From the Journals

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3rd MBRRACE-UK Report (December 2016): Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK

Available at https://www.npeu.ox.ac.uk/downloads/files/mbrrace-uk/reports/MBRRACE-UK%20Maternal%20Report%202016%20-%20website.pdf

The third enquiry into maternal deaths in the UK was published in December 2016. This focused predominantly on maternal deaths from cardiovascular disease between 2012 and 2014. Deaths were collated and patients' notes were anonymised and reviewed by a multidisciplinary team of health care professionals.

There were 8.5 deaths per 100 000 pregnant women during pregnancy or up to 6 weeks after the end of pregnancy, one-quarter of whom died from cardiovascular disease. Thrombosis and thromboembolism remain the leading cause of direct maternal death and cardiovascular disease the primary cause of indirect maternal death. The predominant causes of cardiovascular deaths include sudden arrhythmic cardiac deaths with a morphologically normal heart (31%), ischaemic heart disease (22%), cardiomyopathy or myocardial disease (18%) and aortic dissection (14%). Only 17% of these cardiovascular deaths were in woman with pre-existing cardiac problems.

In many instances clear symptoms and signs of cardiac disease were missed in pregnant and postpartum women, often because the diagnosis was simply not considered in a young pregnant woman.

The pertinent lessons from this enquiry include:

- All consultant-led maternity units should have access to an ECG machine and, ideally, echocardiography.
- Women with prosthetic heart valves are at extremely high risk in pregnancy. New onset of cardiorespiratory symptoms, including the absence of valve clicks, in women with prosthetic heart valves should prompt echocardiography, where available, to exclude valve thrombosis.
- A raised respiratory rate, chest pain, persistent tachycardia and orthopnoea are important signs and symptoms that should always be fully investigated.
- Normal ECG and/or negative troponin does not exclude an acute coronary syndrome.
- Persistent breathlessness when lying flat is not normal in pregnancy and may suggest cardiovascular problems.
- As with any other cardiac arrest, determining the cardiac rhythm early and attempting defibrillation if the patient is in a shockable rhythm (ventricular fibrillation or ventricular tachycardia) is key to improving chances of survival.
- Perimortem caesarean section plays a key role in the resuscitation of a pregnant woman. Ambulance crews should not delay transfer to hospital (see Further reading).
- Blood pressure and proteinuria should be closely monitored during pregnancy. Blood pressure should be kept below 150/100 mmHg and severe hypertension requires urgent treatment.

In other instances, suboptimal management resulted from fragmented care and poor communication between members of the multidisciplinary team.

FURTHER READING

- Johnstone D. Maternal collapse and perimortem caesarean section. *Update Anaesthes* 2007; **23**: 11–13. Available at http://www.wfsahq.org/components/com_virtual_library/media/0ca587ba711f9a11557cd10b30a0d019–42e17a357b96579d8dfa041d8a2b1494-Maternal-Collapse-and-Perimortem-Caesarian-Section--Update-2.pdf

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Difficult Airway Society (DAS) 2015 guidelines for management of unanticipated difficult intubation in adults

Frerk C, Mitchell VS, McNarry AF, Mendonca C, Bhagrath R, Patel A et al. *Br J Anaesth* 2015; **115**: 827–48. Available at https://www.das.uk.com/guidelines/das_intubation_guidelines

The updated 2015 DAS guidelines include some important changes to managing the unanticipated difficult airway in an adult. The guidelines are written by the UK's DAS working group based on findings from a comprehensive literature review and expert opinion.

The guidelines state that a thorough airway assessment should be performed prior to administration of any anaesthetic. In order to maximise the likelihood of successful intubation at the first attempt or, failing that, to minimise trauma caused by repetitive laryngoscopy, patients should be optimally positioned (head-up positioning and ramping) and pre-oxygenated (with 100% oxygen via facemask seal until the end-tidal oxygen fraction is 0.87–0.9) prior to induction.

The administration of oxygen by nasal cannulae in addition to standard preoxygenation and facemask ventilation, is recommended in high-risk patients (e.g. when a difficult intubation is predicted and in obese patients). Gentle mask ventilation after the application of cricoid pressure and before tracheal intubation prolongs the time to desaturation. This is most useful in those with poor respiratory reserve, sepsis or high metabolic requirements.

A maximum of three attempts at intubation can be made, with purposeful adjustments on each attempt to improve success, including patient position, laryngoscope, adjuncts such as introducers, adequate neuromuscular block and release of cricoid pressure. A fourth attempt by a more experienced colleague is permissible. DAS recommends training with, and the immediate availability of, video-laryngoscopy.

If tracheal intubation fails, supraglottic airway devices (SADs) are recommended to provide a route for oxygenation while reviewing how to proceed. Second-generation devices are suggested.

If both tracheal intubation and SAD insertion have failed, consider waking the patient whilst oxygenating with facemask ventilation. If facemask ventilation is impossible, ensure that the patient is paralysed. A 'cannot intubate, cannot oxygenate' (CICO) situation arises when attempts to manage the airway by tracheal intubation, SAD and facemask ventilation have all failed. Hypoxic brain damage and death will occur if the situation is not rapidly resolved. Recognition and declaration of an airway emergency is important to focus the team, and scalpel cricothyroidotomy should follow immediately. This 'front of neck' access consists of neck extension, palpation and identification of the cricothyroid membrane, incision through the skin and cricothyroid membrane with a scalpel and insertion of a bougie and then cuffed tracheal tube. The DAS points out that high-pressure oxygenation through a narrow-bore cannula is associated with serious morbidity and should be avoided.

This guidance from the DAS limits choice and simplifies decision-making in stressful circumstances. Although serious airway complications are rare, rehearsal for such events is important.

Therapeutic hypothermia after out-of-hospital cardiac arrest in children

Moler FW, Silverstein FS, Holubkov R, Slomine BS Christensen JR, Nadkamy VM et al. *N Engl J Med* 2015; **372**: 1898–908

Therapeutic hypothermia is widely used after out-of-hospital ventricular fibrillation or ventricular tachycardia cardiac arrest in adults to improve neurological outcomes. Data are lacking for similar management in children. This multicentre study, conducted in paediatric intensive care units in North America, had two randomised treatment arms: therapeutic hypothermia (33°C) or therapeutic normothermia (36.8°C), maintained for 120 hours. Children older than 48 hours and younger than 18 years were included if they had had a cardiac arrest and remained dependent on mechanical ventilation after return of circulation.

The researchers looked at survival, as well as age-adjusted cognitive performance, at 12 months in the 295 subjects. The median age was 2 years.

There was no significant difference in neurobehavioural scores between the two groups. Survival at 12 months was not significantly different (38% in the hypothermia group versus 29% in the normothermia group; $P = 0.13$), although hypothermic patients survived significantly longer (149 ±1 4 days vs. 119 ± 14 days; $P = 0.04$). There was also no significant difference between groups in rates of infection, bleeding and significant arrhythmias.

The authors conclude that, in children who survive out-of-hospital cardiac arrests, therapeutic hypothermia offers no significant benefit compared with therapeutic normothermia with regards to 12-month survival and neurobehavioural outcome. The authors do suggest that controlled normothermia may be of benefit in these patients as fever can develop after hypoxic–ischaemic brain injury.

Incidence of mechanical complications of central venous catheterization using landmark technique. Do not try more than 3 times

Calvache JA, Rodríguez MV, Trochez A, Klimek, Stolker RJ, Lesaffre E. *J Intens Care Med* 2016; **31**: 397–402

Central venous catheters (CVCs) are widely used in critically ill patients in intensive care units for delivering medications, fluids, parenteral nutrition or dialysis. Insertion of CVCs carries the risk of

complications, including failure to place the catheter, incorrect positioning, pneumothorax, haemothorax, arterial puncture, dysrhythmia and death. This single-centre prospective observational cohort study in Colombia looked into the incidence of these complications. Insertion of 300 lines, using landmark technique, was independently witnessed and patients were observed for 24 hours for complications.

Seventy-two per cent ($n = 218$) of lines were inserted via the subclavian approach, with 87% inserted successfully on first attempt. Complications occurred in 17% of patients: 13% ($n = 40$) required a change in anatomical site for insertion and 5% ($n = 16$) experienced a major complication (arterial puncture, pneumothorax, haemothorax). There was an increased incidence of complications in patients mechanically ventilated during the procedure. There was a strong relationship between number of punctures and the incidence of mechanical complications during CVC insertion: complication rates are linearly correlated with number of attempts have a linear relationship until three punctures, at which point the relationship becomes exponential. The authors recommend performing no more than three punctures at the same site, after which another site should be sought.

Ultrasound guidance is recommended for CVC insertion; however, in many low- and middle-income countries this is unavailable and a landmark technique must be used.

Neurodevelopmental outcome at 2 years of age after general anaesthesia and awake regional anaesthesia in infancy (GAS): an international multicentre, randomised control trial

Davidson AJ, Disma N, de Graaf JC, Withington DE, Dorris L, Bell G et al. *Lancet* 2016; **387**: 239–50

Animal data have suggested that a variety of general anaesthetic agents have a detrimental effect on the developing brain. Whether these findings translate into humans is not entirely clear, and confounding factors have limited any conclusions drawn. For this reason, it is often regarded as wise to delay non-urgent surgery in the first year of life.

The authors of this study set out to identify whether general anaesthesia in early childhood has implications for adverse effects on infant neurodevelopment. The primary outcome is neurodevelopment at 5 years and the secondary outcome neurodevelopment at 2 years, and the 2-year data are presented in this publication.

The study was conducted across several countries and the design was a prospective, observer-blinded, randomised controlled equivalence trial. Infants of older than 26 weeks gestational age and less than 60 weeks postmenstrual age undergoing inguinal herniorrhaphy were randomised to regional anaesthesia (spinal or caudal anaesthesia) or general anaesthesia. Exclusion factors included contraindications to either form of anaesthetic or risk factors for neurodevelopmental delay. For assessment of the secondary outcome, the Bayley III neurodevelopmental assessment was utilised and performed within 2 months of the child's second birthday by a trained psychologist.

A total of 722 infants were recruited across seven countries, with 292 patients in the regional anaesthesia group and 295 in the general anaesthesia group attending for follow-up assessment. The overall results suggested equivalence within the various facets of the Bayley III neurodevelopmental assessment (cognitive, language and motor scales). The median duration of general anaesthesia was 54 minutes.

The authors conclude that in this first randomised control trial there is equivalence in neurodevelopmental assessment at 2 years of age between general anaesthesia, provided for less than 1 hour, and regional anaesthesia. They suggest that definitive conclusions should be limited until the primary outcome can be analysed in 2018. They also acknowledge that, whilst it appears general anaesthesia of just less than 1 hour duration compares equally with awake regional anaesthesia, the same may not be true in situations where general anaesthesia is provided for longer periods of time or when an infant is exposed to multiple general anaesthetics.

Safety of perioperative glucocorticoids in elective noncardiac surgery: a systematic review and meta-analysis

Toner AJ, Ganeshanathan V, Chan MT, Ho KM, Corcoran TB. *Anaesthesiology* 2017; **126**: 234–48

The increased use of perioperative glucocorticoids for their well-documented antiemetic properties has raised concerns about their safety profile. Whilst these agents undoubtedly provide useful anti-inflammatory properties, it has been postulated that they may increase the risks of wound infection due to their immunosuppressive effects and hyperglycaemia. Studies investigating these adverse outcomes have not provided conclusive evidence of a causal link.

Fifty-six randomised control trials were identified, including 5607 patients undergoing non-cardiac and non-obstetric surgery. Dexamethasone was the most common agent used in the analysed trials. Glucocorticoids were shown to have no effect on wound infection (odds ratio (OR) 0.8; 95% confidence interval (CI) 0.6 to 1.2) and caused only a minor increase in measured plasma glucose levels, said by the authors to be 'clinically unimportant'. Other outcome measures that were evaluated in this meta-analysis were anastomotic leak (OR 1.0; 95% CI 0.5 to 2.2), impaired wound healing (OR, 1.0; CI, 0.5 to 2.1) and postoperative haemorrhage (OR 1.4; 95% CI 0.7 to 2.7), all of which had similar rates in both the glucocorticoid and control groups.

The authors concluded that this meta-analysis supports many of the previous publications that have suggested that the use of perioperative single-dose glucocorticoids is safe with regards to the aforementioned risks in patients having non-cardiac and non-obstetric procedures.

Apnoeic oxygenation in pregnancy: a modelling investigation

Pillai A, Chikhani M, Hardman JG. *Anaesthesia* 2016; **71**: 1077–80

Apnoeic oxygenation is well described in non-pregnant patients as a simple method to prolong the time to desaturation during airway management. This technique is of particular use in situations when difficulty with airway management is anticipated. Rapid sequence induction (RSI) in pregnancy presents significant challenges owing to the associated anatomical and physiological changes, with risks of hypoxia even with timely securing of an endotracheal tube. Apnoeic oxygenation offers potential benefits by prolonging the time to desaturation in this situation.

This study utilised a computer-based model, which replicates the respiratory and cardiovascular systems in pregnancy. Virtual subjects were created to simulate common patients who might be encountered such as patients with a body mass index (BMI) of 35 $kg\,m^{-2}$ or 50 $kg\,m^{-2}$, patients in labour, with sepsis, with anaemia and in those with a twin pregnancy. These virtual patients were modelled on pre-existing physiological measurements. A protocol was applied in which the virtual patient was pre-oxygenated for 3 minutes with 100% oxygen and then apnoea was commenced with supply of a variety of concentrations of oxygen at the open glottis until the SaO_2 decreased to 40%. Conditions replicating events during RSI were introduced. Measurements of SaO_2, pH, PaO_2 and $PaCO_2$ were obtained at 1-second increments.

The results demonstrated that administration of 80–100% oxygen to an open airway extended the time to desaturation (SpO_2 of 40%) from 4 minutes 28 seconds to 58 minutes in the average pregnant patient (likely to be achievable only with high-flow nasal cannulae). This time was markedly reduced in the labouring, septic and high-BMI modelled patients. $PaCO_2$ was shown to rise by 1.13 $kPa\,min^{-1}$.

The authors acknowledged the difficulties in translating the findings into clinical practice but that ultimately apnoeic oxygenation can delay the duration to critical hypoxia in parturients. They highlighted that a patent airway is required for apnoeic oxygenation to be effective and that the evidence for the use of standard nasal cannulae as opposed to high-flow nasal cannulae requires further investigation. Their results suggested that, using standard nasal cannulae during apnoea, an FiO_2 of 0.4–0.6 could be delivered, thus providing a small increase in the time to desaturation, and with the use of high-flow nasal cannulae an FiO_2 of approaching 1.0 could be delivered, thus showing the most impressive increases in time to desaturation.

Standard nasal cannulae are relatively inexpensive and hence may be a viable option for apnoeic oxygenation to improve safety during high-risk airway management in pregnant patients in areas of the world with limited resources.

Guidelines for the management of severe traumatic brain injury, 4th edn

Carney N, Totten AM, O'Reilly C *et al* (for the Brain Trauma Foundation). *Neurosurgery* 2016. [Epub ahead of print]. Available at https://braintrauma.org/uploads/03/12/Guidelines_for_Management_of_Severe_TBI_4th_Edition.pdf

This new document updates the previous guidelines published by the Brain Trauma Foundation in 2007. The authors provide a comprehensive analysis of the current evidence base for therapeutic interventions, monitoring and treatment thresholds in patients with traumatic brain injury (TBI).

In total, 28 recommendations are provided, 14 of which are new or revised from the third edition of the guidelines.

Treatment recommendations

Decompressive craniectomy (DC)

- Not recommended to improve outcomes at 6 months in patients with severe TBI with diffuse injury, and with intracranial pressure (ICP) elevation to values > 20 mmHg for more than 15 minutes in an 1-hour period refractory to first-tier therapies.
- A large frontotemporoparietal DC is recommended over a small frontotemporoparietal DC for reduced mortality and improved neurological outcomes in patients with severe TBI.

Prophylactic hypothermia

- Early, short-term prophylactic hypothermia is not recommended to improve outcomes in patients with diffuse injury.

Hyperosmolar therapy

- Mannitol is effective for controlling ICP; arterial hypotension should be avoided to ensure that the cerebral perfusion pressure is maintained.
- Restrict use prior to ICP monitoring to patients with signs of transtentorial herniation or progressive neurological deterioration not attributable to extracranial causes.

Cerebrospinal fluid (CSF) drainage

- An external ventricular drainage (EVD) system zeroed at the midbrain with continuous drainage of CSF is more effective in lowering ICP than intermittent use.
- Use of CSF drainage to lower ICP in patients with an initial Glasgow Coma Scale (GCS) score <6 during the first 12 hours after injury may be considered.

Ventilation therapies

- Prolonged prophylactic hyperventilation with a $PaCO_2$ of ≤ 25 mmHg (3.3 kPa) is not recommended. Hyperventilation is recommended as a temporising measure for the reduction of elevated ICP. Hyperventilation should be avoided during the first 24 hours after injury when cerebral blood flow (CBF) may be critically reduced.

Anaesthetic, analgesics and sedatives

- Administration of barbiturates to induce burst suppression measured by electroencephalography (EEG) as prophylaxis against the development of intracranial hypertension is not recommended.
- High-dose barbiturate administration is recommended to control elevated ICP refractory to maximum standard medical and surgical treatment. Haemodynamic stability is essential before and during barbiturate therapy.
- Although propofol is recommended for the control of ICP, there is no evidence of improvement in mortality or 6-month outcomes.

Steroids

- The use of steroids is not recommended for improving outcome or reducing ICP. In patients with severe TBI, high-dose methylprednisolone is associated with increased mortality and is contraindicated.

Nutrition

- Feeding patients to attain basal caloric replacement ideally by day 5 and at the latest by day 7 post injury is recommended to decrease mortality.
- Transgastric jejunal feeding is recommended to reduce the incidence of ventilator-associated pneumonia.

Infection prophylaxis

- Early tracheostomy is recommended to reduce mechanical ventilation days when the overall benefit is thought to outweigh the complications associated with such a procedure. However, there is no evidence that early tracheostomy reduces mortality or the rate of nosocomial pneumonia.
- The use of povidone-iodine oral care is not recommended to reduce ventilator-associated pneumonia and may cause an increased risk of acute respiratory distress syndrome.
- Antimicrobial-impregnated catheters may be considered to prevent catheter-related infections during external ventricular drainage.

Deep vein thrombosis prophylaxis

- Low-molecular-weight heparin (LMWH) or low-dose unfractionated heparin may be used in combination with mechanical prophylaxis. However, there is an increased risk for expansion of intracranial haemorrhage.
- In addition to compression stockings, pharmacological prophylaxis may be considered if the brain injury is stable and the benefit is considered to outweigh the risk of increased intracranial haemorrhage.
- There is insufficient evidence to support recommendations regarding the preferred agent, dose or timing of pharmacological prophylaxis for deep vein thrombosis.

Seizure prophylaxis

- Prophylactic use of phenytoin or valproate is not recommended for preventing late post-traumatic seizures (PTS).
- Phenytoin is recommended to decrease the incidence of early PTS, within 7 days of injury, when the overall benefit is thought to outweigh the complications associated with such treatment. However, early PTS have not been associated with worse outcomes.
- At the present time there is insufficient evidence to recommend levetiracetam (Kepra) over phenytoin in terms of efficacy in preventing early post-traumatic seizures and toxicity.

Monitoring recommendations

Intracranial pressure monitoring

- Management of patients with severe TBI using information from ICP monitoring is recommended to reduce in-hospital and 2-week post-injury mortality.
- ICP should be monitored in all salvageable patients with a TBI (GCS score 3–8 after resuscitation) and an abnormal computed tomography (CT) scan. An abnormal CT scan of the head is one that reveals haematomas, contusions, swelling, herniation or compressed basal cisterns.
- ICP monitoring is indicated in patients with severe TBI with a normal CT scan if two or more of the following features are noted at admission: age > 40 years, unilateral or bilateral motor posturing or systolic blood pressure < 90 mmHg.

Cerebral perfusion pressure (CPP) monitoring

- It is recommended that patients with severe TBI are managed following guidelines for CPP monitoring to decrease 2-week mortality.

Threshold recommendations

Blood pressure thresholds

- Maintaining systolic blood pressure at ≥ 100 mmHg in patients aged 50–69 years or at ≥ 110 mmHg in patients aged 15–49 years or ≥ 70 years may be considered to decrease mortality and improve outcomes.

Intracranial pressure thresholds

- Treating ICP > 22 mmHg is recommended because values above this level are associated with increased mortality.
- A combination of ICP values and clinical and brain CT findings may be used to make management decisions.

Cerebral perfusion thresholds

- The recommended target CPP value for survival and favourable outcomes is between 60 and 70 mmHg. Whether 60 or 70 mmHg

is the minimum optimal CPP threshold is unclear and may depend upon the autoregulatory status of the patient.

- Avoiding aggressive attempts to maintain CPP >70 mmHg with fluids and vasopressors may be considered because of the risk of adult respiratory failure.

Whilst not all of these recommendations will apply to lower resourced health care systems the guideline as a whole provides a useful approach to constructing a local evidence based protocol for managing patients with severe TBI.