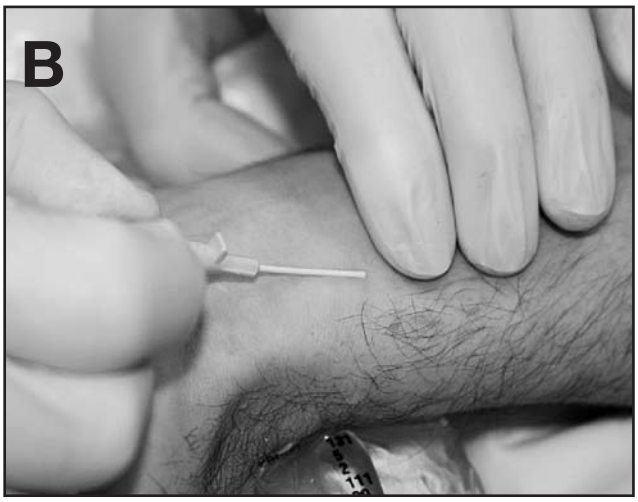


Figure 6: Two 20G arterial cannulae. The lower cannula has a guidewire that can be slid into the artery through the needle to allow smooth placement of the cannula (inset).





Figures 6a and 6b.: See text on page 40 for explanation of technique

- After attaching the catheter to the saline column take great care to ensure there are no air bubbles in the system before flushing it.
- If you suddenly obtain a very high blood pressure reading, check the position of the transducer; it may have fallen on the floor!
- If you lose the waveform on the monitor or it decreases in amplitude, the catheter may be kinked or blocked with a blood clot, or there may be an air bubble damping the trace. After checking that your patient has a pulse, you can try making sure the wrist is extended, aspirate any air bubbles and then flush the catheter, or withdraw the catheter slightly to check it is not kinked.
- Note that over or under-damped traces will give false blood pressure values. An under-damped trace will overestimate systolic pressure and underestimate diastolic pressure as the system 'over oscillates'. A low amplitude, over-damped trace will underestimate the systolic blood pressure and overestimate the diastolic blood pressure. Fortunately, the value for the mean arterial blood pressure is little affected and can usually be taken as accurate.

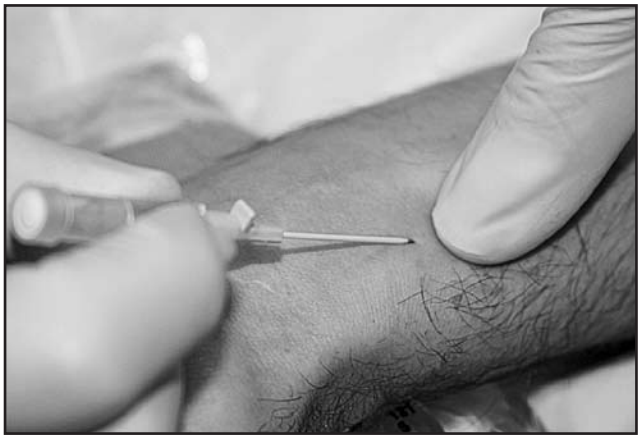


Figure 7: If location of the artery is difficult an alternative method involves positioning your thumb so that the radial pulse is running directly under the centre of your thumb. Then advance the cannula at 30 degrees under the centre point of your thumb.

Pulse Contour Analysis

Useful clinical information can be obtained by looking at the pattern of the arterial waveform on the monitor.

- A large 'swing' or variation in peak amplitude of the systolic pressure that coincides with the ventilatory cycle often indicates that the patient is hypovolaemic.
- Conscious patients who are in respiratory distress may also have a large swing on the arterial pressure trace, due to large swings in intrathoracic pressure.
- A narrow width, high amplitude pulse combined with tachycardia tends to indicate hypovolaemia.
- The angle of the upstroke of the arterial waveform may give an estimate of myocardial contractility; a steeper upstroke indicates greater change in pressure per unit time and higher myocardial contractility. In practice, this only provides a rough assessment of myocardial contractility.

Analysis of the arterial waveform has been developed mathematically to calculate cardiac output. The term 'pulse contour analysis' is usually used to refer to the cardiac output monitoring systems employed in the PiCCO™ (Pulsation Medical Systems, Germany) and LiDCO™ Plus (LiDCO Ltd, UK) monitors.

The PiCCO™ and LiDCO™ systems both measure cardiac output using both the shape and the area under the arterial pulsation curve. For both techniques a haemodilution method is used to calculate the cardiac output and calibrate the pulse contour analyser. Note that this means that both systems require central venous access. By knowing the exact shape and area under the arterial pulsation curve at the time of calibration, future arterial pulsation curves can be compared and the cardiac output at that point in time extrapolated.

The way in which these two systems calculate the initial cardiac output differs in that the PiCCO™ uses haemodilution of cold saline and the LiDCO™ uses haemodilution of lithium. The LiDCO™ cannot be used in patients on lithium therapy or for up to two hours following the administration of non-depolarizing muscle relaxants. Both systems need regular recalibration by re-measuring the cardiac output using haemodilution. All the factors previously mentioned that alter the accuracy of the arterial waveform (air bubbles, kinking etc) will affect the cardiac output value that the system gives. The two systems also alter in terms of the mathematical modelling they use to perform the pulse contour analysis. Further description of these techniques can be found in *Update 21*.

Summary
Invasive arterial monitoring is a highly useful tool, which allows close blood pressure monitoring for patients undergoing major surgery and the critically ill. It is also useful for repeated arterial blood gas analysis and as an access point for obtaining other blood samples. It is important to understand the principles of biological measurement systems in order to optimise their performance and allow trouble-shooting when performance is poor.

Further reading

• J S Gravenstein and David A Paulus. Clinical Monitoring in Practice (2nd edition). Published by J B Lippincott, Philadelphia, 1987

• M K Sykes, M D Vickers, C J Hull. Principles of measurement and monitoring in Anaesthesia (3rd edition). Published by Blackwell Science Publications, 1991.

CORRESPONDENCE

Dr Alex Polishchuk, Oshakati, Namibia

Lateral intubation for difficult intubation

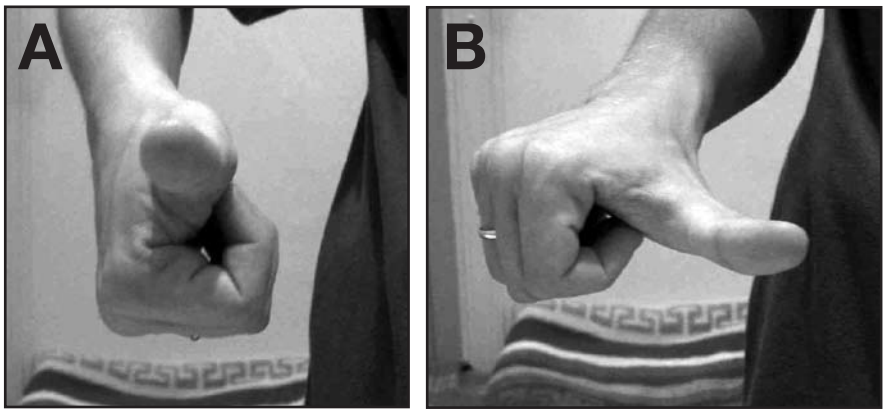
I have received correspondence for Dr Alex Polishchuk, originally from the Ukraine, and now working in Oshakati, Namibia, regarding a potentially useful intubation technique that is widely reported in Russian-language texts, but does not appear in UK textbooks or on the internet. An edited version of Dr Polishchuk's email, with photos, is shown below. Further correspondence of reader's experience with this technique would be welcomed.

Dear Editor, I recently read an Update article about difficult endotracheal intubation (http://www.nda.ox.ac.uk/wfsa/html/u09/u09_025.htm). In this overview article there was no mention of **lateral intubation**. Perhaps Western doctors have never heard of this technique? The technique was shown to me by an old doctor and has helped me many times. I have read about this technique, but only in Russian books. The method is as follows:

- After 3 unsuccessful attempts at conventional intubation turn the patient's head to face to the right side. Insert the laryngoscope in the left corner of the mouth, passing it forward in between the tongue and the upper teeth.
- Keep the laryngoscope handle parallel to the table surface, as during a conventional intubation. Pass the tip of the laryngoscope blade posteriorly, aiming to direct it between the left palatine arch (on the left of the blade) and the base of the tongue (on the right of the blade). Your laryngoscope blade will pass towards the patient's left piriform fossa, with the epiglottis coming into view on the right side of the blade, and the larynx straight ahead. Some anticlockwise rotation of the blade may be necessary to achieve this view.
- Move the larynx with your right hand to improve the view of the vocal cords.

Dr Polishchuk's photographs below demonstrate the lateral approach to the epiglottis and vocal cords.

During this technique, the larynx-mouth distance becomes shorter due to the rightward position of the head and the epiglottis disturbs your view less, because it is to the right of the blade.



The thumb represents the epiglottis and the orifice between the curled fingers, the laryngeal opening, (A) during conventional laryngoscopy and (B) during lateral laryngoscopy.

AN INTRODUCTION TO ANAESTHESIA FOR NEUROSURGERY

Barbara Stanley, Norfolk and Norwich University Hospital, UK
Email: drshoos@doctors.org.uk

Introduction
Anaesthesia for neurosurgical procedures requires understanding of the normal anatomy and physiology of the central nervous system and the likely changes that occur in response to the presence of space occupying lesions, trauma or infection.

In addition to balanced anaesthesia with smooth induction and emergence, particular attention should be paid to the maintenance of an adequate cerebral perfusion pressure (CPP), avoidance of intracranial hypertension and the provision of optimal surgical conditions to avoid further progression of the pre-existing neurological insult.

Aims of neuroanaesthesia

- To maintain an adequate cerebral perfusion pressure (CPP)
- To maintain a stable intracranial pressure (ICP)
- To create optimal surgical conditions
- To ensure an adequately anaesthetised patient who is not coughing or straining
- To enable rapid return to consciousness to allow neurological assessment postoperatively

General considerations for craniotomy
The patients

- Acute neurological condition or injury possibly with intracranial hypertension
- Medical therapy – anticonvulsants
- Pre-existing medical problems

The procedure

- Long operation time
- Blood loss
- Surgical stimulation / brain stem manipulation

The practicalities

- Position
- Access (intravenous and access to the airway)
- Invasive monitoring

Postoperative care

- Rapid recovery and neurological assessment
- Balanced analgesia to avoid sedation

General considerations for other procedures e.g. burr holes and shunts
The patients

- Often extremes of age
- Intracranial hypertension
- Associated conditions or trauma

The procedure

- Short procedure time
- Great surgical stimulation whilst shunt is tunnelled

The practicalities

- Supine position
- Invasive monitoring for burr hole

Postoperative care

- Rapid recovery and neurological assessment

Physiological Principals
Cerebral perfusion pressure and the intracranial pressure/volume relationship
Maintenance of adequate blood flow to the brain is of fundamental importance in neuroanaesthesia. Cerebral blood flow (CBF) accounts for approximately 15% of cardiac output, or 700ml/min. This equates to approximately 50ml/100g of brain tissue per minute under normal conditions. The brain is contained within the cranial vault which is non distensible and has a fixed volume. Cerebral blood flow is therefore affected by the pressure within the cranial vault and a useful measure of this is the cerebral perfusion pressure, the effective pressure which results in blood flow to the brain. Cerebral perfusion pressure (CPP) is the difference between the mean arterial pressure (MAP) and the sum of the intracranial pressure and the central venous pressure (CVP):

CPP = MAP - (ICP + CVP)

Under normal conditions, the ICP remains at 5-12 mmHg, the venous pressure at the base of skull is zero, and CPP varies with the individual's MAP. CPP is reduced in the presence of raised ICP, raised venous pressure or low MAP. Therapeutic measures to maintain optimal CPP are therefore aimed at maintaining MAP whilst lowering ICP and avoiding venous obstruction or hypertension.

Autoregulation is the ability of the brain to maintain stable CBF in the face of a changing MAP/CPP. As shown in figure 1, this is achieved by alterations in cerebrovascular resistance. The calibre of intracranial vessels alters automatically – vessels dilate if perfusion pressure is low (or if metabolic activity in one region is high). Under normal conditions, cerebral blood flow is kept at a stable level over a range of cerebral perfusion pressures between 50 and 150mmHg.

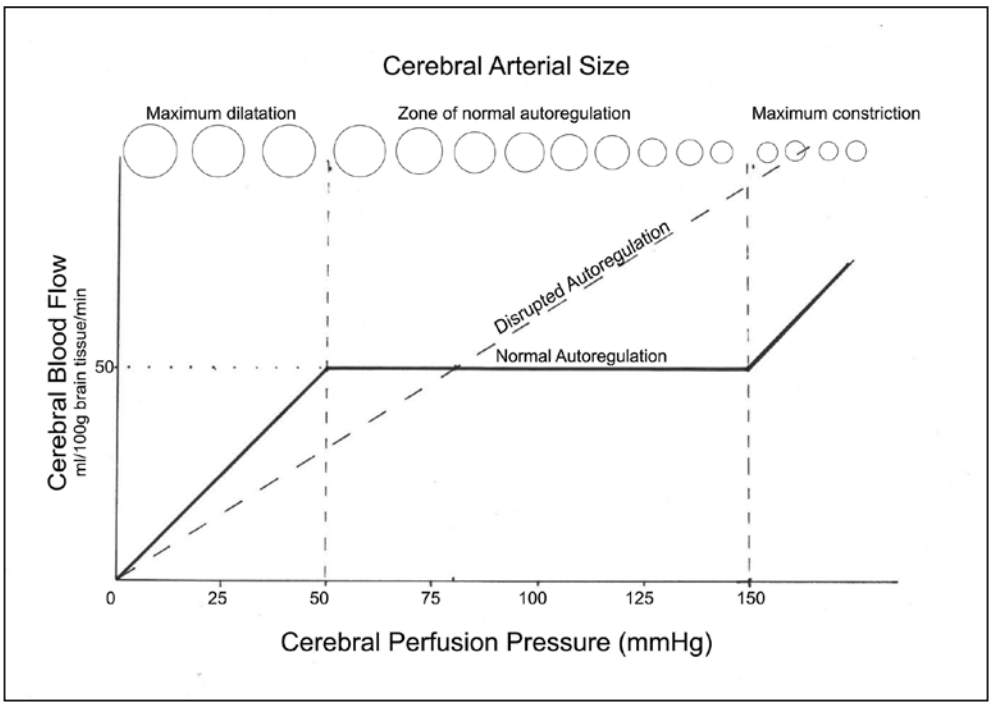


Figure 1: The relationship between cerebral blood flow and cerebral perfusion pressure. CBF is maintained at a constant value over a range of CPP (between 50 and 150mmHg) by alterations in cerebral vascular resistance. Decreased CPP causes vasodilation, increased CPP results in vasoconstriction. Conditions such as head injury disrupt autoregulation and the relationship becomes 'pressure-passive'.

In the presence of a space-occupying lesion (e.g. blood, tumour or oedema), the brain has limited compensatory ability before ICP increases. To avoid a rise in ICP, an increase in the volume of one component of the contents of the rigid cranial vault must be compensated by a reduction in the volume of another. As the volume increases in the vault (figure 2), the pressure is initially controlled by a reduction in CSF and cerebral venous blood volume. Once this mechanism is exhausted, then small increases in volume of the lesion lead to steep increases in intracranial pressure and eventually may cause displacement of brain tissue and cerebellar tonsillar herniation through the foramen magnum (coning).

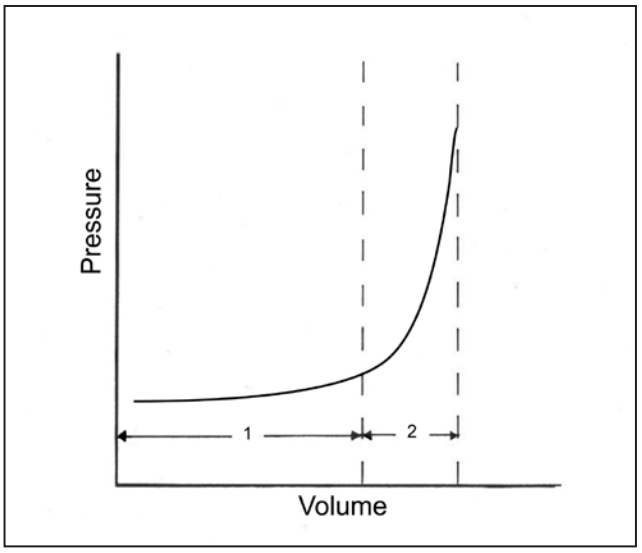


Figure 2: As the volume of a space occupying lesion within the intracranial vault rises, compensatory mechanisms allow intracranial pressure to remain stable (1). Once these mechanisms are exhausted, intracranial pressure rises very sharply (2).

Flow-metabolism coupling

Under normal circumstances, the brain is able to alter the supply of oxygen (by changing blood flow) to specific areas of the brain which have increased metabolic activity.

Arterial oxygen and carbon dioxide tensions

Carbon dioxide tension in the blood has a marked effect on the cerebral vasculature. A rise in arterial carbon dioxide ($PaCO_2$) causes cerebral vasodilation, an effect magnified in the presence of a reduced arterial oxygen tension. Cerebrovascular vasodilation causes an increase in intracranial volume that can cause coning under circumstances of raised ICP.

> In patients with raised intracranial pressure it is vital to control the $PaCO_2$ to normal and to ensure provision of adequate oxygen to avoid hypoxia.

Pathophysiological consequences of injury or disease

The pathophysiological consequences of injury depend upon the speed of onset and whether the compensatory mechanisms are overwhelmed. For example, a sudden catastrophic increase in ICP due to intracerebral haemorrhage can cause otherwise normal tissue to infarct, whereas slow increases due to hydrocephalus allow compensation, but may give rise to the symptoms of headache and nausea.

Once CBF falls below 18ml/100g/min, alterations in cellular activity occur, with intracellular acidosis and cessation of protein metabolism. At less than 12ml/100g/min electrical activity ceases and at 8ml/100g/min cell death occurs.

Autoregulation in injured parts of the brain is impaired

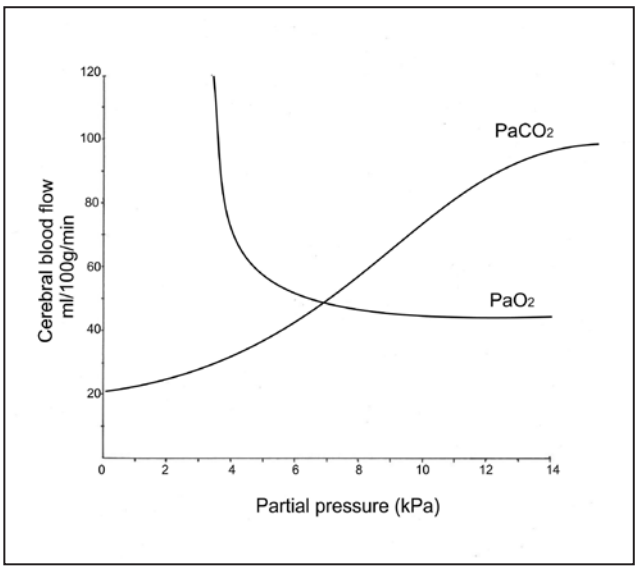


Figure 3: The effects of changes in $PaCO_2$ and PaO_2 on cerebral blood flow. A rise in $PaCO_2$ causes a marked rise in CBF. Fall in oxygen tension has a little effect on CBF until PaO_2 reaches a value of less than 8kPa.

and the threshold at which the vasculature can maintain CBF is elevated, from CPP of 50mmHg to 60–70mmHg. Hypoxia and hypercapnia cause secondary brain injury through ischaemic mechanisms. Hypercapnia causes vasodilation, an increase intracranial volume, subsequent reduction in CPP, further increase in $PaCO_2$ and a downward spiral in blood flow and worsening ischaemia.

The effects of anaesthetic agents on cerebral blood flow

Most anaesthetic agents reduce neuronal activity and so reduce the brain's cerebral metabolic requirement for oxygen ($CMR0_2$). They provide a protective mechanism when oxygen demand may outweigh supply. Unfortunately, many anaesthetic agents also reduce the mean arterial blood pressure by causing arterial vasodilatation with a potentially adverse effect on CPP.

Thiopentone

- Causes a dose-dependent fall in $CMR0_2$, also a fall in CBF. These effects are useful during craniotomy in the presence of elevated ICP.
- Anticonvulsant properties are advantageous.

Propofol

- Similar effects to thiopentone but may preserve autoregulation more effectively.
- It is useful for maintenance of anaesthesia and its amnesic and antiemetic properties make it advantageous for a smooth recovery.
- It does cause a fall in MAP which may have disadvantageous effects on CPP.

Ketamine

- This NMDA antagonist has traditionally been avoided because it increases ICP and CBF, although these effects are less marked if $PaCO_2$ is controlled to normal levels.
- It is not routinely used for elective neurosurgical anaesthesia at present, but has gained acceptance as an appropriate agent for emergency induction of anaesthesia and maintenance of sedation in head injured patients, particularly those with multiple injuries and haemodynamic compromise.

Inhalational agents

- Sevoflurane has less cerebral vasodilatory effects than other inhalational agents and preserves CO_2 reactivity. Also it allows a rapid recovery due to its lower blood:gas solubility coefficient.
- Desflurane at 1 MAC has been shown to increase ICP in patients with supra-tentorial space occupying lesions, in contrast to isoflurane.
- Most of the inhalational agents are deemed safe at concentrations of less than 1 MAC.
- Nitrous oxide increases ICP, CBF and $CMRO_2$. These effects, together with its adverse effect on closed gas spaces preclude its use, especially in trauma patients who may also have undetected chest injury.

Opioids

- Remifentanil – has a rapid onset and offset which allows titration to counter stimulating events such as the application of the Mayfield clamp (see below). A dose dependent fall in MAP and rapid offset mean that a longer acting analgesic agent is required prior to cessation of surgery.
- Fentanyl and morphine – these agents have little effect on intracranial pressure or blood flow which makes them suitable for titration to provide post-operative analgesia.

Neuromuscular blocking drugs

- The non-depolarizing agents do not have an effect on ICP.
- Suxamethonium causes a transient rise in ICP, in part due to muscle fasciculation and increased venous pressure. There may also be a slight increase in $CMR0_2$ and cerebral blood flow. These considerations must be weighed against the need for rapid airway control. Suxamethonium is usually reserved for emergency anaesthesia rather than elective cases.

Other drugs

Diuretics

- Mannitol is a large molecule that will not cross the intact blood brain barrier. It is useful in the

prevention and treatment of cerebral oedema and it causes a reduction in ICP. It can cause a transient rise in cerebral blood volume and this effect can last for up to 20 minutes. It also causes a transient rise in CVP. The usual dose is 0.5 – 1g/kg. It has the additional effect of haemodilution which is thought to improve blood flow characteristics. If the blood brain barrier is damaged it may worsen raised ICP.

- Furosemide 1mg/kg produces a reduction in ICP to the same extent as mannitol at 1g/kg. It is advantageous as it also reduces CVP.

Steroids

- Dexamethasone 8-16mg is useful to reduce cerebral oedema associated with tumours. It is less effective for reduction in global oedema.

Anticonvulsants

- For frontal and temporal surgery phenytoin can be given as a loading dose, 15mg/kg intravenously, but should be given slowly as it causes hypotension and can cause arrhythmias.

Drugs to manipulate the cardiovascular system

- α-agonists such as phenylephrine and noradrenaline are used to increase blood pressure as there are fewer alpha receptors in the cerebral vasculature. These agents have a selective effect on systemic vascular resistance and cerebral vascular resistance is relatively unaffected.
- Clonidine, an α_2-antagonist, can be used to treat hypertension at the start of surgery. It has analgesic and sedative properties which are a useful adjunct to anaesthesia but these effects must be weighed against the need for rapid emergence at the end of surgery.

Anaesthesia for craniotomy for tumour or intracranial bleed

General considerations

History and examination is important to detect signs and symptoms such as convulsions, nerve palsies and reduced levels of consciousness (assess GCS).

Posterior fossa tumours occasionally cause bulbar palsies and lower cranial nerve lesions which increase the risk of laryngeal incompetence and thus chronic or acute aspiration of gastric contents and hypoxia.

Subarachnoid haemorrhage can cause massive release of catecholamines which can cause acute heart failure and malignant arrhythmias. Non-specific T-wave and ST segment abnormalities may be seen on the ECG.

The patient's general medical condition must be stabilised, especially any respiratory or cardiovascular disease, as hypoxia, hypercarbia or failure to maintain blood pressure will be detrimental, as will uncontrolled hypertension. Preoperative medications, especially anticonvulsants, steroids and cardiac drugs, should be continued until and including the day of surgery if possible. Antiplatelet drugs should be discontinued if possible, although the risks of stopping these drugs must be considered.

Airway assessment is important because prolonged attempts at laryngoscopy are extremely stimulating and increase cerebral oxygen demand and ICP.

Patients are often anxious and a sedative premedication such as a benzodiazepine can be offered.

Conduct of anaesthesia

Induction needs to be smooth and blood pressure maintained near preoperative values to maintain cerebral blood flow. A bolus of either propofol (0.5-1mg/kg) or opiate should be given immediately prior to laryngoscopy as this is very stimulating. Adequate time should be allowed for non depolarising muscle relaxant to work before intubation is attempted.

Once the patient is draped and surgery underway access to the airway is very limited, so it is absolutely vital that the airway is secured reliably, preferably with waterproof tapes. An armoured cuffed tracheal tube prevents the tube kinking when the patient's head is manipulated, particularly if the patient is to be positioned prone. Meticulous attention to securing the tube is vital. A prone patient whose skull is pinned is very difficult to manage should the tube fall out.

Intravenous access must be of large bore and reliable as sudden massive haemorrhage can occur. Invasive arterial monitoring is very useful for reliable minute to minute blood pressure assessment and also for evaluating arterial blood gasses and haemoglobin levels. Consideration should be given to site the IV access and arterial pressure monitoring before induction of anaesthesia (although not in children).

Central venous access is appropriate as a guide to venous pressure and to administer drug infusions. The sitting position is used much less frequently now, but placement of the tip of a central line in the right atrium should be considered for these patients and others at risk of air embolus, to allow aspiration of air from the heart should this occur.

Anaesthesia can be maintained using a volatile agent in air and oxygen or propofol infusion. The patent's lungs are ventilated to achieve normocapnia - normal areas of the brain vasoconstrict secondary to hypocapnia and total cerebral blood flow will be reduced inappropriately. Hypocapnia is reserved for situations where ICP is very high; it may be life saving in this situation but there can be rebound vasodilation when normal CO_2 levels are achieved subsequently.

Surgical procedures are often very lengthy and so attention must be paid to patient position, protection of pressure areas, including the eyes, and to ensuring unrestricted venous drainage from the head.

The patient must have a urinary catheter for lengthy craniotomy or if diuretics are used. Calf compressors help to reduce thromboembolic risk. Core body temperature should be measured, preferably with an oesophageal probe.

During patient positioning in theatre the skull is often pinned into a clamp (a Mayfield clamp) to maintain optimal surgical positioning. This is stimulating and so a pre-emptive bolus of propofol or an opioid should be given to prevent a sudden rise in blood pressure.

Once the skull is open a bolus of diuretic optimises operating conditions if intracranial pressure is elevated and the surgeon comments that the dura is bulging. Mannitol 0.5mg/kg or furosemide 1mg/kg are appropriate. Mannitol increases the central venous pressure so should be given slowly - especially if the patient's myocardial function is impaired.

During the procedure, maintain low normal end tidal CO_2 (around 4.0 kPa), normotension and normal oxygen levels. Mild hypotension can help improve the surgical field if necessary. Normothermia should be maintained, especially if the procedure is long. Temperature should be allowed to passively drift to about 35 degrees centigrade if the patient's cerebral blood supply is at risk – for instance during aneurysm surgery. Allowing the patient to become hypothermic has consequences of poor clotting function, impaired cardiac contractility and postoperative shivering which increases oxygen demand.

Fluid replacement with glucose-free crystalloid, such as normal saline or lactated Ringers, is appropriate. Hyperglycaemia is associated with worse neurological outcome and tight glycaemic control may help improve outcome and avoids lactate accumulation. Hypotonic intravenous solutions must never be used as they will exacerbate cerebral oedema.

If the ICP is high during surgery

- Place the patient in a slightly head up position.
- Check there is no neck vein kinking or compression and the abdomen can move freely with no diaphragmatic compression.
- Ensure the patient is paralysed.
- Ventilate without PEEP.
- Ensure the blood pressure is adequate.
- Ensure the $PaCO_2$ is not raised and consider reducing it to 4-4.5kPa.
- Ensure the PaO_2 is normal.
- Reduce the brain's metabolic activity – bolus thiopentone 3mg/kg or propofol 1mg/kg, or lidocaine 1.5mg/kg if cardiovascularly unstable .

During surgery, especially posterior fossa surgery, the brainstem may be manipulated, which can cause profound bradycardias. If this occurs, communicate with the surgeon to release traction or pressure and treat with glycopyrrolate 200–400 micrograms (atropine crosses the blood-brain barrier) and allow surgery to resume when the heart rate is normal.

Once surgery is drawing to a close the surgeon closes the dura, cranium and scalp, which can take up to 30 minutes. If anaesthesia is too light the patient may cough as the head is moved to apply the dressings at the end of surgery. Good communication between surgeon and anaesthetist will help with timing of paralysis and cessation of anaesthesia. Remifentanil infusion, if available, helps to smooth out the waking and extubation process, but remember to give a bolus of longer acting opioid to avoid postoperative agitation. Whichever agent has been used, aim for a smooth extubation with a minimum of straining and coughing.

Pain from craniotomy is described as 'mild to moderate' and paracetamol and codeine are popular analgesics. Non-steroidal anti-inflammatory drugs have an anti-platelet effect and should be used with caution. Small (1-2mg) boluses of intravenous morphine are appropriate for patients in severe discomfort. The aim at the end of surgery is to have a comfortable, co-operative and lucid patient whose neurology can be assessed.

Anaesthesia for other neurosurgical procedures

Burr holes

Burr holes are usually performed as an emergency procedure in those who have had an extradural haemorrhage (arterial, usually associated with a skull fracture) or subdural haemorrhage (venous, may be chronic especially in the elderly). Patients will usually have:

- Altered level of consciousness (measure GCS).
- Raised ICP.
- Focal neurology, such as a dilating pupil.

Other injuries may be present that need consideration. Protection of the patient's cervical spine must be considered.

Preoperative interventions include:

- Secure the airway with cervical spine control if GCS is <9/15 or ventilation is inadequate for normal oxygenation and carbon dioxide elimination (rapid sequence induction with thiopentone and suxamethonium is appropriate).
- Maintain normal blood pressure with fluids and inotropes, using non-glucose containing crystalloid and α-agonists if necessary. Aim for a MAP of 90mmHg in adults.
- Nurse the patient 15-30 degrees head up with no tube tie.

- Ventilate the patient to achieve normocapnia and normoxia.
- Sedate, for example using a propofol infusion 1-3mg/kg/hr.
- Insert invasive arterial pressure monitoring
- Monitor the CVP.

Extracranial injuries must be assessed and their management incorporated into the definitive treatment plan.

Communication between the trauma team and neurosurgical/ICU team is of paramount importance. Other life threatening injuries must be dealt with and stabilised and may occasionally take priority over evacuation of an intracranial haematoma. In this situation, intracranial pressure must be assumed to be raised and diuretics and low CO_2 may delay brain herniation. Patients are often transferred to regional neurosurgical centres, making management of raised ICP even more important. Make sure cross-matched blood is available

Patients who have a low GCS preoperatively or who have high ICP intraoperatively should be managed in an intensive care unit postoperatively and kept sedated and ventilated for 24 hours after surgery.

Ventriculoperitoneal (VP) shunt for hydrocephalus
Hydrocephalus can present acutely with a low GCS, or chronically with headaches, neurological symptoms and vomiting. It can result from the overproduction of CSF (non-obstructive and very rare), blockage of CSF absorption (obstructive, communicating resulting from arachnoiditis) or obstruction to normal CSF flow (obstructive, non-communicating).

In treatment of hydrocephalus a fine bore tube with a valve is inserted to drain CSF from the dilated ventricle into the peritoneal cavity.

- Patients may be children.
- The commonest shunt is from the lateral ventricle to the peritoneum.
- The commonest complication of VP shunts are infection and blockage.
- Patients can have an intracranial haemorrhage if CSF is drained too quickly.

The procedure is shorter than full craniotomy and invasive monitoring is not usually required unless the patient is medically unwell. The airway should be secured and attention paid to good oxygenation, normalising $PaCO_2$ and preventing coughing and straining – especially during the stimulating part of surgery when the shunt is being tunnelled subcutaneously. As with craniotomy, arrhythmias or bradycardia can occur as the catheter is placed.

Post-operatively the aim is to have an awake and comfortable patient in recovery that can co-operate with neurological assessment. Paracetamol and codeine phosphate are the mainstay of analgesia and intravenous morphine titrated to effect may also be required.

Further reading

- Matta B, Menon DK, Turner JM et al. Textbook of Neuroanaesthesia and Critical Care. Published by Cambridge University Press, Cambridge, UK
- Clayton T and Manara A. Neurosurgery in the Oxford Handbook of Anaesthesia (second edition). Published by Oxford University Press, Oxford, UK

The author would like to acknowledge the help of Dr Jurgens Nortje in preparing this article.

CEREBRAL CHALLENGE

Compiled by Nicki Bosley and Bruce McCormick, Exeter, UK

Case 1

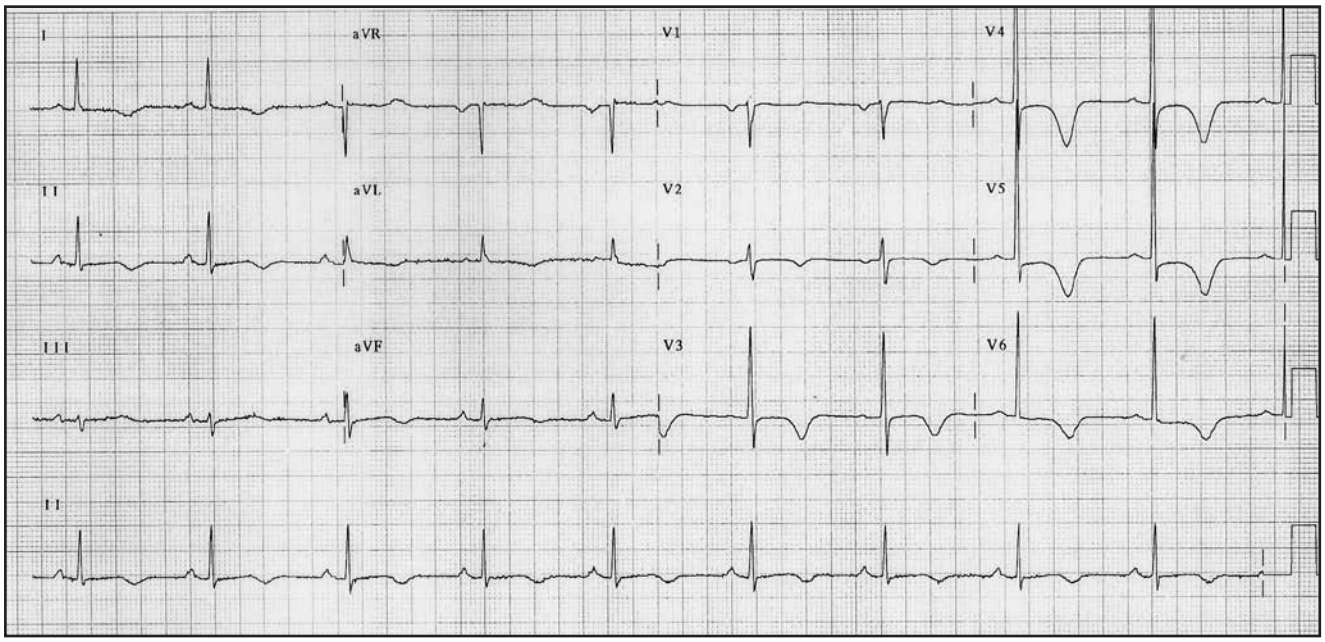


Figure 1: You are asked to anaesthetise a woman of 56 years for abdominal hysterectomy. She says she is fit and well with hypertension treated with a calcium antagonist. She denies any cardiac disease, but does admit to suffering occasional chest pain, but she has not visited her doctor. Her blood pressure is 180/92mmHg and she has had an electrocardiogram (ECG).

What does the ECG show and what are the implications for this woman's anaesthetic management?

Case 2

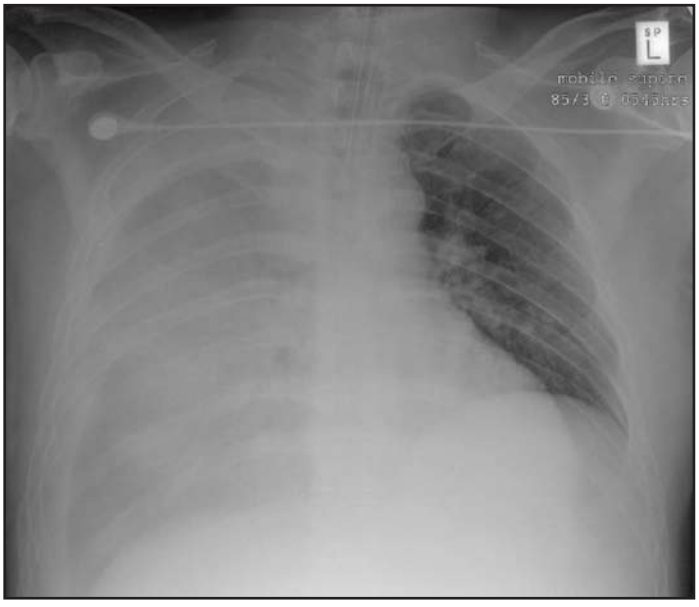


Figure 2: You take over a case from one of your colleagues - a 69-year-old man who is undergoing a laparotomy to relieve bowel obstruction. Your colleague noted that he had a two month history of worsening shortness of breath on exertion and put this down to bronchitis. He has also lost 8kg in weight over the last 3 months. He has been a lifelong heavy smoker with a 40-pack year history. Preoperatively examination showed him to be cachectic, with a respiratory rate of 26 per minute and oxygen saturations of 93% on air. The surgeons have relieved a band adhesion causing small bowel obstruction and have closed his abdomen. When you extubate him his breathing is laboured and he promptly desaturates. You anaesthetise him again, reintubate and ventilate him. Examining his chest, you find dullness to percussion over the right base with absent breath sounds and request a chest Xray (CXR).

What does the CXR show? Are you happy with the CXR that has been taken?

What are the possible underlying causes of his CXR diagnosis?

How would you manage this man from here?

Case 3

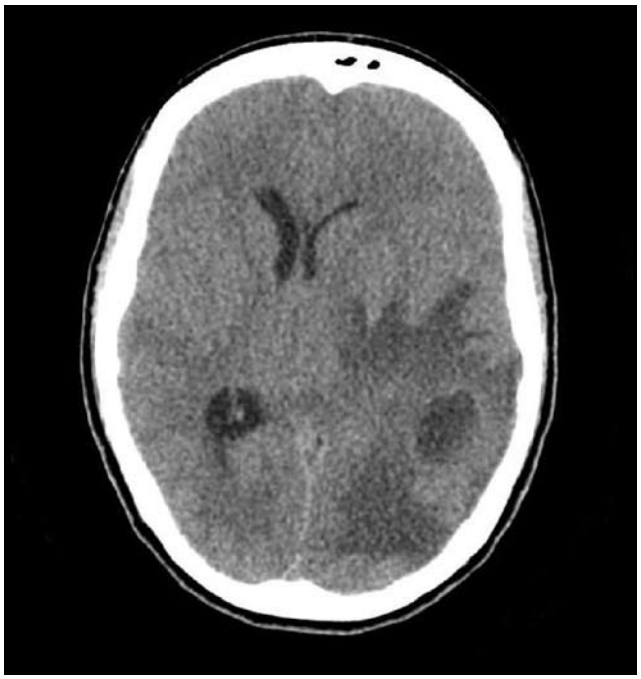


Figure 3a: CT head without contrast

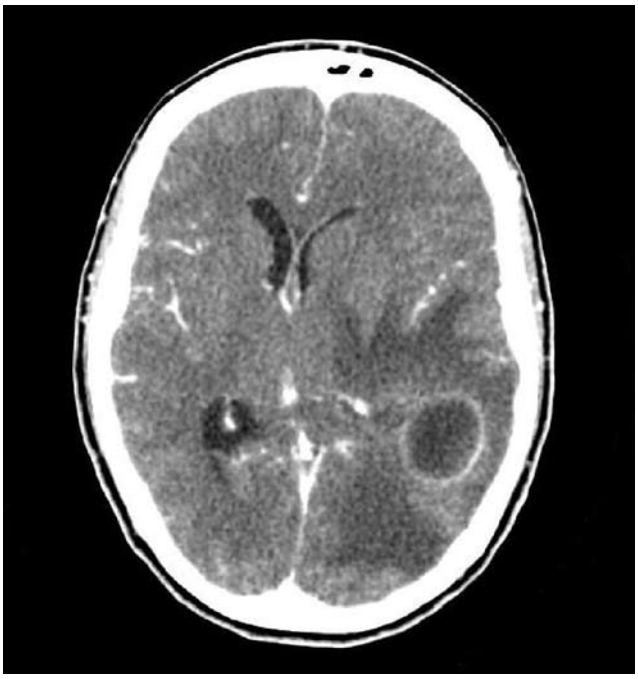


Figure 3b: CT head after IV contrast

A 38-year-old man is brought into the emergency department after having two grand mal seizures at home. He had been feeling generally unwell for a few months and over the last few days had been experiencing headaches. His wife says he has been confused for 3 days and had rigors and fevers this morning.

On arrival in the emergency department he had a Glasgow Coma Score of 8 (Eyes 2, Vocal 1, Motor 5). His pupils are equal but dilated and slow to react. He is haemodynamically stable, with a blood pressure of 138/74 and a heart rate of 106/min. He is pyrexial at 39°C. He has had a CT scan of his head.

What does the CT show?

What are the likely causes of this abnormality?

Discussion

Case 1

The ECG shows sinus rhythm of 60 beats per minute. There is T wave inversion through out the chest leads, V2 to V6. It is likely she has suffered a subendocardial myocardial infarction at some stage in the past, meaning that the innermost layer of heart muscle has been damaged by ischaemia, but the damage is not affecting the full thickness of the myocardium. Full thickness infarction of the heart muscle results in T wave inversion with formation of Q waves in the ECG leads lying over the area of damaged heart muscle.

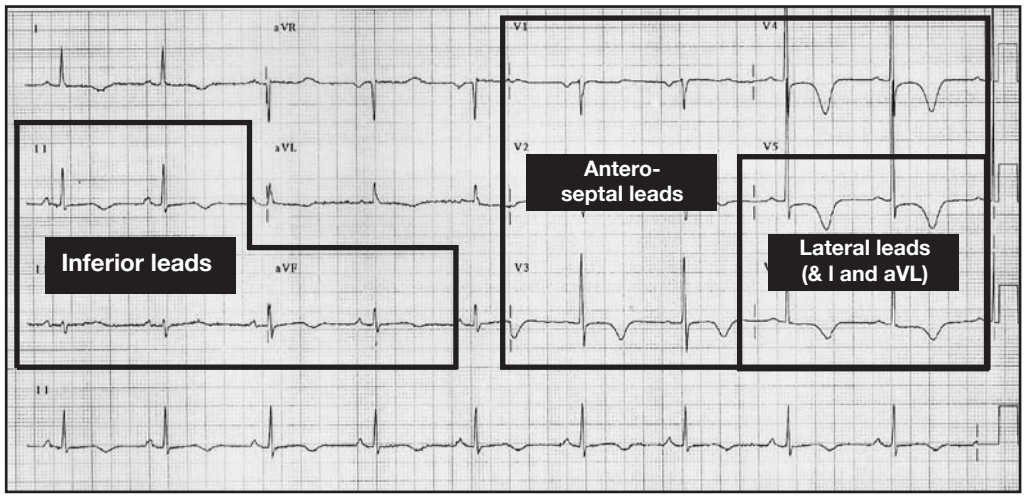


Figure 4: Assuming the leads are properly positioned on the patient, the outlined areas on the ECG correspond to the stated areas of the heart.

There are no Q waves visable on this ECG. It is possible to identify which area of heart muscle is involved by a pathological process by determining which leads show electrical abnormalities (figure 4).

The other common cause of T wave inversion on an ECG is acute ischaemia. Diffuse T wave inversion is occasionally seen in patients with intracranial pathology, such as subarachnoid haemorrhage.

This woman suffers occasional chest pain and has not sought medical advice. Her ECG suggests that she may have had a myocardial infraction in the past that she was unaware of – this may have been recently or months or years ago. Her blood pressure is poorly controlled and the voltages in the chest leads of her ECG are slightly high, suggesting that she is developing left ventricular hypertrophy (LVH) as a consequence of this. This is another possible cause of the T wave inversion.

Her surgery is elective and since she is still complaining of chest pain, it is sensible to postpone her operation until she has been reviewed by a cardiologist. It is highly likely that she will be investigated further, with an exercise test or angiography, if available. She should be started on aspirin 75mg daily straight away, as secondary prevention of further myocardial infarction. A β-blocker is an appropriate agent to introduce to help control her hypertension, since it also has a role as an anti-anginal and also as a secondary preventative measure post myocardial infarction.

Criteria for diagnosis of left ventricular hypertrophy

There are several ways of diagnosing LVH using the voltages on the ECG. Sokolow's criteria are to add the height (number of little squares, mm) of the S wave in V1 to the height of the R wave in V5 or V6 (whichever is larger). If this is greater than 35mm, LVH is present. In this woman it is about 38mm and so she has LVH.

Case 2

The CXR is an AP portable film. 'AP' is short for antero-posterior, meaning that the Xrays have passed from in front of the patient to the Xray plate behind them – if the film is not labelled it is an AP film.

The obvious abnormality is diffuse shadowing of the right lung field – a 'white-out' of the right lung. The principal differential diagnoses are either complete collapse of the right lung, a right pleural effusion or, in trauma, a haemothorax. Your examination of the patient (decreased air entry with dullness to percussion on the left) would fit with either of these. Note that the film has been taken with the patient lying supine (stated at the top right of the film) and also that you can see the border of the partially inflated lung behind the opacity (shown by arrows in figure 5). This is a typical CXR appearance of a pleural effusion when the patient is supine - the effusion lies at the back of the pleural cavity and gives a 'veiling' opacity over the full area of that lung. Note also that the endotracheal tube is correctly placed with its tip at the aortic knuckle and that the left hemidiaphragm is elevated.

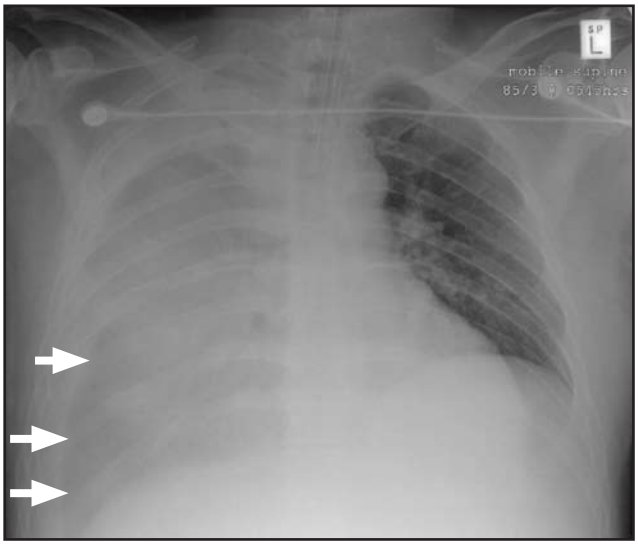


Figure 5: The border of the partially inflated right lung is just visible (arrows).

It is worth clarifying the diagnosis by performing an erect CXR which will show the pleural effusion more clearly (see figure 6).

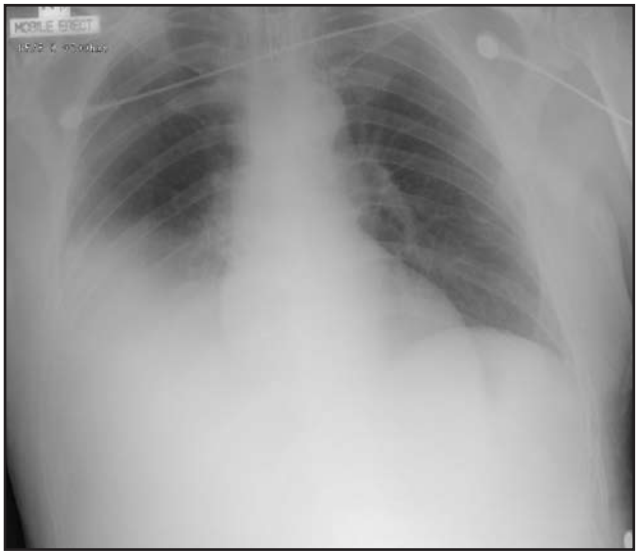


Figure 6: An erect CXR of the same patient.

Clinically and on CXR a pleural effusion and complete collapse of one lung can be differentiated by the position of the trachea. In complete collapse the trachea will be pulled towards the side of the collapse (figure 7). In an effusion the trachea will usually be central.

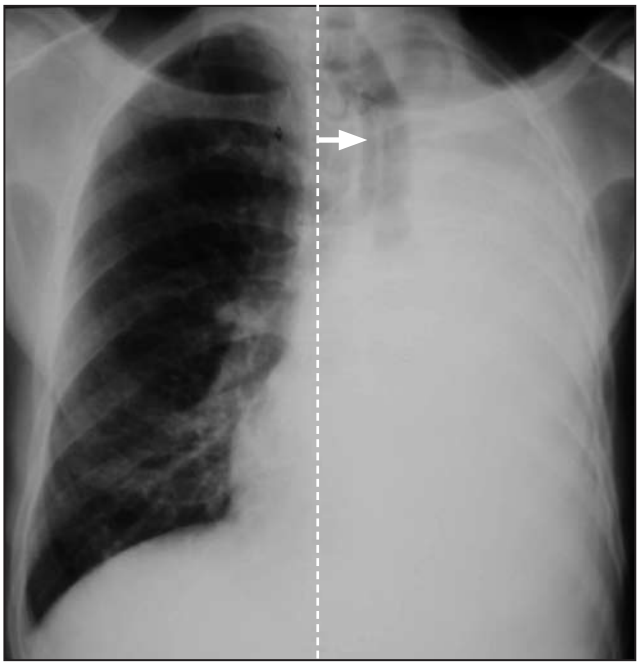


Figure 7: CXR showing left lung collapse/atelectasis with marked deviation of the trachea towards the side of collapse (arrow).

A pleural effusion is an accumulation of fluid within the pleural space. It can be detected clinically when there is more than 500ml present and radiologically when there are 300ml or above.

The causes of a pleural effusion can be divided into two broad categories:

Transudates	Exudates
Heart failure	Parapneumonic effusion
Hypothyroidism	Carcinoma of the bronchus
Constrictive pericarditis	Pulmonary infarction
Hypoproteinaemia (e.g. nephrotic syndrome, hypoalbuminaemia)	Tuberculosis
	Connective tissue disease
	Mesothelioma
	Sarcoidosis (rarely)
	Acute pancreatitis
	Empyema
	Meigs syndrome

This patient's further management should involve further investigation of the effusion. His underlying history is suspicious of bronchial malignancy, but other diagnoses such as TB are possible. Pleural fluid aspiration can be performed by simple needle aspiration using aseptic technique.

Lights criteria are used to differentiate between transudates and exudates - an exudate has one or more of the following:

- Pleural fluid protein divided by serum protein ratio > 0.5
- Pleural fluid lactate dehydrogenase (LDH) divided by serum LDH ratio > 0.6
- Pleural fluid LDH above the upper limit of normal serum LDH.

In addition samples should be sent for:

- Biochemistry
  - pH < 7.2 suggestive of empyema or malignancy,
  - protein > 30g/l - exudate is more likely
  - glucose - low in infection
  - amylase
- Microbiology (gram stain, culture and sensitivity, acid alcohol fast stain)
- Cytology (malignant cells)

Further investigation of his effusion is warranted, initially with a pleural tap and cytology, followed where available by computer tomography (CT) of the thorax. This will identify any underlying masses, enlarged lymph nodes or pleural thickening that could be suitable for CT guided needle biopsy for a tissue diagnosis.

It is the likely that the effusion contributed to this man's respiratory collapse after extubation. The effusion should be drained, after which he should be weaned and extubated.

Case 3

CT scans are viewed as if looking up through the patient's body from their feet. So as the patient lies, looking upwards, their right side is on the left as we look at the scan.

Bone is bright white, fresh blood appears white, cerebrospinal fluid is black and brain parenchyma is varying shades of grey.

Figures 3a and 3b show a round lesion in the left cerebral hemisphere.

This man should be resuscitated with attention to his airway, breathing and ventilation. With a Glasgow Coma Score of 8, where the facilities are available, he should be sedated, intubated and ventilated, whilst appropriate antibiotics are started. A preventative anticonvulsant such as phenytoin should be started (15mg/kg IV slowly).

Further history from the man's wife indicates that he is HIV positive. The most likely causative organism in an immunocompromised patient is Toxoplasma

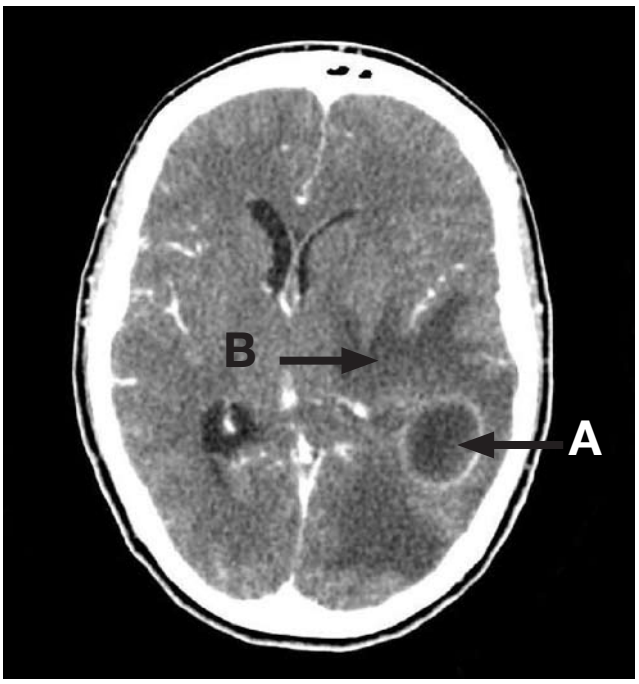


Figure 8: The border of the lesion shows up brightly after contrast – it is a 'ring-enhancing' lesion (arrow A). This appearance is characteristic of a brain abscess, although less commonly it can be caused by certain types of brain tumour or cerebral lymphoma. There is oedema of the brain around the lesion, which shows up darker since it contains more water that other areas of the brain (arrow B). The midline is shifted to the right and the left lateral ventricle is effaced ('squashed').

gondii, which can cause either single or multiple abscesses. Other organisms to consider include: TB, staphylococcus, streptococcus, salmonella, nocardia, listeria, cryptococcus, histoplasma and candida.

Toxoplasmosis is an obligate intracellular parasite. Cats are the definitive hosts and domestic cats play a major role in its transmission. Ingesting undercooked or raw meat, blood transfusions, organ transplants and congenital infections are other methods of infestation. The most severe forms of toxoplasmosis are seen in the immunocompromised (AIDS, organ transplant patients, malignancies), usually resulting from reactivation of latent Toxoplasmosis gondii infection.

Clinical features may include confusion, headaches, fever, speech disturbances, motor weakness, visual field defects, cerebellar dysfunction, cranial nerve abnormalities, meningism, seizures and shortness of breath.

Laboratory investigations are:

- Serology – immunoglobulin M immunoflourescent antibody test (IgM-IFA), titre 1:160 or greater or IgM enzyme linked immunosorbent assay (IgM-ELISA) titre, 1:256 or greater is diagnostic.
- Cerebrospinal fluid examination – mononuclear pleocytosis, elevated protein, normal glucose.

Imaging:

- CT brain – single or multiple ring enhancing lesions.
- MRI brain – may detect multiple lesions mainly involving the basal ganglia and corticomedullary region, not seen on CT. This is the most reliable imaging for diagnosing T. gondii encephalitis.

Histology

- Where facilities exist, brain biopsy is indicated in patients who have a single lesion on MRI, multiple lesions whilst on T. gondii prophylaxis, negative serological findings and failure to respond to empirical treatment after 14 days or deterioration after day 3 of treatment.

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Anaesthesia

Journal of the Association of Anaesthesia of Great Britain and Ireland

Volume 62, Supplement 1. December 2007

In December 2007, the Association of Anaesthetists published a supplement to Anaesthesia as part of the Council of Science Editors Global Theme Issue on Poverty and Human Development. This supplement contains many articles of great interest and relevance to anaesthetists working both in well and poorly-resourced countries.

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Typeset by: Sumographics: www.sumographics.co.uk or e-mail: info@sumographics.co.uk

Printed by COS Printers

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