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Update in Anaesthesia

Education for anaesthetists worldwide

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The Journal of the World Federation of Societies of Anaesthesiologists

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WFSA and Lifebox advocate for global anaesthesia and surgery at the World Health Assembly

The 70th World Health Assembly (WHA), held in Geneva in May 2017, was an opportune occasion to discuss the role of anaesthesia and surgery within the global health agenda with stakeholders and decision-makers from around the world.

Recent seminal papers have highlighted major discrepancies in the provision of safe anaesthesia and surgery worldwide.[1,2] The Lancet Commission on Global Surgery estimated that five billion of the world's seven billion people do not have access to safe, affordable anaesthesia and surgical care when needed.[1] Despite these findings, the essential role that anaesthesia and surgery play within health systems is still not understood by key decision-makers and has been given a lower priority than other areas of global health.

WFSA and Lifebox are amongst a small but growing group of organisations dedicated to working in partnership with our colleagues in low-resource settings to improve access to safe anaesthesia and safe surgery. Locally led projects, such as Lifebox's pulse oximetry and education work, and the WFSA's Fellowships and SAFE courses play an immediate role; but bringing this evidence-based impact to bear through advocacy at the highest international level is crucial for long-term change.

The WFSA's delegation included Drs Jannicke Mellin-Olsen, Adrian Gelb and Wayne Morriss, who joined WFSA and Lifebox staff in Geneva to represent our activities and aims to member states, to our other partners in the World Health Organization (WHO), to industry, and to other non-government, non-corporate bodies working on behalf of the neglected surgical patient. Over the week we learned more about how we can impact global health policy, listen to, and support partners in countries addressing critical safety and access issues. Through direct conversation, strategic and procedural support, we helped to influence further decision making that will prioritise surgical and anaesthesia care around the world.

STRENGTHENING EMERGENCY AND ESSENTIAL SURGICAL CARE AND ANAESTHESIA AS A COMPONENT OF UNIVERSAL HEALTH COVERAGE

The Assembly marked the 2-year anniversary of a potential game-changer for the five billion people named by the Lancet Commission: Resolution 68.15, passed by the WHA on 22 May 2015, calls for 'Strengthening emergency and essential surgical care and anaesthesia as a component of universal health coverage'.[3] The WFSA, as a non-state actor in official liaison with WHO, made four statements at the Assembly, one unequivocally supporting Resolution 68.15 and outlining WFSA's contributions towards progressing the Resolution, and others on the workforce crisis in anaesthesia and on the global shortage of medicines. The WFSA commended states that have initiated the development of national surgical, obstetric and anaesthesia plans (NSOAPs), and urged others to do the same. However, the WFSA highlighted concern about the massive funding gap that exists for this area of global health despite the huge number of people who die from conditions that could be treated by surgery.

'We need to change the way we regard surgery', explained Dr Jabbin Mulwanda, Permanent Secretary of the Zambian Ministry of Health, at an event co-hosted by Lifebox and the WFSA. 'We need to see it as essential. And this will require advocacy to change the way decision-makers think, particularly those that allocate resources.'

Thanks to the hard work of a number of country delegations, and organisations working to progress the Resolution, member states approved an amendment calling upon the Director-General to provide a progress report on WHA Resolution 68.15 every 3 years until 2030. The Kenyan delegation also delivered a statement on behalf of the African region, supported by Zambia and Namibia among other states, calling for a Global Action Plan to guide and facilitate the implementation of commitments to Resolution 68.15.

A statement delivered on behalf of WFSA by Lifebox, noted that 'It is imperative that a Global Action Plan for emergency and essential surgical care and anaesthesia be developed alongside national action plans in order to mobilize the resource sharing and finances needed for their successful implementation.'[4]

Development of this Global Action Plan is being led by a WHO Global Surgery, Obstetrics and Anaesthesia Partnership, with technical committees focusing on the critical components of a perioperative ecosystem: advocacy and research, surgical systems, information management, essential medicines and health workforce.

The next step will be discussions with the newly appointed Director-General of the WHO, Dr Tedros Adhanom Ghebreyesus, who has stated his strong support for global anaesthesia and surgery, and the introduction of an agenda item specifically addressing this request at the next assembly in 2018.

HUMAN RESOURCES FOR HEALTH

The WFSA and Lifebox also held a side-event at the WHA entitled 'What next for surgery and anaesthesia? Civil society & global solutions', which explored the future of global surgery and anaesthesia and invited views from InciSioN, a student global surgery network, Operation Smile, the G4 Alliance and the Zambian Ministry of Health.[5]

Zambia played a leading role in the passage of Resolution 68.15, and continued its high-profile commitment by launching a NSOAP during the WHA.[6] Dr Nthele Mzaza, of the Zambian Ministry of Health, talked about the challenges of leading by example, and the importance of partnership in planning and addressing surgical and anaesthesia need.

Kris Torgeson shared an example of how planning, partnership and engaging local leadership can support change in practice from the immediate to the long term. A photo from a recent visit to a district hospital in Zambia, part of a Lifebox pulse oximeter distribution and training programme, showed 'not only how [the nurse anaesthetist] put the pulse oximeter into practice to better serve her patients, but how she had enabled teamwork in the entire OR to implement the WHO Surgical Safety Checklist as well.'

The event was also an opportunity to discuss the importance of human resources for health, particularly in relation to Universal Health Coverage (UHC). There cannot be Universal Health Coverage without a scale-up of surgical services worldwide, and in order to increase the body of evidence highlighting the current workforce shortage, and subsequent impact, the WFSA officially launched a landmark online resource tool mapping the total number of anaesthesia providers worldwide.

The *WFSA Global Workforce Map*, which shows data for countries representing more than seven billion people, highlights the huge shortage in anaesthesia workforce worldwide and the gap between high-income and low-income countries.[7] It also shows that over 70 countries reported a total anaesthesia provider number of less than 5 per 100 000 population, detailing the current crisis in the surgical and anaesthesia workforce that has left five billion people without access to safe and affordable anaesthesia and surgical care.

'The crisis in anaesthesia is perhaps most apparent in terms of workforce. Safe anaesthesia requires a trained provider and yet across large parts of Sub-Saharan Africa, South-East Asia, and beyond, ratios of far less than 1 trained provider per 100,000 population are commonplace. In high income countries we are used to ratios of 20 per 100,000 or higher, yet in low income countries we actually have examples of there being 1,000 times fewer trained providers and 1,000 times higher mortality rates. It's wrong', Julian Gore-Booth, WFSA Chief Executive, explained.

Wayne Morriss, Director of Programmes at the WFSA, confirmed the significance of the findings: 'We know that there is a problem, and we know that there is a solution. Anaesthesia provision is affordable with research from the World Bank highlighting a return on investment as high as ten to one.[2] The map shows that substantial investment in the education of all anaesthesia providers is required as soon as possible, and the WFSA is well placed to work with the WHO, its own member societies, other specialist medical organizations, governments, NGOs and country level health systems to correct the workforce gap and achieve safe anaesthesia for all by 2030.'

SIGNPOSTS TOWARDS NEXT YEAR

Such evidence is critical for framing policy – but it's also an access point for more mainstream media, and the public appetite for action needed to carry a global health movement home. With the world's lens on the election process for a new WHO Director-General, media engagement at this year's WHA was always going to be a challenge – even for a movement increasingly vocal about its relevance to global health.[8] However the selection of Dr Tedros from Ethiopia, is an exciting opportunity to push anaesthesia and surgery to a bigger stage.

'As Minister of Health of Ethiopia, I saw first-hand the pain and suffering in communities where life-saving surgical options were not available," said Dr Tedros, in a letter to the four surgical colleges in Great Britain and Ireland.

'Access to surgical services and anesthesia is something to which I am deeply committed … If elected Director-General, I will work in consultation with Member States to build national capacity for emergency and surgical care to implement WHA 68.15.'

As Dr Tedros frames his vision for the next 5 years of WHO priorities, it is up to the global anaesthesia and surgical community to ensure our research, partners, and patients are involved. To work together

to turn paper into policy, words into action, global need into global access. The invitation has been formally issued, but the door won't open if we don't push.

Niki O'Brien
WFSA Advocacy and Communications Officer

Julian Gore-Booth
WFSA Chief Executive Officer

Sarah Kessler
Director of Communications and Strategic Partnerships
Lifebox

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Update in
Anaesthesia

Evolution and change

On 14 April 1859, Charles Darwin's book *On the Origin of Species*, in which he put forward his theory of evolution of life on planet Earth, was published. Based on observations on the voyage of the *HMS Beagle,* his theory has been hotly debated ever since, with those who find his arguments compelling staunchly defending this thesis. There are those who reject Darwin's conclusions as vehemently as those who accept them. No matter where an individual falls in the spectrum of the debate, the important issue is how Darwin's thoughts were made public: by publishing them. In our current world of medical and scientific learning, the most up-to-date theories and knowledge is found in journals.

Update in Anaesthesia, an official journal of the World Federation of Societies of Anaesthesiologists (WFSA), is about to undergo an evolution itself. Bruce McCormick, a Consultant Anaesthetist at the Royal Devon and Exeter NHS Foundation Trust, in the UK, has been the editor-in-chief of this periodical since he took over from its founder, Iain Wilson, in 2006. He has laboured long and hard to produce this outstanding world-wide vehicle for anaesthesia-related education. This edition is his fourteenth: an amazing record of publication given that through most, if not all, of his tenure as editor-in-chief he has worked virtually alone. Bruce has devised editorial content, found authors willing to write, helped edit papers from those who spontaneously contributed, and seen the articles through the typesetting and printing stages. Quite honestly, *Update in Anaesthesia* would not currently exist were it not for Bruce's dedication and hard work.

Over the past year, Bruce has made the very difficult decision to step down as editor-in-chief, and this is in fact his last edition of the journal in that role. Thus, the WFSA Publications Committee has been charged with the very difficult task of defining what the journal has the potential to become, what the organisation believes it should be, and finding the proper leadership to fulfil this vision. Since the World Congress last September, the Committee has been working hard at these tasks.

The Committee's vision is that over the next decade *Update in Anaesthesia* will become a formally peer-reviewed journal. This means that each article will be reviewed and commented upon by individuals who are experts in the area the manuscript addresses. This process is important for several reasons. First, it helps validate the conclusions expressed in the article. Second, it serves as a mechanism to prevent plagiarism. Third, it allows scrutiny of data to assess their validity and possible falsification. While no peer review process is completely accurate, it is the standard for journals across the world. We will continue to produce themed editions of the journal that help disseminate the latest knowledge on various practice areas in anaesthesia, with particular emphasis on the challenges of providing anaesthesia in low- and middle-income countries (LMICs).

Once our vision for *Update in Anaesthesia* was agreed, the Publications Committee, with the outstanding support of the WFSA Secretariat, put out a call for those interested in the job of editor-in-chief. A number of highly qualified individuals submitted their curriculum vitae with a covering letter outlining their expertise and suitability for the position. Three candidates were short-listed and interviewed by internet video link. The WFSA Secretariat was invaluable in overcoming the complex issues of linking candidates and interviewers who were spread across the world in six different time zones – amazingly no one was on line at 2 o'clock in the morning!

After considerable deliberation, Alan Jay Schwartz was chosen as the editor-in-chief. Dr Schwartz is a paediatric anaesthetist at the Children's Hospital in Philadelphia, Pennsylvania, in the United States. Alan has been in practice for the better part of four decades and has extensive editorial experience at both *Anesthesiology* and *Anesthesia and Analgesia*. He has deep passion for education and great enthusiasm for, and understanding of, the needs, goals and aspirations of the WFSA. His belief in our shared vision for *Update in Anaesthesia* will allow the publication to continue to serve its target readership in LMICs, whilst achieving our long-held goal of becoming indexed in the National Library of Medicine's PubMed Index. This will make the journal far more accessible to its readers in all parts of the world.

This recruitment process also identified two other outstanding editorial candidates, and Dr Schwartz reached out to them to join the editorial board as Associate Editors. Victoria Howell, a Consultant Anaesthetist with an interest in paediatrics, works at The Queen Elizabeth Hospital, King's Lynn, in the UK and brings a wealth of experience in anaesthesia in LMICs. She has served as the Head of the Anaesthesia

Department in the CCBRT (Comprehensive Community Based Rehabilitation in Tanzania) Disability Hospital, Dar es Salaam, Tanzania. The other appointed Associate Editor is Professor Aina Christina Lungren, who currently serves as the Chief Specialist and Head of the Anaesthesia Department at the Chris Hani Baragwanath Hospital in Soweto. She is also Academic Head of Anaesthesia at the University of the Witwatersrand. Christina edited the *South African Journal of Anaesthesia* for over 13 years and this editorial experience is essential to moving *Update* forward.

Dr Schwartz and his team are currently investigating software to facilitate electronic submission of manuscripts to the journal. This program will also track where the article is in the publication process – Is it under peer review and with whom? Has it been returned to the author for revision? Has it been accepted? and in which edition of the journal will it be published? The next set of challenges for Alan and his team is to recruit an editorial board and to begin to develop a publication schedule with the goal to produce two editions each year. There is much work to be done, but there are also many individuals willing to help.

While Charles Darwin's work was controversial when published and remains so, the work of Bruce McCormick stands as a testament to one man's belief and hard work. He is handing over *Update in Anaesthesia* as a strong publication. Alan Jay Schwartz has made remarkable progress in a short period of time, largely because he is inheriting a well-developed platform from Bruce. The WFSA and world community of anaesthesia owes Bruce a debt of gratitude we cannot repay. From the Publications Committee, thank you for a job well done.

Douglas R. Bacon, MD, MA
Chair, Publications Committee, WFSA

Update in
Anaesthesia

WFSA Position Statement on Anaesthesiology and Universal Health Coverage

In May 2017 the General Assembly of the WFSA approved the WFSA Position Statement on Anaesthesiology and Universal Health Coverage by unanimous resolution. Eighty-five Member Societies, representing 80% of total delegate numbers, took part in the vote.

The Position Statement together with the International Standards for a Safe Practice of Anaesthesia[1] and the Workforce Survey[2] provide a framework for the work of the WFSA over the coming years as we seek to ensure improved patient care and access to safe anaesthesia worldwide.

The text of the statement is reproduced in full below.

The World Federation of Societies of Anaesthesiologists (WFSA) is a non-profit organisation representing anaesthesiologists in 150 countries. It exists to improve patient care and access to safe anaesthesia worldwide; this mission directly contributes to the United Nations' Sustainable Development Goal 3 which aims to achieve Universal Health Coverage by 2030.

Anaesthesiology is the medical science and practice of anaesthesia. It includes anaesthesia for surgical, obstetric and trauma care, and areas of practice such as perioperative medicine, pain medicine, resuscitation, and intensive care medicine.

An *anaesthesiologist* is a qualified physician who has completed a nationally recognized specialist training programme in anaesthesiology. In some countries, the term *anaesthetist* is used instead of *anaesthesiologist*.

There is an urgent need to address deficiencies in access to safe anaesthesia care.[3] An additional 1.27 million surgical, obstetric and anaesthesia providers will be required by 2030 to achieve Universal Health Coverage.[4] In many countries, particularly those with limited resources, anaesthesia is associated with unacceptably high mortality rates. Training and ongoing maintenance of standards are essential for increasing the number of providers and increasing the safety of anaesthesia for patients worldwide.

In some countries, the anaesthesia need will be met by training anaesthesiologists. In other countries, especially those with limited resources, the need may, in part, be met by training non-anaesthesiologist providers.

Anaesthesia is complex and potentially hazardous, and optimal patient care depends on anaesthesia being provided, led or overseen by an anaesthesiologist. The WFSA recognises that effective teamwork is a vital component of patient safety.

The WFSA, representing anaesthesiologists worldwide, and in official relations with the World Health Organisation, is well positioned to lead the development of standards and implementation of safe, universal anaesthesia coverage. Effective development and oversight of safe anaesthesia services will require anaesthesiologist leadership at governmental, organisational, academic, teaching and clinical levels.

The WFSA is committed to working with governments and non-governmental organisations to improve patient care and access to safe anaesthesia worldwide. Anaesthesiologist-led development of anaesthesia services is vital if we are to achieve Universal Health Coverage by 2030.

WFSA Board and Council

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Update in
Anaesthesia

Rapid sequence induction

Will Ross and Louise Ellard

Correspondence: Louise.ellard@austin.org.au

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Summary
Rapid sequence induction (RSI) is intended to reduce the risk of aspiration by minimising the duration of an unprotected airway. Preparation and planning – including technique, medications, team member roles and contingencies – are desirable prior to every RSI. Substantial variability in practice exists; therefore, institutional factors and clinical circumstances should be considered when determining how to perform an RSI..

INTRODUCTION

Rapid sequence induction (RSI) is a method of achieving rapid control of the airway whilst minimising the risk of regurgitation and aspiration of gastric contents. Intravenous induction of anaesthesia, with the application of cricoid pressure, is swiftly followed by the placement of an endotracheal tube (ETT). Performance of an RSI is a high priority in many emergency situations when the airway is at risk, and is usually an essential component of anaesthesia for emergency surgical interventions. RSI is required only in patients with preserved airway reflexes. In arrested or completely obtunded patients, an endotracheal tube can usually be placed without the use of medications.

History of RSI

RSI was originally described in 1961 by Sellick[1] as:

- emptying of the stomach via a gastric tube, which is then removed;
- pre-oxygenation;
- positioning the patient supine with a head-down tilt;
- induction of anaesthesia with a barbiturate (e.g. thiopentone) or volatile and a rapid-acting muscle relaxant (e.g. suxamethonium);
- application of *cricoid pressure*;
- laryngoscopy and intubation of the trachea with a cuffed tube immediately following fasciculations.

The above classic method is now very rarely followed in full. In current clinical practice, a number of modifications have been made to the traditional RSI technique (Table 1). The term 'modified RSI' is sometimes used to describe such variations, but this term lacks a commonly accepted definition.

Table 1. *Common modifications of RSI technique in current practice*

Omitting the placement of an oesophageal tube
Supine or ramped positioning
Titrating the dose of induction agent to loss of consciousness
Use of propofol, ketamine, midazolam or etomidate to induce anaesthesia
Use of high-dose rocuronium as a neuromuscular blocking agent
Omitting cricoid pressure

CRICOID PRESSURE

Cricoid pressure is the application of force to the cricoid cartilage of the patient (Figure 1). The rationale is that the upper oesophagus is occluded by being compressed between the trachea and the cervical vertebrae, preventing passive reflux of gastric contents and subsequent development of aspiration pneumonitis. A force of 10 newtons (N) is applied by the thumb and index finger of an assistant, increasing

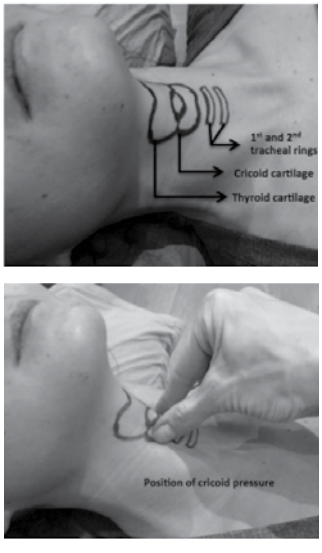

Figure 1. *Surface anatomy for cricoid pressure*

Will Ross
Anaesthesia Fellow
Royal Darwin Hospital
Melbourne University
Melbourne 337
Australia

Louise Ellard
Staff Anaesthetist
Austin Health
145 Studley Road
PO Box 5555
Heidelberg
Victoria
Australia 3084

to 30 N once consciousness is lost (10 N is the equivalent of around 1 kg of pressure). This pressure is maintained until endotracheal tube placement is confirmed. Cricoid pressure should be reduced or released if laryngoscopy is difficult, or if vomiting occurs (to reduce the chance of oesophageal rupture from active vomiting).

INDICATIONS

RSI is indicated in patients who require endotracheal intubation and are at increased risk of reflux and aspiration of gastric contents (Table 2). This means that RSI is almost universally required in situations calling for emergent endotracheal intubation. In fact, non-RSI intubation is almost exclusively the domain of the elective operating environment. Patient factors may dictate the need for certain elements of the RSI to be modified or omitted.

Contraindications to suxamethonium, such as allergy, susceptibility to malignant hyperthermia or hyperkalaemia, should prompt use of an alternative muscle relaxant such as high-dose rocuronium. A laryngeal injury is a contra-indication to cricoid pressure.[2] Unstable cervical spine fractures will require caution in the application of cricoid pressure due to the possibility of exacerbating damage.[3]

PREPARATION

Preparation is vital, both of equipment and of team members – particularly if team members are unfamiliar with the environment or their colleagues. Anticipation of a difficult airway and establishing oxygenation plans prior to conducting RSI are essential.

Many organisations advocate the use of a checklist to ensure that all equipment is available and in working order, and that the planned sequence of events is shared with all team members. An example of an emergency intubation checklist is shown in Figure 2.

Preparation of patient

Explanation should be offered to the patient, providing a description of the planned technique including cricoid pressure. Their cooperation for effective preoxygenation (or denitrogenation) will also be required. An alert patient may be offered a non-particulate antacid beforehand, such as 30 mL of 0.3 mol L^{-1} sodium citrate: this is most commonly used in the obstetric population.

Table 2. *Indications for RSI*

Unfasted patients or patients of unknown fasting status, e.g. trauma patients, patients undergoing emergency surgery or in resuscitation and patients with a reduced consciousness level
Known gastro-oesophageal reflux such as due to hiatus hernia
Conditions leading to delayed gastric emptying, e.g. autonomic gastroparesis (diabetes, Parkinson's disease), history of gastric banding surgery, patient in severe pain or with recent administration of opioids
Pregnancy (from the second trimester onwards)

Preparation of equipment

See Box 1.

Preparation of drugs

Hypnotics

Five drugs are commonly used to induce anaesthesia: propofol, ketamine, etomidate, thiopentone and midazolam (Table 3).

Careful dosing of any drug used is more important than the choice of drug. In shocked patients a very modest dose of hypnotic may be

Box 1. Suggested equipment for RSI

- Oxygen supply (machine)
- Oxygen delivery device
  - self-inflating bag with one-way valve
  - nasal prongs*
- Standard airway equipment
  - facemask
  - laryngoscope handle × 2
  - range of laryngoscope blades
  - cuffed oral endotracheal tubes of appropriate sizing, with a range of alternative sizes available
  - endotracheal tube tie or tape
- **Difficult airway equipment**, as per the difficult airway plan. This may include:
  - oro- and nasopharyngeal airways
  - bougie
  - video-laryngoscope*
- **Supraglottic rescue device**: laryngeal mask airway or alternative supraglottic airway
- **Suction**
- **Monitoring**
  - pulse oximeter
  - waveform capnograph
  - blood pressure cuff and sphygmomanometer, or arterial line
  - electrocardiograph
- **Drugs** (see 'Preparation of drugs' section for further detail)
  - induction agent
  - agent for maintenance of anaesthesia
  - fast-acting neuromuscular blocking agent
  - emergency drugs (vasopressor and adrenaline, atropine)
  - fluids running to act as flush for rapidly delivering drugs to circulation

*Optional.

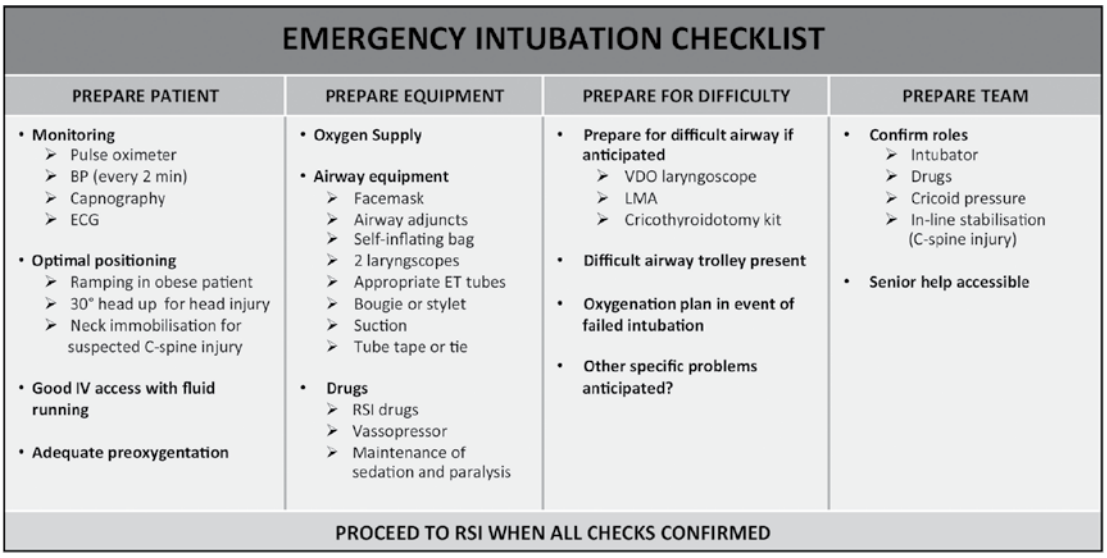

Figure 2. *A checklist used in preparation for emergency intubation to ensure that drugs and equipment are available and that all team members are aware of their roles and the planned sequence of events*

Table 3. *Drugs commonly used to induce anaesthesia*

Propofol 1–3 mg kg^{-1}	Commonly used in the operating theatre for patients who are haemodynamically stable. In elderly or hypovolaemic patients, the dose is drastically reduced: often 0.5–1 mg kg^{-1} is sufficient, although time to effect is increased due to lower cardiac output
Ketamine 1–2 mg kg^{-1}	Increasingly used in pre-hospital settings and in unstable patients. The usual effect is an elevation in heart rate and variable but modest blood pressure changes. Secretions increase, which may necessitate suctioning or premedication with an anti-sialagogue such as atropine or glycopyrrolate
Etomidate 0.3 mg kg^{-1}	Also has very limited haemodynamic effects. Use has been limited by concerns of adrenal suppression, and there is limited availability in some countries
Thiopentone 3–5 mg kg^{-1}	Has the most rapid and predictable effect, with less haemodynamic instability than propofol. However, there may be issues with poor availability, and the harmful sequelae following extravasation or intra-arterial injection should be considered
Midazolam 0.1–0.2 mg kg^{-1}	May be used, although the time to effect may be very prolonged. It is most suitable in patients who are already obtunded and primarily require amnesia rather than true anaesthesia

sufficient as these drugs can easily lead to circulatory collapse and cardiac arrest. Resuscitation drugs should be readily available.

Neuromuscular blocking agents and reversal agents

For many decades, **suxamethonium** (succinylcholine) has been the standard of care for RSI. It is usually easily available and reliable. In full dose (1–2 mg kg^{-1}) it produces fasciculations, paralysis and excellent intubating conditions within one circulation time (15–45 seconds).

Adverse effects are well recognised, although uncommon. Myalgia is the most common, but bradycardia, hyperkalaemia-induced cardiac arrest, anaphylaxis and triggering of malignant hyperthermia can all occur. Many clinicians continue to use suxamethonium unless there is evidence of susceptibility to one or more of these severe adverse events, for example recent burns, spinal cord injury or a history of muscular dystrophy.

Rocuronium is an alternative agent. In high dose (a range of 0.9–1.6 mg kg^{-1} has been described) profound relaxation is obtained within 45–60 seconds.[4] One disadvantage is a lack of fasciculations, so other methods of ensuring adequate laryngeal paralysis must be used. The prolonged duration of action must be taken into account if the airway is likely to be difficult and if the specific reversal agent is not available. Anaphylaxis is still a possibility, but the risks of myalgia, hyperkalaemia and malignant hyperthermia are avoided.

A further benefit of rocuronium is the existence of a specific reversal agent. Sugammadex binds avidly to rocuronium, making it unavailable to bind at the neuromuscular junction and reversing the effect. This is useful for elective reversal preceding extubation, and

also for restoring neuromuscular function rapidly if required by the difficult airway plan. Sugammadex 16 mg kg^{-1} can rapidly reverse the effect of rocuronium but its use may be inhibited by the high cost and resulting limited stock. It may also be completely unavailable in some settings, and there can be issues with unfamiliarity with its use. Side effects include interaction with hormonal contraceptive drugs. There is only limited availability in some countries (Sugammadex achieved US FDA approval only in December 2015). Other common neuromuscular blocking agents are too slow in onset to provide sufficiently rapid intubating conditions and so would require prolonged mask ventilation of the patient.

Pharmacological adjuncts

In shocked patients, no adjuncts may be required. However, in systemically well patients, or patients at risk of severe hypertension during induction (for example patients with pre-eclampsia, head injury or an unprotected intracranial aneurysm), ablating the pressor response to laryngoscopy is often desirable.

Opioids are commonly used: **fentanyl** (1–2 μg kg^{-1}), **alfentanil** (10–15 μg kg^{-1}) and **remifentanil** (0.5–1 μg kg^{-1}) are all sufficiently rapid-acting for use in RSI. **Lidocaine** (lignocaine) (1–1.5 mg kg^{-1}) is also effective at reducing cough and bronchospasm, solely or in combination with an opioid.[5]

Preparation of team members

Tasks that need to be allocated and performed include:

- pre-oxygenation
- intubation
- assisting the intubator (passing equipment, etc.)
- drug administration
- cricoid pressure application (if used)
- manual in-line stabilisation (if indicated).

A minimum of two people are required to fill these roles. Commonly the lead intubator will also pre-oxygenate and administer drugs, while the assistant applies cricoid pressure, and passes equipment to the intubator. A third person may be required for manual in-line stabilisation of the neck if cervical spine injury is suspected.

RSI TECHNIQUE

The patient should be positioned appropriately for pre-oxygenation and intubation; this may involve ramping, manual inline stabilisation or a semirecumbent position for pre-oxygenation if respiratory function is impaired by lying supine.

A reliable intravenous cannula should be placed, and a carrier fluid should run freely to maximise drug delivery to the central circulation. Alternatively, a large syringe of saline may be used to flush medication following administration.

Pre-oxygenation, or denitrogenation, should be performed as completely as possible having regard to the clinical urgency. At a minimum, 3 minutes of tidal breathing, or eight vital capacity breaths in one minute should be performed with an inspired oxygen concentration of 100%. Alternatively, if a gas analyser is available, the end-tidal oxygen fraction should reach at least 0.8. If the available device offers an option for positive end-expiratory pressure (PEEP) or positive pressure during patient-initiated breaths (pressure support ventilation, bilevel positive airway pressure (BiPAP) or similar), then this may be useful to aid pre-oxygenation in some patients.

When satisfactory pre-oxygenation has been achieved, and all team members are ready to proceed, the chosen medications should be administered and the patient should be observed for evidence of effect. If cricoid pressure is to be used, it should be *in situ* and increased from 10 N to 30 N at the moment consciousness is lost. When intubating conditions are obtained, by observing fasciculations (if suxamethonium is used), waiting for an appropriate time period or using a neuromuscular monitor, intubation should be performed. Given the need to rapidly secure the airway, first-pass success is highly desirable. Accordingly, many practitioners use a bougie or stylet as routine, and if available a video-laryngoscope may maximise chance of success.

If regurgitation is observed, suction should be rapidly applied, and the bed should be placed in a head-down (Trendelenburg) position to minimise the chance of aspiration into the trachea.

Once the endotracheal tube is placed, the cuff is immediately inflated and correct position should be confirmed by multiple means. Observing chest rise and fall, tube misting and a normal feeling of airflow in and out of the endotracheal tube are useful, but neither sufficiently sensitive nor specific. The gold standard is the appearance of a four-phase capnography waveform for five breaths, although this is reliant on cardiac output. Auscultation, in conjunction with the clinical assessment methods described above, must be used if capnography is unavailable. Cricoid pressure, if used, should be released only when endotracheal intubation is confirmed. Auscultation of the chest also helps to exclude endobronchial intubation (although it is poorly sensitive for this diagnosis), and in high-resource environments a chest radiograph is often obtained when prolonged intubation is anticipated (for example, in the intensive care unit following an intubation for head injury). Ongoing sedation should be provided, and if required, a long-acting muscle relaxant may be administered.

FAILED INTUBATION

Inability to intubate the patient during an RSI should prompt the usual approach to a difficult intubation, which should be communicated to the team prior to induction. However, if the indication was, for example, respiratory failure, allowing the patient to wake and breathe spontaneously may not be feasible.

If the initial intubation attempt is unsuccessful, a best attempt at facemask ventilation should be performed while preparing for a supraglottic airway, a different laryngoscopy technique or a new operator. Attempts at intubation should be limited, and the persistent risk of regurgitation and aspiration must be remembered. Rarely, a surgical airway may be required, and equipment for this should be available at every RSI.

Several algorithms for managing failed intubation have been produced, including the Difficult Airway Society guidelines[6] and the Vortex approach.[7]

CONTROVERSY AROUND CRICOID PRESSURE

Although routinely performed in many parts of the world – particularly the UK, North America and Australia – cricoid pressure is not established practice elsewhere and is contentious. It is not common practice in Europe, and some pre-hospital organisations do not endorse its use. It may also not be used in areas of the world where there is a lack of dedicated personnel to assist the anaesthetist.

Concerns include:

- reduced quality of laryngoscopy;
- lack of evidence of effectiveness in preventing reflux and aspiration;
- reduced lower oesophageal sphincter tone and therefore increasing reflux risk;
- worsening of undetected laryngeal or cervical spine injury;
- inability to measure the direction and degree of force being applied by the operator and likely highly variable location;[8]
- patient discomfort, gagging or coughing; and
- increasing physical and cognitive workload for the operators.

A recent systematic review has found no data from randomised trials providing any clinically relevant outcome measures.[9] Despite the ongoing controversy, use is considered standard of care in many settings. It is advisable to seek guidance from individual institutions about their expectations and guidelines.

RECENT DEVELOPMENTS

Classically ventilation is not usually provided during the apnoeic period (to avoid inflation of the stomach and associated increased risk of regurgitation), but some anaesthetists may give a single breath, or several gentle breaths, to both confirm that mask ventilation is possible and reduce the development of hypercapnia, acidaemia and hypoxia. Some recent guidelines now advocate use of mask ventilation for this reason in patients at elevated risk of hypoxia, for example pregnant women.[10,11]

Recently apnoeic oxygenation has been increasingly used, especially in critically unwell patients, to provide an oxygen-rich environment in the oropharynx to minimise hypoxia during the apnoeic period of RSI.[12] This is provided by an alternative oxygen source, commonly via nasal prongs with oxygen flow at 10 L min^{-1} or more, or via insertion of tubing carrying oxygen into the oropharynx. Limitations can include difficulty with the facemask seal, pressure-induced damage from misplaced tubing (e.g. gastric rupture) and lack of efficacy in at least one trial.[13]

SPECIFIC CLINICAL SITUATIONS

Obstetrics

Patients in the second or third trimester of pregnancy are at higher risk of aspiration due to anatomical and physiological changes. These patients are also more likely to be difficult to intubate, and desaturate faster, than non-pregnant women.

For these reasons, RSI is employed with meticulous attention to positioning, pre-oxygenation and availability of difficult airway equipment and expertise. Routine, gentle facemask ventilation may be utilised.[10] Use of opioids as an adjunct to induction may be required if the pregnancy is complicated by hypertension or pre-eclampsia.

As with all advanced pregnancies, the woman should be positioned with a left tilt using a wedge or a tilted table.

Paediatrics

Neonates, infants and children desaturate rapidly and can have pronounced vagal responses to laryngoscopy. A standard approach to RSI is generally performed, with a range of appropriately sized equipment, and carefully calculated drug dosages. Required doses may be higher than for adults on a per kilogram basis – for example, a 3-year-old child will often require 5 mg kg^{-1} propofol, several times higher than the proportional adult dose, because of the larger volume of distribution. Atropine as an additional adjunct is often used in a dose of 20 μg kg^{-1} to reduce bradycardia.

Suspected or known cervical spine injury

In patients who have an unstable cervical spine injury, laryngoscopy with attendant manipulation of the head and neck presents a risk of worsening any injury. There is no consensus as to the safest way to intubate these patients, but two alternative approaches are commonly practised. One is to perform a laryngoscopy with minimal movement of the cervical spine, often with a hyper-angulated video-laryngoscope if it is available, whilst the neck is immobilised by an assistant performing manual in-line stabilisation. The second option is an awake fibre-optic technique, using local anaesthesia only.

EMERGENCE

In patients in whom RSI was indicated because of aspiration risk,

emergence remains a high-risk time for further aspiration events. Strong consideration should be given to extubating the patient awake with full reversal of neuromuscular blockade. Left lateral head-down positioning may further reduce the chance of aspiration, at the expense of reduced access to the airway.

CONCLUSION

- Rapid sequence induction is performed to secure the airway in patients at elevated risk of aspiration.
- Preparation of equipment, drugs, the team and the patient is essential; excellent communication should be routine.
- The technique may be tailored to the specifics of the clinical scenario.

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Update in
Anaesthesia

Typhoid enteric fever – part 1

Falan Mouton, Esohe I Ohuoba, Faye M Evans and Ibironke Desalu

Correspondence: bruce.mccormick@nhs.net

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Summary

Typhoid enteric fever is a bacterial infection transmitted by faecal–oral route exclusively through human hosts.

Gut perforation is a potentially lethal complication associated with an inflammatory response at Peyer's patches

Definitive diagnosis requires successful culture from blood, stool, skin, or other infected site. Prompt antibiotic therapy reduces mortality.

Typhoid intestinal perforation is a surgical emergency that is potentially fatal, with children accounting for more than half of cases.

INTRODUCTION

Typhoid fever, otherwise known as enteric fever, is a bacterial infection of the gastrointestinal system that has long plagued humanity. The causative agent is in the family of Enterobacteria, and the genus *Salmonella*. These Gram-negative, facultative anaerobic bacilli are also flagellated, motile and non-spore forming. Although the organism lacks an exotoxin to promote illness, it is strongly antigenic and causes an intense inflammatory response in tissues. Typhoid fever is associated with the *Salmonella* serotypes typhimurium (*S. typhi*) and paratyphimurium (*S. paratyphi*).[1]

While a wide variety of animals can be infected with *Salmonella*, only humans carry the *S. typhi* and *S. paratyphi* serotypes associated with typhoid fever. Thus, livestock, household pets and other animals are neither carriers nor vectors of typhoid fever.[2] Humans acquire the disease from other humans through faecal–oral transmission, most commonly in the setting of contaminated water or food. It is not surprising that the greatest disease burden is found among the world's poorest countries where water and sanitation services are the least robust. Non-typhoidal salmonellosis (NTS) can be spread by animals other than humans and presents as a milder gastroenteritis. NTS is beyond the scope of our discussion of typhoid fever and will not be elaborated on.[1]

EPIDEMIOLOGY

Typhoid is more common in urban than in rural areas. Worldwide there are over 22 million cases with over 200 000 deaths each year, representing a 1–4% mortality rate.[3,4] The disease burden of typhoid fever is lowest in the developed world and highest in resource-limited settings. North America and Europe have fewer than 10 cases per 100 000 people per year, while Central and Southeast Asia have 10 times that number, achieving the highest rates in the world. The burden of the disease is difficult to estimate in African countries owing to limitations in laboratory testing capacities.[4,5] Outbreaks are more frequent in low-resource countries because they are associated with contaminated food and water and with fields fertilised by sewage, street vendors, uncooked fruits and vegetables, sick contacts, limited toilet access, and limited ability to wash the hands.

PATHOPHYSIOLOGY

Once consumed, typhoid bacteria cross the epithelial layer of the intestinal wall. They are then quickly consumed by macrophages and transported to the aggregates of lymphoid tissue in the small intestine (Peyer's patches), where the immune function of the gut is most concentrated. The typhoid bacteria alter host cell signalling and function in such a way that host cells ultimately promote the survival and replication of *S. typhi* and *S. paratyphi*.

The incubation stage of a typhoid infection is characterised by the replication and transfer of *S. typhi* and *S. paratyphi* from the Peyer's patches in the gastrointestinal system, through the lymphatics, to the organs of the reticuloendothelial system including the

Falan Mouton
Paediatric Anaesthesia Fellow
Lagos University Teaching Hospital
Lagos
Nigeria

Esohe I Ohuoba
Consultant anaesthetist
Lagos University Teaching Hospital
Lagos
Nigeria

Faye M Evans
Anaesthesiologist
Boston Children's Hospital
Boston, MA
USA

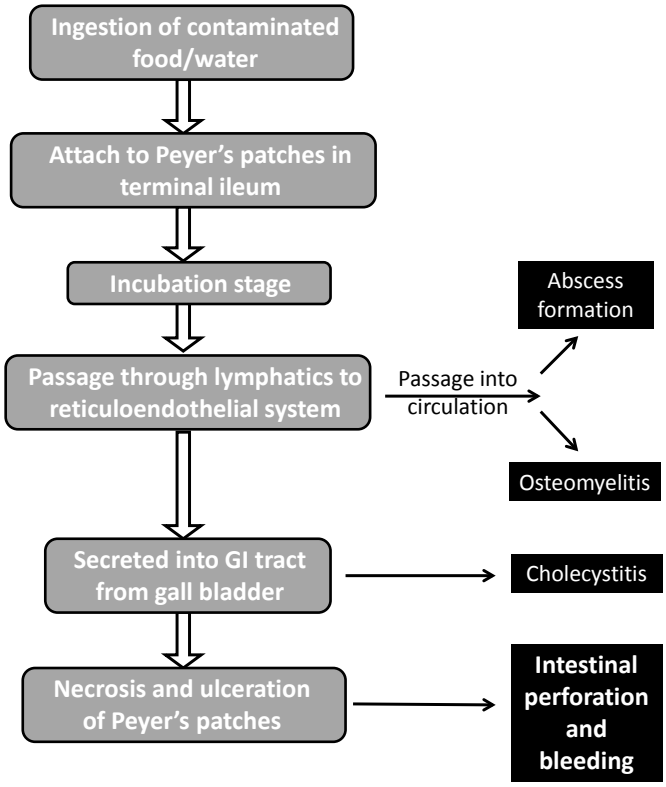

Figure 1. *Aetiopathogenesis of typhoid intestinal perforation and other complications*

lymph nodes, spleen, bone marrow and liver. Once in the gallbladder, *S. typhi* and *S. paratyphi* are secreted back into the gastrointestinal tract. Having been previously exposed to the organism, the Peyer's patches respond with an intense inflammatory reaction, leading to congestion and clogging of the microcirculation and capillaries with release of lytic lysosomal enzymes and other inflammatory mediators.[1,3] This results in varying degrees of necrosis and ulceration of Peyer's patches, of which the clinical manifestation is bleeding and perforation. The terminal ileum is the most common site of perforation, but perforation has also been reported to occur anywhere from the duodenum to the colon including the gall bladder and appendix (Figure 1).[3]

Depending on the strength of the host's immune system and the size of the inoculum, the incubation phase may last 3 days to 3 weeks.[1] During this interval, a patient may have no symptoms or vague complaints of fever and abdominal pain. Once the bacterial load reaches a critical mass, an individual is said to have an active typhoid infection.

SIGNS AND SYMPTOMS

Although *S. typhi* is four times more common than *S. paratyphi*, in general, the clinical appearances of *S. typhi* and *S. paratyphi* infections are virtually indistinguishable. Signs and symptoms of the infection consist mostly of abdominal complaints including fever associated with frontal throbbing headache, nausea, vomiting, abdominal pain, anorexia, diarrhoea, constipation, gastrointestinal bleeding and hepatosplenomegaly. Systemic complaints are also common, and more than 75% of patients report having flu-like symptoms. Neurological problems include meningitis, Guillain–Barré syndrome and a delirium that features muttering and picking at clothes and imaginary objects. Disseminated intravascular coagulation, haemolytic–uraemic syndrome, renal failure, cardiac failure and respiratory failure have all been reported as a consequence of severe infection. While no specific constellation of symptoms is pathognomonic of the disease, a transient skin rash, described as rose spots, can be biopsied to confirm the diagnosis.[1]

The severity and duration of typhoid fever depends on several host factors including age, integrity of the immune system and gastrointestinal tract, and alkalinisation of the stomach. It has been found that a more acidotic environment in the stomach is bactericidal, while a concomitant *Helicobacter pylori* infection, which increases gastric pH, promotes the disease.[1] Up to 4% of patients with untreated disease that resolves spontaneously will become asymptomatic carriers and continue to shed the bacteria in urine and stool.

COMPLICATIONS

S. typhi has the capacity to affect virtually every organ system; as a result patients are vulnerable to a wide variety of complications. Intestinal perforation, occurring in 1–3% of cases, is associated with the highest mortality.[1,3,4] Even when aggressively treated, mortality with perforation can be as high as 40%. In contrast, in unperforated cases treatment reduces the mortality rate to only 1%. Perforations can occur anywhere from the duodenum to the colon, though the ileum is the most common site. Gall bladder perforation has also been reported. In children, multiple perforations are frequently present.[3] Anaesthesia in a child with typhoid intestinal perforation will be discussed later in this article.

Additional complications include heart failure from myocarditis or endocarditis, liver failure from hepatitis or pancreatitis, renal failure from pyelonephritis or glomerulonephritis and respiratory failure from pneumonia, as well as disseminated intravascular coagulation, arthritis and orchitis.[1]

Although both sexes are infected equally, some evidence suggests that males suffer significantly more intestinal perforations than females.[5] Typhoid fever can affect people of all ages, but the burden is heaviest among children aged 5–10 years. In endemic regions, children account for greater than 50% of intestinal perforation cases.[5]

In one published report of an outbreak in Uganda from 2007–2009 there were 577 cases with 249 intestinal perforations and 47 deaths. resulting in an incidence rate of 8092 cases per 100 000 people.[4] Although this is unlikely to represent the incidence rate of the

population as a whole, it does emphasise that during an outbreak the burden of the disease can be tremendous.

DIAGNOSIS

The diagnosis of typhoid cannot be confirmed based on clinical presentation alone. Because the symptoms of typhoid fever are so variable, the differential diagnosis can be quite broad. Other diseases such as malaria, HIV infection, hepatitis, gastrointestinal viral infections and bacterial infections such as *Clostridium difficile* or *Escherichia coli* must be excluded. Suspicion of more common causes of fever such as malaria frequently delays diagnosis of typhoid. Malignancy, rheumatic processes and inflammatory bowel diseases should also be considered.

Definitive diagnosis requires isolation of the causative organism from tissues. Punch biopsies from rose spots on skin, or cultures from blood, urine, bone marrow or stool are often adequate for diagnosis. Bone marrow cultures are the most sensitive, at 55–90%, and can grow *S. typhi* even in the setting of 5 days of antibiotic treatment. Unfortunately, even samples from patient with active typhoid can sometimes fail to grow the bacteria in culture.[1]

In such settings, Widal's test has some efficacy and remains the most commonly used serological test. It evaluates agglutination between antibodies in the patient's blood to the H (flagella) and O (somatic) antigens of *S. typhi*. The test is plagued by a high false-positive rate as antibodies from other infectious disease such as dengue, malaria and non-typhoidal salmonella also cross-react with the *S. typhi* antigens. Previous immunisation or exposure to the disease can also cause false-positives in acute disease. Poor commercial antigen preparation is responsible for both false-positives and false-negatives. Additionally, *S. typhi* carriers and others with low antibody production can have false-negative results in the setting of acute infection.[6,7]

In regions of the world where typhoid is endemic, laboratory resources are also very limited. PCR identification of *S. typhi* solves many of the shortcomings of cultures and Widal's test, but these studies are expensive and require some of the most advanced technologies available. As a result of the laboratory limitations, practitioners must have a high index of suspicion for the disease and rely on the familiar constellation of symptoms previously described.

MEDICAL MANAGEMENT

Medical management is the preferred treatment for typhoid fever. Prompt diagnosis and initiation of appropriate antibiotic therapy is critical to treatment success and mortality reduction. The majority of uncomplicated cases do not require hospitalisation. When possible, typhoid should be cultured and susceptibilities noted to help guide antibiotic therapy. If laboratory testing is not available, antibiotics should be selected based on regional susceptibilities.

Fluoroquniolones, such as ciprofloxacin and ofloxacin, are the first-line antibiotic treatment for *S. typhi* and *S. paratyphi*. Chloramphenicol, amoxicillin, and TMP-SMX (trimethoprim–sulfamethoxazole (Bactrim)) are all known to be efficacious against susceptible strains of typhoid. For drug resistant strains or empirical treatment, antibiotic coverage is broadened to include ceftriaxone and azithromycin.[1,5]

Antibiotics can be administered orally (PO) or intravenously (IV) depending on the drug, and treatment courses rarely exceed 21 days. Steroid therapy with dexamethasone in conjunction with antibiotics has been shown to reduce mortality and is considered standard therapy for management of the disease. Chronic carriers of typhoid require a longer, 4- to 6-week, course of antibiotics with amoxicillin, TMP-SMX or ciprofloxacin.[1]

Surgical intervention is recommended only in the case of intestinal perforation. If no perforation has been identified, surgery is not indicated as it could spread infection. In addition, it is difficult to identify which areas to resect, as the disease can be ubiquitous in the bowel.[3]

Surviving sepsis

The recently revised Surviving Sepsis guidelines provide an excellent framework for managing cases of typhoid fever that have been complicated by intestinal perforation.[8] The child or adult presenting for laparotomy because of typhoid perforation will almost always have concomitant septic shock. The definition of sepsis is a documented or suspected source of infection as well as symptoms of the systemic inflammatory response syndrome. These symptoms include altered mental status, tachypnoea, fever or hypothermia, leucocytosis or leucopenia, tachycardia (possibly bradycardia if the child is less than 1 year old) and systemic hypotension. There is also evidence of end-organ dysfunction including an elevated lactate or creatinine or a new coagulopathy.

Mortality in sepsis in minimised when the condition is promptly diagnosed and treated. The current Surviving Sepsis guidelines for adults recommend that within 3 hours of diagnosis cultures are drawn, empiric antibiotics are administered, a lactate level is measured, and a fluid bolus is given of 30 mL kg^{-1}. Within 6 hours the objective is to address hypotension and end-organ perfusion by measuring a central venous pressure (CVP) and mixed venous saturation if available. Vasopressors can then be added to maintain a mean arterial pressure (MAP) of 55–65 mmHg with a goal of a CVP > 8 mmHg or a venous oxygen saturation (SvO_2) > 70%.

Haemodynamic goals are similar in paediatric patients, but there are some management differences in the Surviving Sepsis guidelines. A child in respiratory distress should initially be managed with high-flow nasal cannula or continuous positive airway pressure (CPAP). Fluid resuscitation should start with 20 mL kg^{-1}crystalloid or an albumin equivalent with a goal of maintaining a capillary refill time of < 2 seconds, normal blood pressures, baseline mental status,

urine output of 1 mL kg^{-1} h^{-1} and ultimately SvO_2 of 70%. Empiric antibiotics should be administered within 1 hour of diagnosis. American College of Critical Care Medicine-Pediatric Life Support (ACCM-PALS) guidelines should be followed if the child is in shock and blood should be given to an initial goal of haemoglobin concentration of 10 g dL^{-1}. Once stable, haemoglobin of 7 g dL^{-1} can be allowed.

In both paediatric and adult patients, vasopressors should be added to maintain haemodynamic goals if shock is refractory to fluid boluses. Lung-protective ventilation strategies should be employed. These typically involve low tidal volumes of 6–7 mL kg^{-1}, higher respiratory rates, application of positive end-expiratory pressure (PEEP) and permissive hypercapnia. In children, if hypotension does not respond to fluid boluses and vasopressors, adrenal insufficiency should be considered and managed with steroids.[8]

PREVENTION

Prevention is the preferred method of management of typhoid. Strategies include improved sanitation services, sewage disposal, water treatment services and early identification and minimisation of outbreaks.

Vaccinations are available for several of the typhoid serotypes, but their effectiveness is limited. Additionally, there is no vaccine for *S. paratyphi*, which accounts for up to 25% of cases of typhoid fever. The potential of vaccinations is limited because they are ineffective at preventing disease in the event of a large inoculum. Discretion is advised when food choices are made while travelling in a typhoid-endemic area. Despite this limitation, vaccinations are still warranted as they will behave as an adjunct to treatment and limit the extent and duration of the disease.

There are two forms of the *S. typhi* vaccine that are currently commercially available; however, neither form is available for children below 2 years of age. The live attenuated oral vaccine, Ty21a, is administered every other day for three doses. It has an efficacy of 67–80% and provides some cross-protection against *S. paratyphi*. It requires a booster vaccination every 5 years, and is not generally given until the age of 6 years. The Vi CPS vaccine is an alternative parenteral form featuring the Vi polysaccharide of the *S. typhi* bacterial capsule. It can be administered to children as young as 2 years old but requires a booster every 2 years and it has an efficacy of 55–72%. Typhoid vaccination is recommended for persons visiting endemic or high-risk areas, but not for those who reside in them, and not for those with an acute infection.[9]

CONCLUSION

Typhoid fever is an infectious disease that exclusively affects humans and is transmitted by faecal–oral routes. Though it typically results in gastrointestinal symptoms, typhoid enteric fever may present as a multisystemic disease when infection is severe. Management strategies involve prompt diagnosis or a high index of suspicion, appropriate antibiotic therapy and early initiation of sepsis management. Typhoid intestinal perforation is a serious complication if prompt surgical intervention is not available.

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Update in
Anaesthesia

Typhoid enteric – part 2: anaesthesia in a child with typhoid intestinal perforation

Falan Mouton, Esohe Ohuoba and Ibironke Desalu

Correspondence: bruce.mccormick@nhs.net

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Summary

Typhoid intestinal perforation is a surgical emergency that is potentially fatal.

Children account for more than half of cases.

The role of the anaesthetist in the management includes aggressive fluid resuscitation, correction of electrolyte imbalance, use of intravenous broad-spectrum antibiotics, formulation of an appropriate anaesthetic plan and postoperative management in a HDU/ICU.

Vigilance by the anaesthesia provider is critical to the patient's survival.

INTRODUCTION

Typhoid fever is a common infection in developing countries and where unhealthy environmental conditions prevail. The annual global incidence of typhoid fever according to the World Health Organization is 21 million cases, with 1–4% mortality.[1] In sub-Saharan Africa, it predominantly affects children below the age of 15 years with a mortality of 24%.[2]

Typhoid intestinal perforation, which is the most serious complication of typhoid fever, has a global incidence rate of 0.6–4.9%; however, in West Africa, higher rates, of 10–33%, have been reported.[3] Children account for more than 50% of these cases of typhoid intestinal perforation, with boys and girls equally affected. Typhoid infection is caused by the bacteria *Salmonella typhi* (also known as *Salmonella enterica* serotype *typhi*), a Gram-negative flagellated rod found only in humans, and also by *Salmonella paratyphi*. The bacteria are transmitted by ingestion of food or water contaminated with faeces. The organism has no exotoxin; however, it is strongly antigenic causing an intense inflammatory reaction in tissues where it is present. The commonest site of intestinal perforation is the terminal ileum, though it can occur anywhere in the intestine.[1,3]

MANAGEMENT OF TYPHOID INTESTINAL PERFORATION

History and presentation

Many patients seek professional medical attention late, after weeks of symptoms, and following attempts at treatment with antibiotics or traditional medications. Though symptoms may be atypical in infants and toddlers less than 5 years old, the classical form displays some typical presenting features (Table 1).[1]

Assessment

On general examination, a child with typhoid intestinal perforation will be ill-looking and toxic. There may be pyrexia, pallor and jaundice. If the illness has lasted several weeks, the child may appear wasted and demonstrate an altered level of consciousness.

Physical examination of the abdomen frequently reveals distension with associated guarding and rigidity. Plain abdominal radiograph (erect film) will show air under the diaphragm. Children too sick to stand erect may have a lateral decubitus film which will show pneumoperitoneum (Figure 1). Abdominal ultrasound can be used to exclude other intra-abdominal conditions that can complicate typhoid fever such as cholecystitis or intraperitoneal abscesses.[1]

Preoperative optimisation

High-flow oxygen should be commenced via a facemask with a reservoir bag. If the child is obtunded, the airway should be secured with an endotracheal tube. Abdominal distension can result in splinting of the diaphragm, leading to respiratory compromise.

Falan Mouton
Paediatric Anaesthesia Fellow
Lagos University Teaching Hospital
Lagos
Nigeria

Dr Esohe I Ohuoba
Consultant anaesthetist
Lagos University Teaching Hospital
Lagos
Nigeria

Ibironke Desalu
Professor of Anaesthesia
University of Lagos
Lagos
Nigeria

Table 1. *Presenting features of typhoid intestinal perforation*

Fever	Earliest symptom and commonly precedes abdominal pain (differentiates it from appendicitis, in which abdominal pain precedes fever), often associated with throbbing frontal headache.
Abdominal pain	Usually begins 2–30 days (average of 9 days) after onset of fever. It is initially vague but gradually becomes generalised. With perforation, abdomen distension is commonly noted.
Diarrhoea	Common in the early stages of but constipation is predominant later in the course of the illness.
Gastrointestinal bleeding	A history of passage of frank or altered blood in stools may also be present.

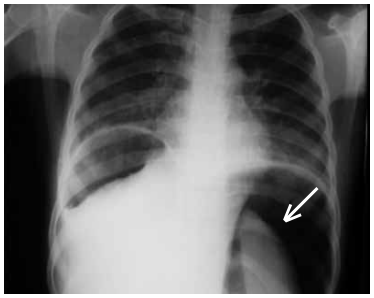

Figure 1. *Plain chest radiograph showing massive pneumoperitoneum (arrow) (photograph supplied by Professor Emmanuel Ameh, Paediatric surgeon, National Hospital, Abuja, Nigeria)*

In some cases, pneumonia may develop. An appropriately sized nasogastric tube (NGT) should be inserted and the stomach decompressed by low-pressure suction or intermittent aspiration.

The haemodynamic condition of the patient must be evaluated. Tachycardia, hypotension, a capillary refill time (CRT) of longer than 3 seconds, and oliguria are all suggestive of dehydration and shock and will require immediate intervention. Intravenous access via two wide-bore cannulae should be secured and samples drawn for relevant investigations. When adequate peripheral access cannot be obtained, a central venous or intraosseus line should be obtained. Fluid resuscitation with a bolus of 20 mL kg^{-1} isotonic crystalloids such as 0.9% saline should be commenced as soon as possible, after which the patient should be reassessed. Fluid boluses may need to be repeated depending on how the patient responds to the initial bolus. Inotropes, vasopressors or a combination of both should be added if shock is not responding to fluid resuscitation (see 'Management of paediatric sepsis', page 33 in this edition of *Update in Anaesthesia*).

A full blood count may reveal anaemia with leucocytosis or even leucopenia. Serum biochemistry may show clinically significant alterations in potassium and sodium concentrations with a metabolic acidosis. Urea and creatinine may be elevated, heralding renal compromise. Clotting profile is indicated if there is evidence of coagulopathy. The Widal test (an agglutination test that detects the presence of serum agglutinins H and O in the serum of patients with typhoid and paratyphoid fever) has been found to be non-specific with limited usefulness in management of these patients.[1] Regardless of laboratory findings, the diagnosis of typhoid intestinal perforation requires a high index of suspicion as tests may not be readily available in areas where typhoid is endemic.

Intravenous broad-spectrum antibiotics (directed against Gram-negative and anaerobic bacteria) should be commenced immediately once the diagnosis of typhoid perforation is suspected. The antibiotics may be changed later if there is no improvement and when culture results are available.

In areas such as sub-Saharan Africa where there is a high prevalence of multidrug-resistant (MDR) strains, the following combinations are currently recommended:[1,4]

A quinolone, e.g. ciprofloxacin 10 mg kg^{-1} (max. 400 mg 8-hourly) + metronidazole 7.5 mg kg^{-1} (max. 500 mg 8-hourly)

or

A third-generation cephalosporin, e.g. ceftriaxone 50–75 mg kg^{-1} (max. 4 g day^{-1}) + metronidazole 7.5 mg kg^{-1} (max. 500 mg 8-hourly)

In areas where the prevalent strain of bacterium is still susceptible, the following regimen can be used:

Chloramphenicol 100 mg kg^{-1} day^{-1} in divided doses IV + metronidazole

or

Amoxicillin 100 mg kg^{-1} day^{-1} in divided doses IV + metronidazole

or

Trimethoprim–sulphamethoxazole 20 mg kg^{-1} day^{-1} in divided doses IV + metronidazole

Blood should be typed and cross-matched for correction of anaemia and for intraoperative use.

The definitive treatment for typhoid intestinal perforation is operative evacuation of faecal matter to avoid further contamination. Surgical options include resection of the affected intestine, simple closure of perforations and enterostomy, which is performed if the child is too sick or the intestinal oedema too extensive for safe anastomosis or simple closure.[1,5]

Measures to optimise the patient's preoperative status are summarised in Table 2.

ANAESTHETIC MANAGEMENT

Preoperative preparation

Children presenting to the theatre for repair of typhoid perforation are usually quite ill: American Society of Anesthesiologists (ASA) classification 3 or 4E. The anaesthetist must be prepared for a potentially unstable and challenging paediatric patient. Adequate IV access must be ensured with two large-bore cannulae. The patient may be volume depleted or vasoconstricted, making peripheral access challenging; in such cases, a central venous line is an acceptable alternative. An intraosseus line should be considered if attempts at insertion of a peripheral or central line fail. The patient should be adequately resuscitated before induction is attempted.

Standard anaesthesia monitoring should be instituted prior to induction. Plethysmography and measurement of oxygen saturation and blood pressure are particularly useful in monitoring oxygenation and circulation. Capnography is useful in determining correct placement of an endotracheal tube, monitoring and modifying ventilation as well as monitoring adequacy of circulation. Clinical parameters such as capillary refill time, warmth at peripheries and urinary output of at least 0.5 mL kg^{-1} h^{-1} are as important as equipment monitoring. If available, an arterial line is useful in detecting sudden haemodynamic shifts, obtaining frequent blood samples and guiding resuscitation efforts.

Table 2. *Summary of preoperative optimisation*

Oxygen supplementation	High-flow oxygen via a facemask with reservoir bag
	Secure airway with tracheal tube if child is obtunded
Nasogastric tube	Placed NGT to decompress the distended abdomen
	Decompression either by low-pressure suction or intermittent aspiration
Fluid resuscitation	Fluid bolus of 20 mL kg^{-1} isotonic crystalloids
	Reassess child, check CRT and urinary output
	Fluid bolus repeated if necessary
Correct electrolyte derangement	Correct hypokalaemia (or hyperkalaemia), hyponatraemia, hypochloraemia and metabolic acidosis
Intravenous broad-spectrum antibiotics	Ciprofloxacin/ceftriaxone and metronidazole in areas where strains are multidrug resistant
	Chloramphenicol, amoxicillin or trimethoprim–sulphamethoxazole in areas where strains are susceptible

Temperature homeostasis is of particular concern because of pre-existing fluid losses, large area of potential intraoperative evaporative loss and large volumes of resuscitation fluid that may need to be administered. Temperature can be maintained by keeping the theatre warm, warming intravenous and irrigating solutions, covering the exposed gut with warm saline packs, covering the head and extremities with warm towels and using a heat and moisture exchange filter on the breathing circuit. A warming mattress or convection warming is ideal.

Induction

Patients with typhoid intestinal perforation may have significant hypotension at induction of anaesthesia as a result of the active systemic inflammatory response and resultant vasodilation. Volume resuscitation should be started prior to induction and continued throughout the operative period. Despite preoperative fluid boluses and inotropes/vasopressors, the anaesthesia provider should be prepared for cardiovascular collapse at induction or during the procedure.

The anaesthetic technique of choice is general anaesthesia with endotracheal intubation and ventilation. Patients with typhoid fever should be regarded as having a full stomach. After pre-oxygenation, a rapid sequence induction with cricoid pressure should be used to secure the airway as patients are at risk of regurgitation and aspiration. A competent assistant should be available to provide cricoid pressure ensuring that it does not compromise laryngeal view and therefore intubation. Prior to induction, the nasogastric tube must be suctioned. Despite adequate pre-oxygenation, the child will still be prone to a period of severe desaturation at intubation as the distended abdomen decreases the functional residual capacity (FRC). To improve FRC, patients may be intubated in the reverse Trendelenburg position.

Anaesthetic drugs for induction and maintenance should be carefully selected to help maintain haemodynamic stability and minimise additional peripheral vasodilation. Drugs that increase vasodilatation, such as propofol, should be avoided if possible. Drugs that maintain sympathetic tone should be selected as they will help to support haemodynamic stability. In many settings, ketamine is the drug of choice as it supports circulation, especially if hypovolaemia is still suspected. It should be used at a dose of 1–2 mg kg^{-1} IV. Thiopentone may also be used, but with caution, especially where fluid resuscitation has not been completed. Suxamethonium, at a dose of 2mg kg^{-1}, offers rapid relaxation and optimal intubating conditions; rocuronium at 0.9–1.2 mg kg^{-1} may also be used. Etomidate should be employed with caution because of its association with adrenal insufficiency. Adrenal suppression in these critically ill patients may contribute to postoperative hypotension and impair their immune response. Narcotics, benzodiazepines and inhaled agents can potentiate

hypotension at high doses, but when used in moderation and titrated to effect they can also contribute to a stable anaesthetic.

Maintenance

Maintenance of general anaesthesia can be accomplished with inhalational agents such as isoflurane, sevoflurane or desflurane. In some areas halothane is the only inhalational agent available and may also be used. Deep anaesthesia should be avoided, and special additional attention should be paid to cardiac depression if halothane is employed. The low blood gas solubility coefficient of sevoflurane, desflurane and isoflurane ensures rapid awakening after surgery. These agents can be delivered in a mixture of medical air/oxygen. Nitrous oxide should be avoided.

In patients who are hypotensive, maintenance of anaesthesia may be by intermittent boluses of IV ketamine (0.5 mg kg^{-1}) given according to patient's response or via ketamine infusion (25–75 μg kg^{-1} min^{-1}).[6] Controlled ventilation with monitoring of end-tidal carbon dioxide (if available) is important during surgery. Muscle relaxation will facilitate ventilation and optimise surgical exposure.

A multimodal approach to pain management is encouraged. Simple analgesics such as paracetamol (15 mg kg^{-1} IV) may be given intraoperatively. Opioids such as morphine (0.05–0.1 mg kg^{-1}), fentanyl (1–2 μg kg^{-1} per dose as intermittent boluses) or pentazocine (0.5 mg kg^{-1}) can also be given, but with caution, as they may cause hypotension. Local infiltration of the surgical incision site with bupivacaine can help to decreases the opioid requirement in the postoperative period.

Adequate fluid management is vital in these patients and must take into account preoperative fluid deficits, maintenance requirements and intraoperative losses.[7] Should a patient remain hypotensive despite adequate volume resuscitation, inotropes or, vasopressors, such as dopamine, phenylephrine, noradrenaline or adrenaline, via infusion, should be started and titrated to effect to help maintain haemodynamic stability. It can be helpful to dedicate one IV line to vasoactive agents and maintenance fluids with a second infusion line for replacing fluid deficits and on-going losses and giving bolus injections of drug. Electrolyte derangements are corrected via the maintenance fluid. If a patient is severely acidotic, treatment with sodium bicarbonate should be considered. Blood loss is typically replaced with non-dextrose-containing crystalloid (e.g. 3 ml of normal saline for each mL of blood lost) or colloid (1 ml of 5% albumin for each mL of blood lost); however, the child's preoperative haematocrit and general status determines when blood transfusion is commenced. Whole blood or packed cells could be transfused and a urinary output of 1–2 mL kg^{-1} h^{-1} should be aimed at.

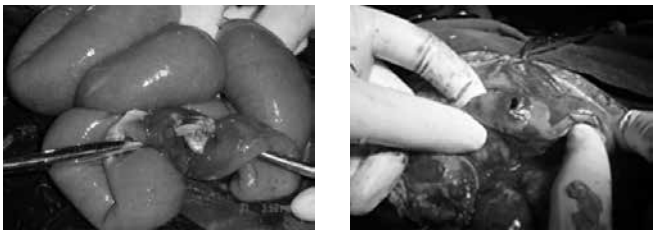

Figure 2. *Perforations on the anti-mesenteric border of the terminal ileum (photographs supplied by Professor Emmanuel Ameh, Paediatric surgeon, National Hospital, Abuja, Nigeria).*

Postoperative management

Depending on their condition, these patients should be managed in an intensive care unit (ICU)/high-dependency unit (HDU) as active resuscitation may be required in the postoperative period. If no ICU is available, patients should be moved close to a nurses' station for close observation as deterioration can occur rapidly. In some cases, the patient can be extubated fully awake and continued on high-flow oxygen via a facemask with a reservoir bag. In many other cases, patients may have to be mechanically ventilated postoperatively. The decision to keep the patient intubated should be based on available resources and the status of the patient. Patients should remain intubated if their ventilatory drive is poor, oxygenation is inadequate, ventilation has been difficult (high pressures have been required to maintain adequate volumes) or if resuscitation has been vigorous and involved large amounts of crystalloid, blood, and vasopressors.

These patients should be considered in critical condition and should be monitored closely. Antibiotics should be continued for at least 2 weeks;[1] vasopressors and blood products should be continued postoperatively as needed. Intravenous replacement therapy should be continued with strict monitoring of urinary output. The nasogastric tube should remain in place postoperatively and be placed on suction or gravity until its drainage is minimal. Analgesics such as paracetamol and small doses of IV opioids can be continued as needed for pain. Corticosteroid therapy, which has been found to reduce mortality in the management of typhoid enteritis, has *not* been conclusively proven to improve the outcome in perforated cases. For nourishment, total parenteral nutrition, if available, should be started and continued until oral intake can be tolerated. These patients are at high risk of multiple organ failure; therefore, a comprehensive daily review of each organ system with appropriate management of any derangements is critical in their management.

CONCLUSION

Typhoid perforation is the most serious complication of typhoid fever and children account for a larger proportion of cases. It typically presents with gastrointestinal symptoms though presentation may be atypical in infants or toddlers. Aggressive resuscitation and antibiotic therapy must be commenced before surgical intervention to reduce mortality. Anaesthetic management is of a critically ill child with a full stomach. Postoperative care is key to recovery in these patients and may need to be done in the HDU/ICU.

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Update in
Anaesthesia

Wrist block – landmark technique

A Girolami, K Russon and A Kocheta

Correspondence: kim.russon@rothgen.nhs.uk

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Summary
Remember to fully prepare the patient and equipment.

Always aspirate before injecting local anaesthetic.

Ensure that the surgical site is known and all the necessary nerves blocked.

A Girolami
Sheffield Teaching Hospitals
Sheffield
UK

K Russon
Rotherham District General Hospital
Rotherham
UK

A Kocheta
Rotherham District General Hospital
Rotherham
UK

INTRODUCTION

A wrist block is the technique of blocking terminal branches of some or all of the six nerves that supply the wrist, hand and fingers. The combination of nerves that need to be blocked depends upon the exact location of surgery. This block can be used to provide regional anaesthesia for a patient undergoing surgery awake or as an analgesic technique to be used in combination with general anaesthesia or brachial plexus block (BPB) using short-acting local anaesthetic (the wrist block will provide prolonged pain relief once the BPB has worn off). It is simple to perform with readily identifiable landmarks, yet remains an underused weapon in the anaesthetist's armamentarium.

INDICATIONS

Anaesthesia and/or analgesia is indicated for many surgical procedures on the wrist, hand and fingers, such as wrist arthroscopy, the correction of Dupuytren's contractures, metacarpal or phalangeal osteotomy, arthrodesis of the metacarpophalangeal joints, fixation of fractures in the hand. It is worth noting, however, that, in an awake patient, the duration of surgery may be limited by the patient's ability to tolerate the tourniquet on the upper arm if a wrist block alone is used.

CONTRAINDICATIONS

Absolute contraindications

- Patient refusal
- Allergy to local anaesthetic
- Active infection at the site of the block

Relative contraindications

- Anti-coagulation or bleeding diathesis

ANATOMY

The wrist, hand and fingers are supplied by six nerves:

- the median nerve
- the ulnar nerve
- the dorsal branch of the ulnar nerve
- the radial nerve
- the posterior interosseous nerve
- the anterior interosseous nerve.

All six originate from the brachial plexus and descend into the forearm to supply the distal structures.

The median nerve

The median nerve arises from the medial and lateral cords of the brachial plexus and takes fibres from nerve roots C5–C8 and T1 (Figure 1). It has no branches above the elbow but in the forearm supplies the flexor muscles of the forearm (except flexor carpi ulnaris), opponens pollicis, abductor pollicis brevis and the first and second lumbricals. Sensory fibres supply the palmar surface of the radial three and a half fingers and their nailbeds. At the level of the wrist, the median nerve traverses the carpal tunnel and terminates as digital and recurrent branches. The digital branches supply the skin of the lateral three and a half digits and, usually, the lateral two lumbricals. A corresponding area of the palm is innervated by palmar branches, which arise from the median nerve in the distal forearm. The recurrent branch of the median nerve supplies the three thenar muscles. It may be seen that the median nerve must be blocked proximally to the exit of the palmar branches in order to provide complete anaesthesia of the hand (Figures 2 and 3).

The ulnar nerve

The terminal branch of the medial cord forms the ulnar nerve, with fibres coming from nerve roots C7–8, T1 (Figure 1). In the forearm, it supplies flexor carpi ulnaris and half of flexor digitorum profundus.

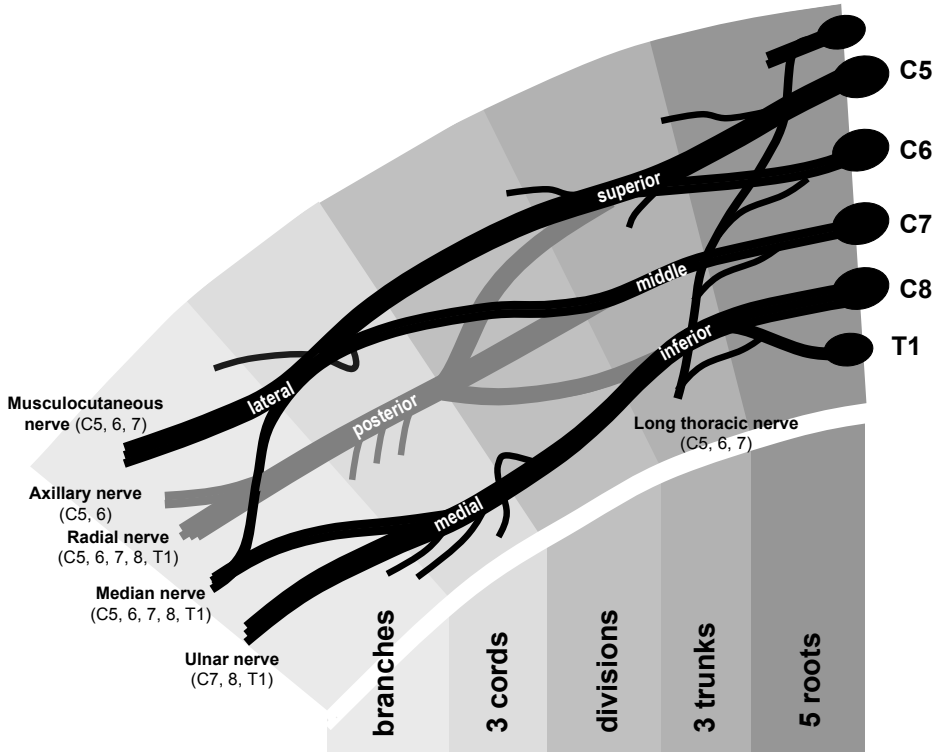

Figure 1. *The brachial plexus*

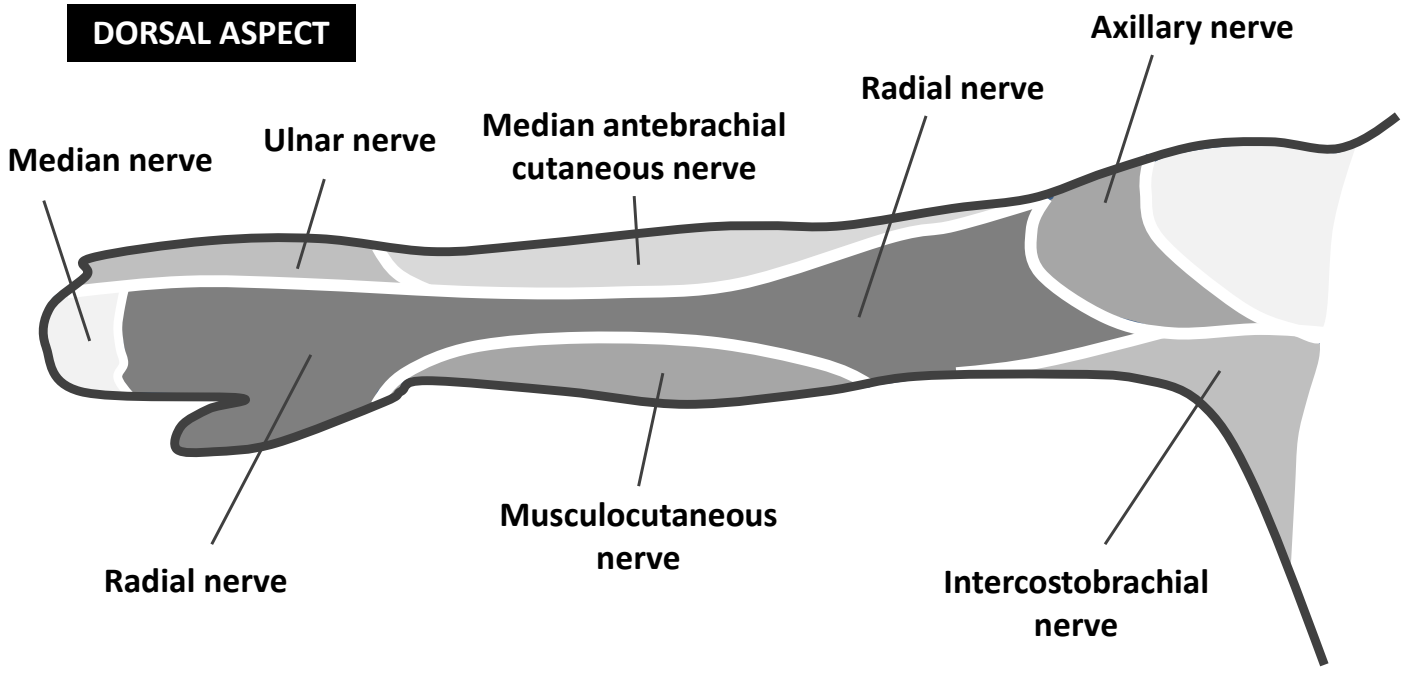

Figure 2. *Nerve supply of the arm, palmar surface*

In the hand, the deep branch of the ulnar nerve accompanies the deep palmar arch and supplies innervation to the three hypothenar muscles, the medial two lumbricals, all the interossei, and adductor pollicis. Digital branches provide cutaneous sensation for the medial one and a half fingers. The medial palm is supplied by palmar branches that arise from the ulnar nerve in the distal forearm.

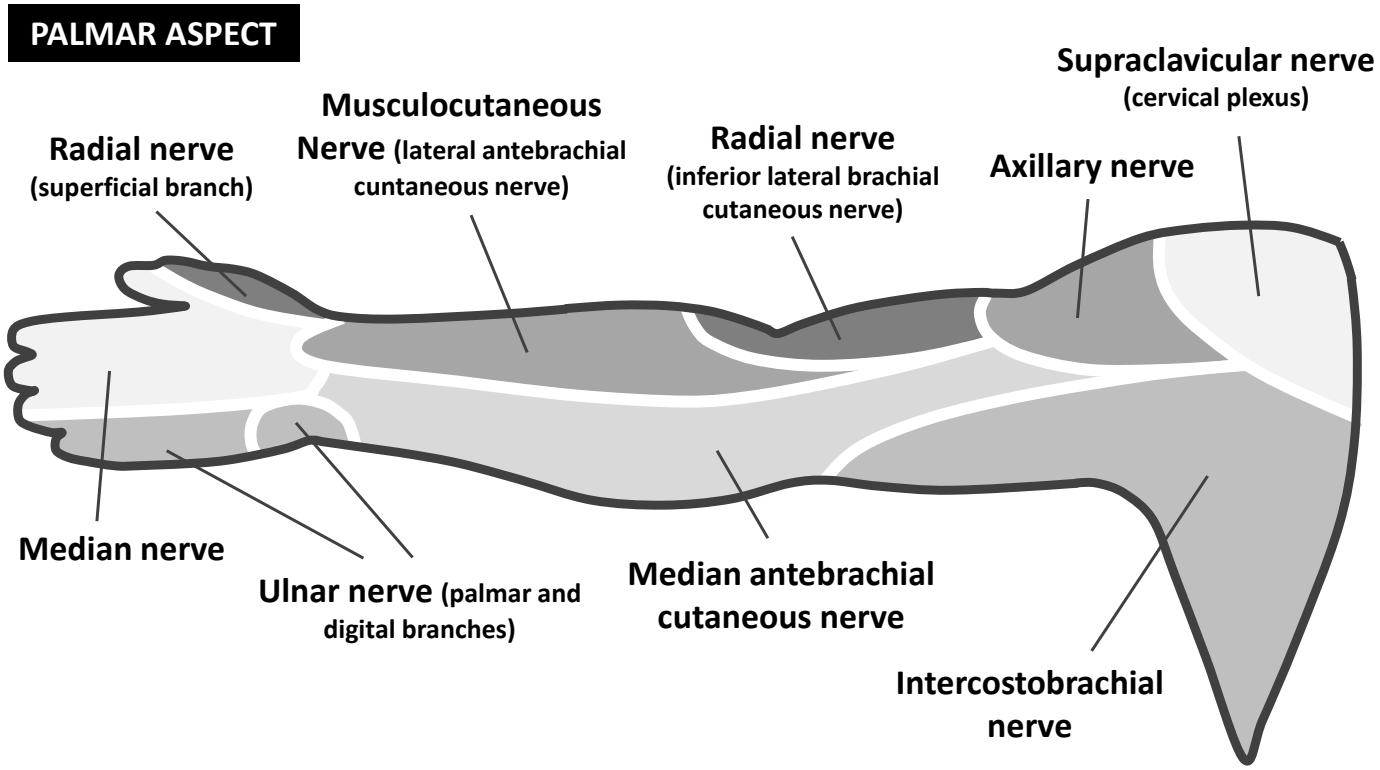

Figure 3. *Nerve supply of the arm, dorsal surface*

The dorsal branch of the ulnar nerve

The dorsal, medial side of the hand is supplied by the dorsal branch of the ulnar nerve, which arises proximally to the wrist crease (Figures 2 and 3).

- Tip: Although there may be variability of innervation of the ring and middle fingers, the skin on the anterior surface of the index finger and thumb is always supplied by the median nerve and that of the little finger by the ulnar nerve.

The radial nerve

The radial nerve is formed from the terminal branch of the posterior cord of the brachial plexus and takes fibres from nerve roots C5–8C andT1 (Figure 1). It travels in the posterior compartment of the upper arm and divides at the level of the elbow into the superficial radial nerve (SRN) and the posterior interosseous nerve (see below). The SRN passes distally on the radial side of the forearm with the radial artery and sensory fibres supply the skin of the lateral aspect of the arm, posterior aspect of the forearm and web space between thumb and index finger (Figures 2 and 3). About 7.5 cm above the wrist, it leaves the artery, pierces the deep fascia to become superficial and divides into two main branches. The external branch, the smaller of the two, supplies the skin of the radial side and base of the thumb. The internal branch communicates with the posterior branch of the lateral cutaneous nerve. On the back of the hand, it forms an arch with the dorsal cutaneous branch of the ulnar nerve but does not anastamose with it.

The posterior interosseous nerve

The posterior interosseous nerve (PIN) is the continuation of the deep branch of the radial nerve, taking fibres from nerve roots C7 and C8. It descends on the posterior surface of the interosseous membrane to the back of the wrist, giving motor supply to the extensor muscle bellies of the forearm. Although it is predominantly a motor nerve, it also provides important sensory fibres to the ligaments and various articulations of the wrist.

The anterior interosseous nerve

The anterior interosseous nerve (AIN) is a branch of the median nerve that accompanies the anterior interosseous artery along the anterior surface of the interosseous membrane of the forearm, in the interval between the flexor pollicis longus and flexor digitorum profundus, ending in the pronator quadratus muscle and wrist joint. Like the PIN, it is a predominantly motor nerve but contributes important sensory fibres to the wrist joints.

TECHNIQUE

Preparation and positioning

Fully prepare the equipment and patient, including obtaining informed consent. Also ensure that intravenous access, monitoring and full resuscitation facilities are available. For a more detailed explanation on preparation, see Russon et al.[1]

The patient is in the supine position with the arm abducted. Prepare the skin with antiseptic solution.

The radial nerve

Landmarks (Figure 4)

The SRN runs along the medial aspect of the brachioradialis muscle. It then passes between the tendon of the brachioradialis and radius to pierce the fascia on the dorsal aspect. Just above the styloid process of the radius, it gives digital branches for the dorsal skin of the thumb, index finger and lateral half of the middle finger. Several of its branches pass superficially over the 'anatomical snuff box'.

Technique (Figure 4)

The radial nerve is essentially a 'field block' and requires a more extensive infiltration because of its less predictable anatomical location and division into multiple, smaller, cutaneous branches. With the wrist held in slight dorsiflexion, local anaesthetic should be injected subcutaneously, 3 cm proximal to the radial styloid, aiming medially and towards the radial artery but not piercing it. The infiltration is then extended laterally, using up to 5 mL of local anaesthetic.

The median nerve

Landmarks (Figure 5)

The median nerve is located between the tendons of the palmaris longus (PL) – present in approximately 85% of the population – and the flexor carpi radialis (FCR). The PL tendon is usually the more prominent of the two; the median nerve passes just deep and lateral to it.

Technique (Figure 5)

The median nerve is blocked by inserting the needle 2.5 cm proximal to the wrist crease between the tendons of palmaris longus and flexor carpi radialis with the forearm supinated. The needle is inserted until it pierces the deep fascia (3–5 mm), then 3–5 mL of local anaesthetic is injected. Although the piercing of the deep fascia has been described to result in a fascial 'click', it is more reliable to simply insert the needle 3–5 mm as the fascia here is relatively thin and the classical click will not be felt. The median nerve is superficial at this level, proximal to the carpal tunnel, and can easily be penetrated by the needle. Any lancinating symptoms into the fingers felt by the awake patient on needle insertion should prompt withdrawal of the needle because this may indicate that the needle is intraneural. Injection should be easy and with relatively low pressure. Pain in the fingers should not be felt by the awake patient during injection.

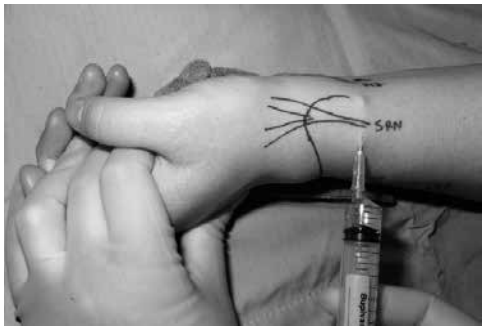

Figure 4. *Blocking the superficial branch of the radial nerve (SRN)*

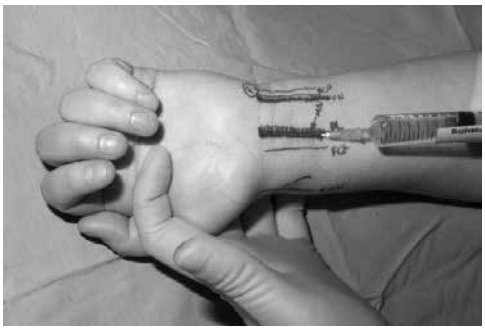

Figure 5. *Blocking the median nerve (the needle is inserted between palmaris longus and flexor carpi radialis). FCU, flexor carpi ulnaris; UN, ulnar nerve; PL, palmaris longus; FCR , flexor carpi ulnaris*

The ulnar nerve

Landmarks (Figure 6)

The ulnar nerve passes between the ulnar artery and tendon of the flexor carpi ulnaris (FCU). The tendon of the FCU is superficial to the ulnar nerve, which is the medial to the artery.

The dorsal cutaneous branch of the ulnar nerve (which must be blocked if anaesthesia to the ulnar aspect of the back of the hand is required) curves around the ulnar aspect of the wrist, 1 cm distal to the ulnar styloid in the mid-axial plane to reach the skin of the back of the hand.

Technique (Figures 6 and 7)

The ulnar nerve is anesthetised by inserting the needle under the

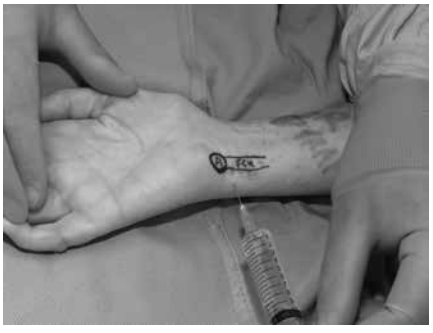

Figure 6. *Blocking the ulnar nerve (the needle is inserted under the FCU)*

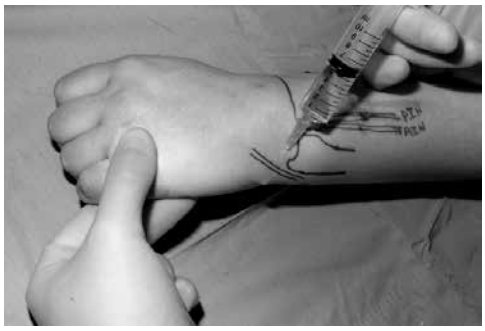

Figure 7. *Blocking cutaneous branches of the ulnar nerve*

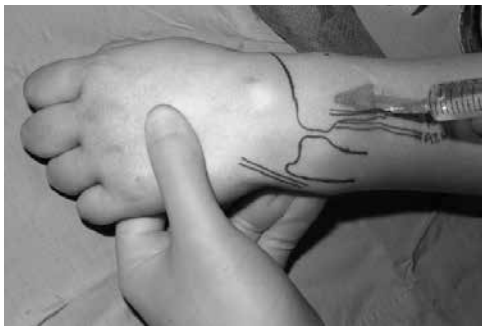

Figure 9. *Blocking the PIN*

tendon of the FCU muscle close to its distal attachment just above the styloid process of the ulna. The needle is advanced 5–10 mm to just past the tendon of the FCU and 3–5 mL of local anaesthetic solution is injected. If blood is aspirated prior to the injection, redirect the needle more superficially and medially as the ulnar artery has been pierced. As with the medial nerve injection, any lancinating symptoms into the fingers felt by the awake patient on needle insertion should prompt redirection.

A subcutaneous injection of 2–3 mL of local anaesthesia just distal to the ulnar styloid with the forearm pronated is also advisable in blocking the cutaneous branches of the ulnar nerve, which often extend to the hypothenar area and the back of the hand.

The posterior interosseous nerve

Landmarks (Figure 8)

The distal articular branch of the PIN lies alongside Lister's tubercle at the level of the wrist, before passing proximally between extensor carpi radialis longus and extensor digitorum.

Technique – PIN block (Figure 9)

With the forearm pronated, the PIN is blocked by an injection of local anaesthetic at the palpable ulnar border of the distal radius, 3 cm proximally to the level of the palpable ulnar head. The needle is inserted until it contacts the radial cortex and the anaesthetic is injected onto the periosteum where the nerve lies; 2 mL is adequate.

The anterior interosseous nerve

Landmarks (Figure 8)

Although the distal articular branch of the AIN is an anterior structure, it is best reached from the posterior aspect of the wrist. Its landmark, therefore, is the radial border of the distal ulna.

Technique – AIN block (Figure 10)

Having blocked the PIN, the needle is walked off the ulnar border of the radius and passed between the radius and ulna, through the interosseous membrane, where a 'click' is felt. A further 2 mL of anaesthetic solution is delivered just anterior to the interosseous membrane where the AIN lies.

LOCAL ANAESTHETIC

The choice of the type and concentration of local anaesthetic for wrist block depends upon the preferences of the individual operator. Whatever the requirements, the total dose should be well within the therapeutic limit/safe dose because the volumes required are not large. To provide anaesthesia and postoperative analgesia, the authors use 15 mL of a mixture of equal parts of 2% lignocaine and 0.5% levobupivacaine, occasionally increasing this to 20 mL. For postoperative analgesia alone, the authors use up to a total of 15 mL of 0.5% levobupivacaine. In order to ensure a consistent 'feel' for the injections, the authors also always use a 10 mL syringe and 23G (blue) needle, whatever the volume used.

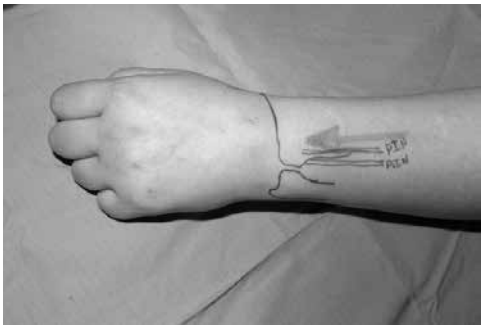

Figure 8. *The anatomy of the posterior interosseous nerve (PIN) and the anterior interosseous nerve (AIN)*

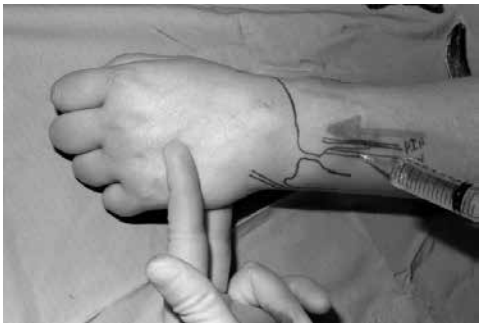

Figure 10. *Blocking the AIN*

COMPLICATIONS

- Block failure – in experienced hands the success rate is 98–100%.
- Bleeding and haematoma.
- Inadvertent vascular injection.
- Infection.
- Nerve damage – this can result from direct trauma, haematoma or high concentrations of local anaesthetic and vasopressor. Incidence ranges from 1 in 2000 to 1 in 50 000.

WEB LINKS

- The New York School of Regional Anaesthesia – www.nysora.com
- Neuraxiom – www.neuraxiom.com
- RA Education – www.raeducation.com
- Nerveblocks.net – www.nerveblocks.net

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ACKNOWLEDGEMENTS

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Update in
Anaesthesia

Update on opioid pharmacology

Woon-Shin Chong and Donald S Johnson

Correspondence: Donald.Johnson@health.wa.gov.au

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Summary

- Opioids bind to G-protein-coupled receptors.
- Opioid analgesia is a result of direct inhibition of peripheral and dorsal horn nociceptive neurons and activation of descending inhibitory pathways.
- Knowledge of the pharmacological differences between opioids is relevant to effective analgesia and patient safety.

INTRODUCTION

Opioid analgesics are the gold standard in systemic analgesia for severe acute pain. There are many different compounds in clinical use around the world. Cost, regulations and clinical setting dictate their availability. There is intra-patient and inter-patient variability in response to opioids. Incomplete cross-tolerance occurs when a patient is switched from one opioid to another, the clinical implication being that equivalent opioid doses need to be reduced when commencing a new opioid to avoid overdose. Knowledge of the pharmacological differences between opioids can be applied to select the appropriate drug for the relevant clinical setting and minimise the impact of side-effects. Over the last 20 years more information regarding the pharmacodynamics and pharmacokinetics in terms of opioid receptor dimers and oligomers, second messenger system effects and genotyping has come to light.

Opioid analgesics exert their pharmacological actions through the μ-opioid receptor, MOP, with some also having κ-opioid receptor, KOP activity.

OPIOID RECEPTORS

Classic opioid receptors

The opioid receptor is a G-protein-coupled (GPCR) with seven transmembrane regions. Opioid receptors are currently classified into:

1. δ-opioid receptors, DOP (named after the tissue it was first isolated from, vas **d**eferens);
2. κ-opioid receptors, KOP (named after the first ligand, **k**etocyclazine);
3. μ-opioid receptors, MOP (named after morphine, proposed 1976, cloned 1993).

The receptors were temporarily renamed in 1996 by the International Union of Pharmacology (IUPHAR) as OP1, OP2 and OP3. Prior to this they were known as DOR, KOR and MOR. Owing to the large body of literature using the Greek nomenclature, IUPHAR has recommended that the original δ, κ and μ nomenclature can be used interchangeably with DOP, KOP and MOP. Their actions are listed in Table 1.

Location

These receptors are located within the central nervous system in midbrain and brainstem areas associated with descending modulatory pathways and in the dorsal horn of the spinal cord. There are also peripheral sites including the vas deferens, knee joint, gastrointestinal tract, heart and immune system.

Opioid analgesia

Activation of midbrain opioid receptors indirectly stimulates descending inhibitory pathways. These descending pathways involve serotonergic and noradrenergic transmission, which results in inhibition of nociceptive traffic in the substantia gelatinosa of the dorsal horn of the spinal cord. In addition, opioids can act directly on nociceptive neurons in the dorsal horn and periphery.

Nociceptin receptor

This receptor, known as NOP, was discovered in 1984. Its endogenous ligand is nociceptin/orphanin FQ. Unlike the classical opioid receptors, it does not bind naloxone, which has led to the suggestion that it should not be classified as part of the opioid receptor family. It does, however, have a very similar structure and intracellular mechanisms.

Although, to date, only three types of opioid receptors have been cloned (DOP, KOP and MOP), at least 13 different opioid receptor subtypes were characterised using pharmacological methods over 10 years ago. Research is ongoing to discover the reason for this discrepancy. Postulated explanations are:

- There are splice variants of the receptor (however, expression is low in the central nervous system and

Woon-Shin Chong
Royal Perth Hospital
Perth
Western Australia

Donald S Johnson
Royal Perth Hospital
Perth
Western Australia

Table 1. *Actions mediated by opioid receptors*

Receptor	Action
DOP	Spinal and supraspinal analgesia, reduced gastric motility
KOP	Spinal analgesia, diuresis, dysphoria
MOP	Analgesia, sedation, itch, bradycardia, respiratory depression, inhibition of gastrointestinal transit, opioid tolerance and hyperalgesia, endocrine effects including regulating prolactin, growth hormone, testosterone, and other hormones, and immunological effects
NOP	Spinal analgesia and hyperalgesia and allodynia, supraspinally pronociceptive/antianalgesic due to inhibition of opioid tone

the intracellular C-terminal domain of the receptor is affected rather than the ligand-binding, extracellular N-terminal).

- Functional heterodimeric opioid receptors such as DOP-KOP and DOP-MOP may exist.
- Ligand-directed GPCR signalling may produce differential effects on second messenger systems such as β-arrestin, i.e. biased agonism.

INTRACELLULAR EVENTS

Once a ligand has bound an opioid receptor, the associated intracellular G-protein is activated. The α-subunit exchanges bound GDP for GTP and the βγ-subunit dissociates and is free to interact with intracellular second messenger systems and ion channels. With classical opioid receptor binding there is a decrease in cyclic adenosine monophosphate (cAMP) production as adenylate cylase is inhibited and also potassium conductance is increased with a reduction in calcium conductance through the cell membrane. This causes cell hyperpolarisation and reduced neuronal excitability with reduced neurotransmitter release. This is a tenable mechanism for the clinical effects of opioids but it is surprisingly unproven to date.

Other second messenger systems are coupled to activation of opioid receptors such as mitogen-activated protein (MAP) kinases and the phospholipase C-mediated cascade, leading to the formation of inositol triphosphate and diacyl glycerol.

The concept of ligand-directed GPCR signalling has recently been proposed (Figure 1). GPCR activation can lead to either equal/unbiased signalling or unequal/biased signalling through G-protein and β-arrestin-mediated intracellular signalling pathways. The implication is that analgesia and adverse effects may be differentially transduced by these two pathways. In β-arrestin knockout mice the anti-nociceptive effect of morphine was enhanced and prolonged whereas respiratory depression, constipation and naloxone induced withdrawals were attenuated.

LONG-TERM OPIOID ADMINISTRATION

Prolonged exposure to opioids leads to multiple adaptations in second messenger signalling systems that may be responsible for tolerance, sensitisation and withdrawal symptoms.

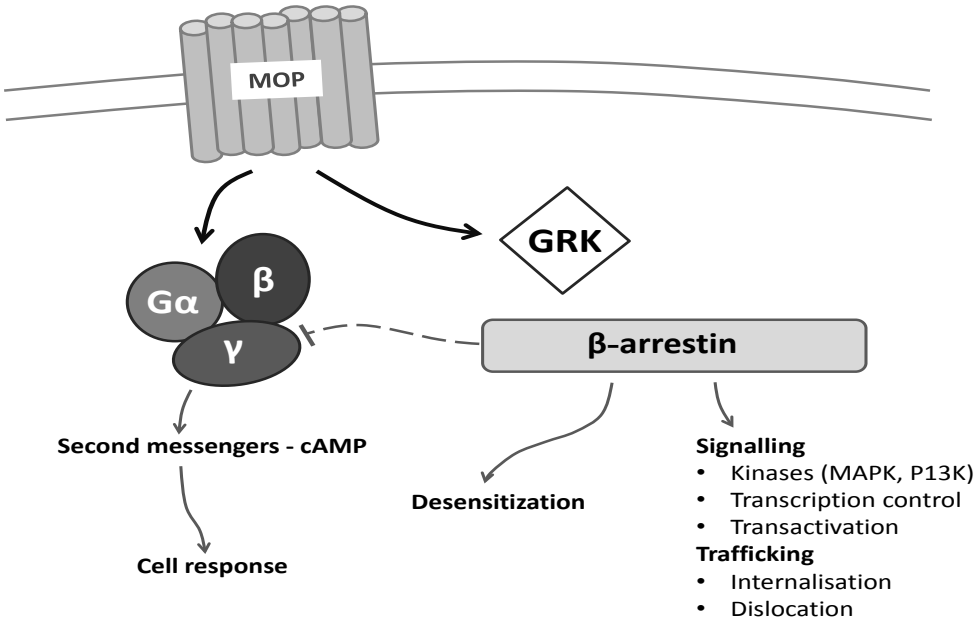

Figure 1. *Opioid receptor and intracellular cascade. MAPK, mitogen-activated protein kinase; PI3K, phosphoinositide 3-kinase; GRK, G-protein-coupled receptor kinase*

Intracellular protein kinases are responsible for an acute phosphorylation of the MOP and DOP opioid receptors, which results in tolerance to the effects of an agonist.

Internalisation of receptors is common to all GPCRs and is controlled by mechanisms separate from the agonist receptor interaction. GPCR kinases (GRK) phosphorylate agonist-bound receptors, promoting interactions with β-arrestins, which interfere with G-protein coupling and promote receptor internalisation. Receptor internalisation can have divergent responses – either receptor degradation, causing loss of function, or receptor dephosphorylation and recycling to the cell surface, leading to enhanced signalling.

Superactivation of adenylyl cyclase occurs with a chronic administration of opioid agonists. The alteration in levels of cAMP brings about numerous secondary changes.

Opioid-induced hyperalgesia

Opioid-induced hyperalgesia is a paradoxical response to an opioid agonist resulting not in an analgesic or antinociceptive effect, but an increase in pain perception.

Evidence for the mechanism of opioid-induced hyperalgesia includes:

- upregulation of excitatory neurotransmitters such as substance P and CGRP in primary afferent fibres and the spinal cord;
- increased evoked release of excitatory transmitters in the spinal cord;
- upregulation of spinal dynorphin levels, promoting enhanced input from afferent nociceptors;
- activation of descending pan-facilitation from the rostroventral medulla;
- increased cholecystokinin (CCK) in the brainstem acting via descending pathways;

TRPV1 (transient receptor potential cation channel subfamily V member 1) receptor antagonists have been shown to reverse opioid-induced hyperalgesia;

- *N*-methyl-D-aspartate (NMDA) receptor mechanisms in keeping with central sensitisation;
- glial activation via Toll-like 4 receptors.

DUAL OPIOID THERAPY

Combinations of analgesics often yield pharmacological effects greater than the sum of the individual effects. This phenomenon is termed synergy. Methadone and morphine have been demonstrated to act synergistically in animal models of analgesia. Interestingly, the effects of these drugs on gastrointestinal transit did not show synergy.

GENETICS

Splice variants

A single gene (OPMR1) has been associated with MOP. Genes consist of exons and introns. In the normal situation the introns are spliced out so the combined exons can be transcripted into mRNA and then translated into receptor proteins. Alternative splicing (splice variants) is one way a single gene can produce a vast array of different proteins. Mice lacking exon 1 of MOP are insensitive to morphine ,and those lacking exon 2 are sensitive to morphine but do not have an antinociceptive response to diamorphine (heroin), fentanyl or morphine-6-glucuronide. The relevance of these findings to clinical variability is unclear at present.

Genetics come into play when metabolism of opioids is considered, and codeine is an interesting case. Codeine can be considered a pro-drug and is metabolised via three pathways in the liver. The product of cytochrome P 3A4 (CYP3A4) is norcodeine, whilst codeine-6-glucuronide is produced by UGT 2B7 (over 80% of codeine metabolism). Codeine-6-glucuronide has been postulated to be responsible for the analgesic effect of codeine, but the CYP2A6 pathway is widely accepted as the most important (despite being responsible for less than 5% of codeine metabolism). The product of the CYP2A6 pathway is morphine. There are several phenotypes of CYP2A6; codeine lacks efficacy in poor metabolisers, whereas in ultrarapid metabolisers there is increased formation of morphine, leading to a higher risk of toxicity. This is highlighted by a case report of the death from opioid toxicity of an infant of a breastfeeding mother. The mother was an ultrarapid metaboliser taking 60 mg of codeine a day.[1]

RECEPTOR DIMERISATION

Opioid receptors exist as single entities but can also exist as homodimers such as KOP–KOP or MOP–MOP and heterodimers such as DOP–MOP and DOP–KOP. This dimerisation alters the receptors' pharmacological properties, with affinity for highly selective agonists and antagonists being reduced. Partially selective agonists and endogenous opioids have a greater affinity for these dimeric complexes. These heterodimers may explain the variability in molecular and pharmacological properties of opioid receptors.

SOME SPECIFIC OPIOIDS

Morphine

Morphine is a phenanthrene derivative that is an agonist at MOP and KOP receptors. Along with codeine it is the on the WHO essential medicines list published in March 2011. Codeine may be removed from the WHO list in the next edition subject to review. It has a bioavailability of 15–50% due to an extensive first-pass metabolism.

It is 20–40% protein bound, predominantly to albumin ,and the volume of distribution (V_D) is 3.4–4.7 L kg^{-1}. Degree of analgesia and plasma concentration are not clearly related. Metabolism occurs in the liver to morphine-3-glucuronide and morphine-6-glucuronide and normorphine. Morphine-6-glucuronide has analgesic effects and morphine-3-glucuronide has effects on arousal. Excretion occurs predominantly in the urine as the glucuronide conjugates; 7–10% appears in the faeces as conjugates morphine. The clearance is 12–23 mL min^{-1} kg^{-1} and the elimination half life is 1.7–4.5 hours. The peak analgesic effect occurs 30–60 minutes after parenteral administration due to the low lipid solubility (slowing transit to the nervous system) and the duration of effect is 3–4 hours.

Hydromorphone

Hydromorphone has similar pharmacokinetics and duration of action to morphine but is five times more potent with a slightly faster onset of action. Glucuronidation only occurs at position 3, making it better tolerated in patients with renal impairment because of the lack of an active metabolite.

Fentanyl, remifentanil and alfentanil

These opioids are MOP agonists that are commonly used in the peri-operative period. They display pharmacokinetic differences including increased lipid solubility compared with morphine, resulting in faster onset and offset. Remifentanil has a short, context-insensitive half-life of elimination due to metabolism by non-specific tissue and plasma esterases. Remifentanil has been used to generate an experimental model of hyperalgesia.

Buprenorphine

Buprenorphine is a synthetic derivative of the alkaloid thebaine. It acts as a partial agonist at MOP receptors and dissociates slowly, leading to prolonged analgesia compared with morphine. It has a high affinity for, but low intrinsic activity at, KOP receptors. Owing to significant first-pass metabolism the sublingual route is preferred. The bioavailability is highly variable even by the intramuscular route, at between 40% and 90%. The drug is 96% protein bound *in vitro* and the V_D is 3.2 L kg^{-1}. Metabolism occurs in the liver by dealkylation with subsequent conjugation to glucuronide – the polar conjugates then appear to be excreted in the bile and hydrolysed by bacteria in the gastrointestinal tract. Excretion occurs predominantly via the faeces as unchanged buprenorphine, with the remainder excreted in the urine as conjugated buprenorphine and dealkylated derivatives. The clearance is 1 L min^{-1}. The elimination half-life is 5 hours.

As it is a partial agonist, buprenorphine may antagonise the effect of morphine and may precipitate withdrawal in opioid-dependent patients. This tends to occur only at very high doses.

Methadone

Methadone is a synthetic opioid developed in 1942. It is a lipophilic basic drug (pK_a 9.2) and exists as a racemic mixture of two enantiomers, *R*-methadone and *S*-methadone. *R*-methadone is a potent MOP and DOP agonist. The *S*-methadone enantiomer is inactive as a MOP agonist but acts as an NMDA receptor antagonist. Following oral administration, time to peak plasma concentration is 2.5–3 hours. The oral bioavailability is high at around 85%. The V_D is high in humans at 4.2–9.2 L kg^{-1}. At physiological pH, 86% of methadone is bound to plasma proteins, predominantly α_1-acid glycoprotein. Unlike morphine, methadone is biotransformed in the liver rather than conjugated, and at daily doses of less than 55 mg the majority of the metabolites are cleared in the faeces. Methadone is metabolised by the cytochrome P450 enzymes. The main enzyme responsible for the N-demethylation of methadone is CYP3A4, with lesser involvement from CYP1A2 and CYP2D6. The main product of metabolism, 2-ethylidene-1,5-dimethyl-3,3-diphenylprrolidine (EDDP), is inactive. There are large interindividual variations in methadone pharmacology. Renal excretion is variable and pH dependent ,with excretion increasing as urine pH decreases. The elimination of methadone is biphasic. The α-phase is 8–12 hours and the β-elimination phase is even longer at 30–60 hours. Despite this long elimination period, the duration of analgesia is 8–12 hours, and for pain management the daily dose is often divided into two or three administrations. There is a real risk of accumulation and toxicity with repeated doses.

Tramadol and tapentadol

Tramadol is a partial MOP agonist with an additional serotonin and noradrenaline reuptake inhibition action and tapentadol is a MOP agonist with noradrenaline reuptake inhibition. Tramadol is metabolised to an active metabolite M1, which has greater affinity for MOP than it's parent compound.

CONCLUSION

No single mechanism adequately explains the intraindividual or interindividual variability observed with opioids. Available evidence suggests that a constellation of neurobiological, demographic, medical and patient specific factors all contribute to a determining a patient's response to a particular opioid. Opioids remain a key component in acute pain management and in cancer pain. Opioid use in chronic non-malignant pain is limited by tolerance and hyperalgesia.

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Update in
Anaesthesia

Management of paediatric sepsis

Erica Dibb-Fuller and Timothy Liversedge

Correspondence: ericadibbfuller@gmail.com

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Summary

Sepsis and septic shock have recently been redefined. Sepsis results when the host response becomes dysregulated.

The term 'severe sepsis' is no longer in use.

Septic shock is sepsis with a high mortality.

In contrast to adults, two thirds of children present in 'cold shock'.

Give antibiotics within 1 hour of diagnosis.

Traditional fluid resuscitation in septic children has recently been challenged by the FEAST trial.

INTRODUCTION

The aim of this article is to provide the reader with an overview of the current guidelines and evidence for the management of sepsis in children. Sepsis is a major cause of morbidity and mortality in children and, although mortality rates are lower in children than in adults, they are estimated at about 10% in severe sepsis.[1] In 2003, the World Federation of Paediatric Intensive and Critical Care Societies (WFPICCS) launched an international paediatric sepsis initiative to reduce mortality and morbidity from sepsis in children[2] by promoting early diagnosis and guiding effective treatment. The provision of dedicated neonatal and paediatric intensive care units, outreach teams and retrieval teams and the dissemination of guidelines to aid early recognition and treatment has contributed to falling mortality rates in paediatric sepsis.[3]

DEFINITIONS

Adult systemic inflammatory response syndrome (SIRS) criteria are modified to produce paediatric specific definitions.[4] However, sepsis and septic shock have recently been redefined and the term 'severe sepsis' is no longer in use (Table 1).[5] The former definition of sepsis was sensitive but very non-specific. The new definition takes into account that SIRS is an appropriate response to an insult, whereas in sepsis the inflammatory response is *dysregulated* and causes life-threatening organ dysfunction.

PRESENTATION

Adult and paediatric shock can be quite different. Adults tend to present with tachycardia, hypotension, low systemic vascular resistance (SVR) and a reduced ejection fraction, but with a relatively maintained cardiac output.[6] In children, the sympathetic nervous system responds to sepsis by increasing heart rate and SVR to maintain mean arterial pressure (MAP). Loss of this compensatory mechanism leads to hypotension, usually a late sign. Two-thirds of children present in 'cold' shock (normal/low cardiac output and high SVR); adults and the remaining one-third of children present in 'warm' shock (normal/high cardiac output and low SVR) (Table 2).[7] Mortality in children with sepsis is associated with severe hypovolaemia and a low cardiac output. It has been stated that for every extra hour a child remains in shock their mortality rate doubles.[8]

Tissue oxygen delivery is the major limitation to oxygen consumption in children with sepsis and treatment should be targeted to improve this. The use of cardiac output measurements or surrogate measures, such as superior vena cava oxygen saturation ($ScvO_2$) and lactate may act as guides to optimise treatment and improve oxygen delivery.[9]

TREATMENT

Consensus guidelines exist for the management of infants and children with septic shock.[10] There is some evidence that adherence to these recommendations has improved survival.[8,11] The treatment algorithm produced by the American College of Critical Care Medicine (ACCM) is available free at the following address: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4447433/.[10]

Management can be broadly divided into two main phases:

1. **ABCs**. During the first hour of resuscitation, fluid and inotropic drug therapy is directed towards maintaining goals of age-appropriate heart rate and blood pressure, and a normal CRT ≤ 2 seconds (Table 3). Oxygenation and ventilation should be supported as appropriate.
2. **Stabilisation**. Beyond the first hour, management should move to an intensive care setting for further haemodynamic support and

Erica Dibb-Fuller
Great Ormond Street Hospital
London
UK

Timothy Liversedge
Great Ormond Street Hospital
London,
UK

Table 1. *New definitions of sepsis*

SIRS – the definition is unchanged	A response to a stimulus, which results in two or more of the following:[4] • Temperature > 38.5°C or < 36°C • Heart rate more than two standard deviations above normal, or bradycardia in children < 1 year old (< 10th centile for age) • Respiratory rate more than two standard deviations above normal (or $PaCO_2$ <32 mmHg) • Leucocyte count >12 000 cells mm^{-3}, <4 000 cells mm^{-3}, or > 10% band forms • Hyperglycaemia, altered mental status, hyperlactaemia, increased capillary refill time (CRT).
Sepsis is now the old 'severe sepsis'	Life-threatening organ dysfunction caused by a dysregulated host response to infection
Septic shock is defined by its increased mortality compared with sepsis	A subset of sepsis in which profound circulatory, cellular and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone
Clinical criteria for septic shock	Hypotension requiring use of vasopressors to maintain mean arterial pressure ≥ 65 mmHg and Persistent serum lactate > 2 mmol L^{-1} despite adequate fluid resuscitation

goal-directed therapy. Treatment targets include normal perfusion pressure for age, $ScvO_2$ > 70% and cardiac index (CI) 3.3–6 L min^{-1}.

SPECIFIC RECOMMENDATIONS

Antibiotics

Antibiotics need to be administered within 1 hour of identification of severe sepsis, after appropriate cultures have been taken. Early antibiotic therapy and identification of the possible source of infection is critical. Broad-spectrum antibiotics should be commenced first; appropriate to the likely source of infection, the age of the child, and knowledge of local disease prevalence and drug-resistant organisms. Antibiotic cover can then be rationalised as the clinical picture, culture results and local microbiology team advice dictates. Therapeutic drug monitoring should be used to ensure adequate target levels and avoid drug toxicity. Courses of antibiotics must be completed and intravenous conversion to oral drugs taken at appropriate stages. Source control strategies are important and include drainage or debridement of infected tissues and removal of infected devices or foreign bodies.

Table 2. *Types of shock*

Type of shock	Clinical signs
Cold shock	CRT > 3 seconds, reduced peripheral pulses, cool mottled peripheries, narrow pulse pressure, commonly seen with community-acquired sepsis
Warm shock	Instantaneous capillary refill, bounding pulses, warm to edges, wide pulse pressure, more likely to be associated with central venous catheter infections.

Neonatal sepsis

A distinction can be drawn between early (age < 72 hours) and late (age > 72 hours) phases of neonatal sepsis.[13]

In early-onset neonatal sepsis causative agents are organisms commonly present in the maternal genital tract (e.g. group B *Streptococcus*, *Escherichia coli*, *Klebsiella*, *Enterobacter* and *Listeria monocytogenes*).[13] Typical broad-spectrum antibiotic cover is ampicillin and gentamicin (or amikacin), with therapeutic drug monitoring.

Late-onset neonatal sepsis is due to pathogens in the post-natal environment (e.g. transmission from the caregiver, aspiration of feeds and central line contamination). Initial broad-spectrum cover is often similar, ampicillin and either gentamicin or amikacin, but if meningitis is suspected then cefotaxime instead of gentamicin is used.[13] Vancomycin is used for suspected central line sepsis instead of ampicillin.

Paediatric sepsis

Common infecting organisms include *Staphylococcus*, *Streptococcus*, *Pseudomonas* and *Meningococcus.* Antibiotic choice depends on the likely pathogens involved and should vary depending on clinical presentation, e.g. pneumonia, bloodstream infection, intra-abdominal sepsis or meningitis. Antibiotic regimens need to cover both Gram-positive and Gram-negative organisms.

Table 3. *Age-appropriate heart rates and perfusion pressures*[11,12]

Age	Heart rate (bpm)	MAP – CVP (mmHg)
Term newborn	120–180	55
Up to 1 year	120–180	60
Up to 2 years	120–160	65
Up to 7 years	100–140	65
Up to 15 years	90–140	65

Anaesthesia and ventilation

Neonates and infants have a low functional residual capacity and a high work of breathing; early intubation and ventilation must be considered, especially in patients who show little response to aggressive fluid resuscitation and peripheral inotropes.

Induction drugs need to be carefully selected and administered to guard against excessive cardiovascular depression. Avoid large doses of thiopentone, propofol, midazolam and high inspired concentrations of volatile anaesthetic agents. Etomidate is associated with increased severity of illness in septic shock[14] and is generally not recommended. Ketamine (1–2 mg kg^{-1}) is a good alternative. Consider the need for a rapid sequence induction with cricoid pressure, and a nasogastric tube. Preoxygenation with 100% oxygen is desirable, but often practically difficult. There is potential for deterioration in cardiovascular parameters at this time and appropriate fluid boluses and inotropes should be prepared in advance.

Maintain sedation and paralysis post intubation and adopt a lung-protective ventilator strategy, maintaining low lung volumes (6–7 mL kg^{-1} tidal volume) with adequate positive end-expiratory pressure (PEEP) and low mean airway pressure. Evidence for this is derived from adult practice.

High-frequency oscillatory ventilation may be required where conventional ventilation alone proves inadequate.

Fluid resuscitation and intravenous access

Resuscitation should begin with boluses of 10–20 mL kg^{-1} crystalloid or 5% albumin over 5–10 minutes with further aliquots titrated to clinical condition (e.g. heart rate, urine output, CRT and level of consciousness). Aggressive fluid resuscitation is a key stage to improved survival, provided there is also access to inotropic therapy and mechanical ventilation.[15] Large fluid deficits are common and volumes of over 40–60 mL kg^{-1} can often be required (but see below for resuscitation in special circumstances).

The optimal choice of fluid is not known, and a recent systematic review of resuscitation fluid in children was unable to find evidence to support the use of colloid over crystalloid.[16] A large randomised study in adults, the SAFE trial, compared crystalloid and albumin fluid resuscitation, finding a trend towards improved outcomes in septic shock with albumin.[17] The 2007 updated consensus guidelines[9] suggest a preference towards the use of colloid resuscitation and there are two particular studies that support this in children.[18,19]

Malnourished children are a special category of patients who do not tolerate aggressive fluid resuscitation, as they are at greater risk of congestive heart failure from overhydration. Septic shock can be difficult to recognise and treat in these patients. Malnourished children require slow IV rehydration with careful and regular observation (every 5–10 minutes). An infusion of 15 mL kg^{-1} Ringer's lactate–5% glucose should be given over 1 hour; if there are signs of improvement, a repeat bolus can be given slowly, followed by oral or nasogastric rehydration. If the patient does not improve after 1 hour, a blood transfusion should be considered (10 mL kg^{-1} slowly over 3 hours). If the child deteriorates during treatment (increased respiratory rate or heart rate), the infusion should be stopped.[20]

The practice of high-volume fluid resuscitation in sepsis has been challenged by the recent Fluid Expansion As Supportive Therapy (FEAST) study, which investigated fluid resuscitation in a large cohort of children with a diagnosis of sepsis (but without hypotension) in Uganda, Kenya and Tanzania.[21] Resuscitation with a fluid bolus of 20–40 mL kg^{-1} saline or albumin was compared with the local practice of no fluid bolus resuscitation. The results of the study were surprising: mortality at 48 hours was higher in the fluid bolus groups than in the group that did not receive a fluid bolus, and at 4 weeks the risk of death and neurological sequelae was 4% higher. Most deaths were early, 87% occurring in the first 24 hours. The study included many children with malaria (57%), severe anaemia (32%), hypoxia (25%) or coma (15%), and 6% had hypotension. This may represent a population in whom overhydration will not be well tolerated, particularly if mechanical ventilation and inotropic support are not available. The implications of the FEAST study are not completely clear at present, but it is likely that aggressive bolus fluid resuscitation, as traditionally recommended, should not be used in children with severe anaemia or malaria, or other common febrile illness associated with a significant stress response but not hypotension (i.e. associated with antidiuretic hormone release and fluid retention). Particular caution should be used when using aggressive fluid resuscitation in patients in low-income countries given the absence of mechanical ventilation and inotropic support in many centres.[22]

Intravenous access is often difficult to achieve in critically ill children. Early intraosseous access should be considered to avoid repeated or prolonged attempts at venepuncture and enable resuscitation to begin in a timely manner. In children with fluid-refractory shock, CVP and arterial pressure monitoring can guide on-going resuscitation. Ultrasound guidance can be a useful tool to facilitate this.

Inotropic and vasoactive drug therapy

In fluid-refractory shock, persistent hypotension is treated with either inotropes, vasopressors or a suitable combination of both. Regular reassessment of the child with appropriate changes to the choice and rate of cardiovascular drug used is essential.

Dopamine is the first-line agent. If central venous access will delay starting inotropes, then the American College of Critical Care Medicine guidelines recommend the use of peripheral inotropes (not vasoconstrictors) with close monitoring of the IV access site to prevent extravasation injury.[10]

Subsequent inotropic support depends on the clinical presentation of the child: low cardiac output and high SVR (cold shock), high

Table 4. *Recommended infusion rates*

Adrenaline	0.05–2 μg kg^{-1} min^{-1}
Dobutamine	5–20 μg kg^{-1} min^{-1}
Dopamine	5–15 μg kg^{-1} min^{-1}
Noradrenaline	0.05–1 μg kg^{-1} min^{-1}
Glycerine trinitrate	1–5 μg kg^{-1}.min^{-1}
Milrinone	0.3–0.75 μg kg^{-1} min^{-1}
Sodium nitroprusside	1–5 μg kg^{-1} min^{-1}

cardiac output and low SVR (warm shock), or low cardiac output and low SVR. Where dopamine is ineffective, add adrenaline in cases of cold shock and noradrenaline in warm shock (Table 4 gives guide infusion rates). Other agents to consider are vasodilators (e.g. sodium nitroprusside or glyceryl trinitrate) or phosphodiesterase inhibitors (e.g. milrinone) in the case of low cardiac output and high SVR despite adrenaline infusion. Vasopressin is used in adult practice for the treatment of extremely low SVR despite high doses of noradrenaline, but there is currently no clear evidence to support its use in paediatrics.[23]

Therapeutic end points

In the first hour, the aim of resuscitation should be to achieve normalisation of heart rate, a CRT ≤ 2 seconds, normal pulses with no differential between central and peripheral, warm extremities, urine output ≥ 1 mL kg^{-1} h^{-1}, and normal mental status. Progress towards these targets can be used to monitor the progress of resuscitation.

Early goal-directed therapy originated in the management of severe sepsis in adults and has been shown to have the largest mortality reduction of any sepsis study.[24] Timely use of cardiac output monitoring and surrogate markers of organ perfusion is recommended in the management of paediatric sepsis, including lactate, improved base deficit, $ScvO_2$ ≥ 70% or SvO_2 ≥ 65%, CVP 8–12 mmHg or cardiac output monitoring (cardiac output 3.3–6 L min^{-1} m^{-2}).

An indirect measure of oxygen delivery can be made using $ScvO_2$. and a study of children with sepsis compared the use of the ACCM guidelines with and without the goal of $ScvO_2$ > 70%.[8] When this goal-directed approach was used, patients received more crystalloid, blood and inotropic support, resulting in a reduction in 28-day mortality from 39.2% to 11.8% in the $ScvO_2$-monitored group. Normalising lactate clearance may be as effective as the use of $ScvO_2$ as a resuscitation goal in the initial treatment of sepsis.[25]

Cardiac output monitoring in the form of echocardiography, trans-oesophageal Doppler, pulse contour analysis or suprasternal ultrasound cardiac output monitors can be helpful. Blood flow is difficult to determine clinically and blood pressure is a poor substitute, as it is affected by both cardiac output and systemic vascular resistance. There is no good evidence for improved outcome with any of these monitoring tools, only observational data. A large multicentre randomised controlled trial is needed.

Steroids

Evidence for the use of steroids in paediatric sepsis is lacking. A randomised controlled trial in children with septic shock is required and until then steroids should not be used routinely.[26] Current *retrospective* studies of steroids in children with severe sepsis have shown their use to be an independent predictor of increased mortality.[27]

Hydrocortisone therapy is reserved for children with catecholamine resistance and suspected or proven adrenal insufficiency. Children at risk of adrenal insufficiency should be treated with steroids, but the recommended doses of hydrocortisone vary; the dose for stress cover is 1–2 mg kg^{-1} day^{-1} whilst that for shock reversal is 50 mg m^{-2} day^{-1}. Note the different units for these doses. Those at risk of adrenal insufficiency include children taking steroids for chronic disease, those with pituitary or adrenal abnormalities, and cases of catecholamine resistant severe septic shock. Adrenal insufficiency can be identified by random blood cortisol levels < 18 μg dL^{-1} or a cortisol level increase of < 9 μg dL^{-1} after an adrenocorticotrophic hormone (ACTH) stimulation test.

Deep vein thrombosis prophylaxis

In older, post-pubertal, children appropriate measures to consider include unfractionated or low-molecular-weight heparin or mechanical prophylactic devices such as compression stockings. In young children, the majority of thrombotic events are associated with the use of central venous catheters, and there is some evidence that heparin-bonded central venous lines may reduce thrombosis rates.[28] A multicentre randomised controlled trial under way at present is looking at catheter-related infections in children and comparing the effectiveness of heparin-bonded catheters and antibiotic-impregnated catheters for the prevention of hospital-acquired bloodstream infections (CATCH trial[29]). A side-arm of this study will investigate the incidence of thrombosis.

Stress ulcer prophylaxis

Early enteral feeding or, where this is not possible, stress ulcer prophylaxis with H_2 blockers or proton pump inhibitors should be used routinely in patients with severe sepsis. This is aimed at reducing the risk of gastrointestinal bleeds and at the prevention of ventilator-associated pneumonia. H_2 blockers were previously used in nil-by-mouth neonates, but there is now evidence of increased risk of infections, necrotising enterocolitis and fatal outcome.[30]

Glycaemic control

Blood glucose should be kept within the normal range. Hypoglycaemia can cause neurological damage and should be treated promptly with 2 mL kg^{-1} 10% glucose. Neonates will require a 10% glucose infusion (8 mg kg^{-1} min^{-1}) whilst children and adolescents have lower requirements, 5 mg kg^{-1} min^{-1} and 2 mg kg^{-1} min^{-1} respectively. Requirements may be higher in children with metabolic disease or liver failure.

Hyperglycaemia is also a risk factor for increased mortality[31] and should be treated with an insulin infusion and frequent glucose monitoring to avoid inadvertent hypoglycaemia.

Transfusion

Consider targeting transfusion to a haemoglobin goal of greater than 10 g dL^{-1} to achieve an $ScvO_2$ > 70%, so enhancing oxygen delivery.[10]

After the initial resuscitation is complete, we do not know the best haemoglobin level for critically ill children. Common practice is to use conservative blood transfusion thresholds to reduce potential risks and complications. The Transfusion straTegies in Paediatric Intensive Care Units (TRIPICU) study looked at transfusion thresholds in stable, critically ill children.[32] The authors reported that a haemoglobin threshold of 7 g dL^{-1} decreased transfusion requirements without increasing adverse outcomes.

Renal replacement therapy

With large volumes of initial resuscitation fluid being given and often an on-going fluid requirement due to capillary leak, there can be significant tissue oedema and fluid overload. Diuretics, peritoneal dialysis or renal replacement therapy may be required once the child has been stabilised. Early implementation of continuous renal replacement therapy is associated with improved survival compared with late implementation.[33]

Protein C and activated protein C

The use of activated protein C in children is not recommended due to a lack of evidence of benefit and an increase in bleeding complications.[34]

Extracorporeal membrane oxygenation (ECMO)

Extracorporeal membrane oxygenation (ECMO) may be considered in those cases of severe septic shock, which have not responded to all conventional treatment strategies,[35] where it may be associated with improved survival.

Intravenous Immunoglobulin

Intravenous immunoglobulin therapy may be associated with a reduction in mortality and should be considered in severe sepsis.[35]

CONCLUSION

Mortality rates in paediatric sepsis have fallen due to improvements in its management. Early recognition and aggressive treatment in line with protocol-driven algorithms (such as the guidelines produced by the ACCM) form the mainstay of initial management. Subsequent early referral and transfer to intensive care units for on-going care, and the use of early goal directed therapy are essential to improve outcomes. For many therapeutic interventions there is a paucity of good supporting evidence. The guidelines provided by the ACCM provide an expert consensus approach to the management of septic children.

There is some emerging evidence that children in low-income countries represent a patient cohort in whom traditional recommendations of fluid resuscitation may not be applicable.

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Update in
Anaesthesia

Hyponatraemia

Peter Allan and Saibal Ganguly

Correspondence: bruce.mccormick@nhs.net

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Summary

- Sodium disorders are the most common electrolyte abnormalities seen in hospitals.
- Hyponatraemia is often iatrogenic in inpatients, and severe sodium disturbances are associated with considerable morbidity and mortality. Disorders of sodium balance can be confusing.
- Categorisation based on fluid status aids diagnosis of the underlying cause and helps guide treatment.
- The speed with which hyponatraemia develops is important. In acute cases there is a greater risk of cerebral oedema and rapid correction is beneficial.
- However, rapid correction can be dangerous in patients with chronic hyponatraemia.

INTRODUCTION

The presence of hyponatraemia has been demonstrated to be an independent risk factor for increased mortality in hospital inpatients.[1] As hyponatraemia is the most common electrolyte disturbance encountered in clinical medicine,[1] it is vital that doctors and nurses know how to appropriately manage this condition. Severe hyponatraemia has long been recognised to be associated with adverse outcomes.[2] It is also increasingly being recognised that even mild hyponatraemia can be associated with patient harm, with even relatively minor derangements having been shown to be associated with an increased risk of falls and fractures.[3–5]

Appropriate management of hyponatraemia is often challenging because of both numerous pathophysiological mechanisms and multiple underlying pathological conditions.[6] After revising the normal control of sodium balance this article will review the causes, classification, diagnosis and management of hyponatraemia. An algorithm for investigations and treatment is provided at the end of this article.

CONTROL OF SODIUM BALANCE

Sodium is the most prevalent cation in the extracellular fluid (ECF). Total body sodium is therefore proportional to ECF volume. Under normal circumstances serum sodium levels are maintained within a tight physiological range of between 135 and 145 mmol L^{-1}. Despite great variation in the intake of both sodium and water, close control of serum sodium is maintained via control of the excretion of water and sodium.[7] Over 99% of the sodium filtered by the kidney is reabsorbed in the proximal tubule and loop of Henle. This reabsorption occurs at a relatively fixed rate, regardless of total body sodium. It is the smaller proportion of sodium, reabsorbed in the distal tubule and collecting ducts, that exert the most influence on total sodium balance,[8] but serum sodium levels reflect water balance under the influence of antidiuretic hormone (ADH).

THE ROLE OF ANTIDIURETIC HORMONE

The majority of hyponatraemic states involve inappropriately elevated levels of ADH.[9] This causes disproportionate retention of water compared with sodium. The secretion of ADH is influenced by multiple factors such as plasma osmolality and circulating volume. Failure to suppress ADH production in lowered osmolality states is a feature of SIADH (syndrome of inappropriate ADH secretion). By contrast, continued production of ADH despite a lowered serum osmolality is a feature of oedema-forming conditions such as heart failure and liver

Peter Allan
Foundation Doctor
Royal Cornwall Hospitals NHS Trust
UK

Saibal Ganguly
Intensive Care Registrar
Royal Cornwall Hospitals NHS Trust
UK

disease.[10] In these conditions ADH production continues because reduced renal perfusion causes excess aldosterone production.

CAUSES OF HYPONATRAEMIA

True hyponatraemia

As sodium and its accompanying anions are the major effective plasma solutes in the ECF, hyponatraemia and hypo-osmolality almost always coexist. True hyponatraemia is regarded as a low sodium level in the presence of hypo-osmolality.

The situations in which hyponatraemia can occur without hypo-osmolality are discussed later.

True hyponatraemia is characterised by hypo-osmolality. This is because sodium in the ECF and potassium in the intracellular fluid (ICF) (along with their associated anions) determine osmolality, with water moving freely between fluid compartments, in order to maintain the same osmolality between compartments. As a result, plasma hypo-osmolality, and therefore hypotonic hyponatraemia, indicates a relative excess of water to sodium regardless of volume status.

It is an oversimplification to regard hypo-osmolar states as produced by either water excess or solute depletion as often components of both are involved.[11] It can be useful though to classify hyponatraemia on the basis of fluid status. This can facilitate understanding of the processes involved in the development of hyponatraemia and also help guide management.

Categorisation into one of three clearly defined groups based on volume status is not always possible due to multiple aetiologies and patient co-morbidities. However, inappropriate categorisation of hyponatraemia and subsequent mismanagement has been shown to lead to poor clinical outcomes,[12] whilst following a simple algorithm for the diagnosis and treatment of hyponatraemia has been shown to be associated with improved outcomes.[13]

Hypovolaemic hyponatraemia

In hypovolaemic hyponatraemia total body water and total body sodium are both low, but there is disproportionate loss of sodium compared with water. This is a result of the increased ADH secretion seen in hypovolaemic states causing increased water reabsorption. Hyponatraemia is often compounded by thirsty patients consuming hypotonic fluids at a level inadequate to try to restore circulating volume.

Sodium loss can be renal or extrarenal, and establishing the urinary sodium level is important in distinguishing between the two. A urinary sodium level below 20 mmol L^{-1} is suggestive of an extrarenal cause.[12,14] Extrarenal causes are commonly of gastrointestinal origin. Other causes include exercise-associated hyponatraemia (also commonly seen in people working in hot conditions), burns, trauma and pancreatitis. Renal causes include diuretic excess, renal failure, salt-wasting nephropathy, aldosterone deficiency, chronic pyelonephritis, nephrocalcinosis, proximal renal tubular acidosis and ketonuria.[12]

Euvolaemic hyponatraemia

Euvolaemic hyponatraemia is the most common category of hyponatraemia seen in hospital inpatients.[12] SIADH is the most common cause of euvolaemic hyponatraemia and is associated with many different disorders. These can be divided into several major aetiological groups, but a discussion of these this is beyond the scope of this article.

If SIADH is suspected, it can be useful to measure urine osmolality as a urine osmolality > 100 mosm kg^{-1} in the presence of hyponatraemia reflects inappropriate antidiuresis. As SIADH remains a diagnosis of exclusion other potential causes must be investigated and excluded first.

Other common causes of euvolaemic hyponatraemia include:

- Glucocorticoid deficiency – cortisol deficiency may lead to failure of ADH suppression.
- Hypothyroidism – hyponatraemia secondary to hypothyroidism is rare. It is thought to result from impaired water excretion due to decreased glomerular filtration rate (GFR) secondary to the systemic effects of thyroid hormone deficiency on peripheral vascular resistance and cardiac output.
- Low solute intake, e.g. beer potomania – here the primary abnormality is one not of water balance but of sodium balance due to reduced intake.
- In the vast majority of cases excessive water intake in isolation is insufficient to overwhelm the capacity of the kidneys to excrete water. Therefore, severe hyponatraemia due to excess water intake alone is rare in the presence of normal renal function. If water intake exceeds 20 litres per day, as seen in psychogenic polydipsia, it is possible to achieve a transient hyponatraemia, but in the absence of other dysfunction this is rapidly corrected on cessation of fluid intake.[12] It is more likely that patients with high fluid intakes and accompanying hyponatraemia have a concurrent impairment of water excretion that has previously gone unnoticed during periods of normal water ingestion. In patients with known psychiatric disorders who consume large volumes of water, this is often a result of iatrogenic SIADH, for example as a side-effect of selective serotonin reuptake inhibitors. Acute psychosis has also been shown to increase ADH secretion.

Hypervolaemic hyponatraemia

This is a situation characterised by a paradoxical increase in total body sodium, but a simultaneous and proportionally larger increase in total body water, leading to a dilutional hyponatraemia. This reduction in water excretion is secondary to either an excess of ADH secretion or an element of renal impairment limiting the maximal excretion of free water.

Table 1. *Some important causes of SIADH with examples of major groups of causes and descriptions of specific causes*

Cause	Description
Drugs	Commonly thiazide diuretics, vincristine and cyclophosphamide. Many others including selective serotonin reuptake inhibitors, sodium valproate and haloperidol. For a more comprehensive list, see Binu et al.[15]
Central nervous system disorders	Infection, trauma, ischaemia, haemorrhage and psychosis can increase the release of ADH[16,17]
Malignancies	Commonly of the lung, particularly small cell carcinoma.[18] Other tumours can less frequently have a similar effect. These include head and neck, duodenal and pancreatic cancers[15,19]
Pulmonary disease	Pneumonia, asthma and acute respiratory failure have been known to cause SIADH[15]
Surgery	Major surgery can lead to increased secretion of ADH.[20,21] This is thought to involve a pain afferent-mediated response
Nephrogenic SIADH	Due to a vasopressin receptor 2 (VR2) gene gain-of-function mutation. This leads to excess water reabsorption in the renal collecting duct[22]
Infective	Acquired immune deficiency syndrome[23,24]

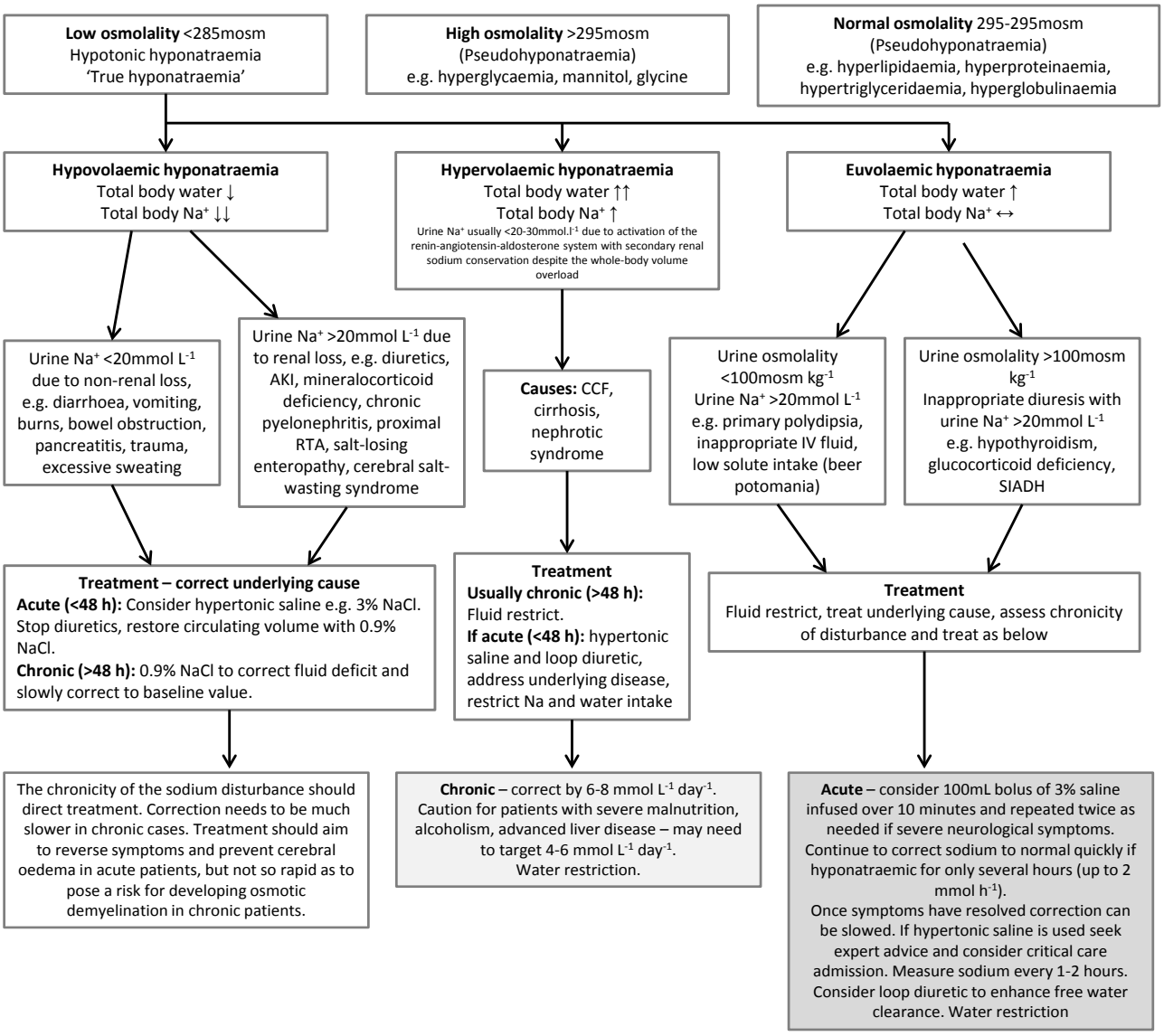

Figure 1. *Hyponatraemia treatment algorithm*

Underlying pathologies include nephrotic syndrome, congestive cardiac failure and cirrhosis (although rarely in the absence of ascites).[10] In all of these situations there is oedema secondary to impairment of the kidney's ability to excrete water maximally. This results from either inappropriate ADH secretion, leading to water retention, or an inappropriate distribution of fluid within the body, preventing intravascular fluid elimination.

Hyponatraemia without hypo-osmolality

As stated previously, hyponatraemia and hypo-osmolality almost always coexist, and this is referred to as 'true hyponatraemia'. Hyponatraemia occurring without hypo-osmolality is referred to as pseudohyponatraemia. Pseudohyponatraemia can occur with a normal or elevated serum osmolality. Pseudohyponatraemia with normal serum osmolality occurs when grossly elevated levels of lipids or proteins lead to an artificial apparent decrease in measured a serum sodium. This is because sodium normally distributes in the aqueous phase of plasma, which accounts for 93% of the plasma volume. A correction factor for whole plasma can be rendered incorrect if the non-aqueous phase is increased due to hypertriglyceridaemia or paraproteinaemia.[17]

The use in laboratories of direct ion-sensitive electrodes eliminates this potential error. Hypertonic hyponatraemia refers to hyponatraemia with an increased osmolality. This occurs when sodium and its associated anions are no longer the major effective solutes present in the plasma. This 'translocation hyponatraemia' is the due to osmotically active solutes in the plasma which are unable to cross the cell membrane. While many solutes, such as urea and ethanol, can enter cells and so cause hypertonicity without cell dehydration, other molecules, such as glycine, cannot. Glucose normally diffuses freely into cells but when insulin is deficient, such as in diabetic ketoacidosis (DKA), glucose is effectively confined to the ECF. When the concentration of glucose rises, water is displaced across the membrane from inside to outside the cell. As well as dehydrating the cell, this leads to a dilutional hyponatraemia. In DKA, the 'true' corrected serum sodium can be estimated from the formula:

$$[Na^+] \text{ corrected} = [Na^+] \text{ measured} + \{(\text{glucose} - 5.6) \times 0.288\}$$

It is an important axiom of treatment of DKA, especially in children, that the corrected sodium concentration should rise slowly as glucose falls, to avoid the risk of cerebral oedema secondary to plasma hypo-osmolality.

SYMPTOMS AND SIGNS OF HYPONATRAEMIA

The symptoms and signs associated with hyponatraemia relate to both the degree of imbalance and the time course over which the imbalance has developed. Neurological symptoms can occur as a result of an osmotic gradient between the ICF ECF compartments. This gradient causes water to move into cells, resulting in tissue oedema.[27,28] This process is clinically most important in the brain as, due to the exhaustion of adaptive mechanisms and confinements of the skull, cell swelling here can lead to raised intracranial pressure and neurological damage. This situation occurs most often when hyponatraemia develops over a short time frame.

If severe hyponatraemia develops over the course of hours or a few days, rather than over many days or weeks, then the ability of the brain to adapt to osmotic changes and cell swelling is more rapidly exceeded. This leads to the development of cerebral oedema.[29] Patients in whom acute severe hyponatraemia has developed in under 48 hours can present with alarming neurological findings such as coma and convulsions. Additionally they are at risk of death as a result of cerebral herniation.[30]

Rapidly evolving severe hyponatraemia is a different disease entity from slowly evolving hyponatraemia. Brain adaptation seen in slowly evolving hyponatraemia may prevent cerebral oedema. This occurs via the transport of sodium, chloride and potassium to the ECF. This compensatory mechanism maintains ICF osmolality equal to equal ECF osmolality and thereby avoids large shifts of water into the cells.[31] Over a period of time organic solutes such as glutamine, glutamate and taurine follow into the ECF to maintain this osmotic stability. These molecules are known as 'organic osmolytes'.

The clinical result of this compensation is that these patients experience fewer and less severe symptoms and generally do not die as a result of brain herniation.[31] Slowly evolving hyponatraemia is frequently asymptomatic, but there are limits to how low levels can get before physiological processes are affected, regardless of the chronicity of the process.[12] Non-specific symptoms generally develop when serum sodium levels drop below 120 mmol L^{-1}. These symptoms include fatigue, lethargy, weakness and confusion. Seizures and coma are uncommon. As well as time frame, symptoms are also dependent on the patient's premorbid state. Certain groups, such as children, hypoxic patients and premenopausal women, are at increased risk of cerebral oedema.[32]

INVESTIGATION

The diagnosis of underlying cause is difficult and should be carried out with the help of an endocrinologist. A careful history with particular reference to the patient's recent medications and fluid intake should be taken. A clinical examination, looking for indicators of volume status, e.g. oedema, jugular venous pressure, signs of adrenocortical insufficiency including pigmentation, postural hypotension, stigmata of hypothyroidism, or any signs related to chest or central nervous system disease, in particular underlying neoplasia, should be carried out.

Assessment of volaemic status using clinical examination is notoriously unreliable, however, and must be made in conjunction with the history and blood and urine tests.

Radiological investigations where indicated might include computed tomography of brain, thorax, abdomen and pelvis. Measurement of

urine osmolality and electrolytes, thyroid function tests, a random cortisol and/or short Synacthen test, blood lipid profile and serum electrophoresis are required.

The algorithm below provides a useful structure for investigating and managing hyponatraemia.

MANAGEMENT

General advice

Because there are inherent risks associated with both hyponatraemia and its rapid correction, appropriate management of hyponatraemia involves balancing these risks. Patients, who have developed a sodium imbalance over a longer period of time are likely to have made appropriate compensatory changes.[31] They are therefore better able to tolerate severe hyponatraemia. Furthermore, in these patients slow correction is much safer, as discussed later. In contrast, in patients who have developed hyponatraemia over a short timeframe, a faster resolution may be appropriate, particularly if there are signs of neurological compromise.

The major risk associated with excessively rapid sodium correction is osmotic demyelination.[33] This can result in severe and permanent neurological impairment or death. Certain patient groups, such as the malnourished, alcoholics, those with burns and those with hypokalaemia, are at increased risk of osmotic demyelination.[12]

Osmotic demyelination occurs as a result of the failure of the adaptations that prevent chronically hyponatraemic patients from developing cerebral oedema. Over-rapid correction in these patients prevents the brain from replacing organic osmolytes at an appropriate speed. The resultant osmotic stress leads to osmotic demyelination.[33,34] This condition has previously been known as central pontine myelinolysis, due to its tendency to affect the pons, which has a dense concentration of heavily myelinated ascending and descending tracts that are particularly vulnerable to osmotic stress. However, these changes have been reported in extrapontine sites also.[35] The key features of osmotic demyelination are described below. While it is known that resolution of hyponatraemia should be tailored to the speed of the acquisition of the imbalance, there is no clear consensus on the absolute safe rate, and it may be that none exists.

Over-rapid correction is extremely common, despite the use of formulae to guide sodium correction. This is because volume repletion, irrespective of the fluid's actual sodium content, can switch off ADH production and cause a rapid rise in sodium level.

Importantly, there are case reports of successful treatment of osmotic demyelination treated by acutely re-lowering the serum sodium with dextrose and/or desmopressin in cases of overshoot correction, thereby buying time for organic osmolytes to recumulate.[36]

Management of acute hyponatraemia

Recommendations for the rate of correction of acute hyponatraemia are based on avoiding brain herniation, something that is almost exclusively seen in acute hyponatraemia.[12,37,38] These patients have the greatest risk of cerebral oedema but a lower risk of demyelination than chronically hyponatraemic patients. Therefore. prompt partial correction of hyponatraemia is indicated. The limited literature available suggests that an increase in serum sodium of 4–6 mmol L^{-1} or to exceed the seizure threshold of 120 mmol L^{-1} is adequate to reverse the most severe manifestations of acute hyponatraemia.[38]

In acute hyponatraemia severe neurological symptoms may be treated with a 100 mL bolus of 3% hypertonic saline.[32,39] This can be given intravenously over 10 minutes. This bolus may be repeated twice if severe neurological symptoms persist.[12] The aim of this emergency treatment is to address neurological complications such as cerebral oedema, hyponatraemic seizures or reduced level of consciousness-ness. Importantly, the aim is not to return serum sodium levels to within the normal range. In acute hyponatraemia, once symptoms have resolved, it becomes less important to rapidly correct the sodium level, and in these instances an increase in serum sodium rates of up to 2 mmol L^{-1} h^{-1} may be appropriate.[40]

If hypertonic saline (3% sodium chloride) is used in acute symptomatic patients, specialist advice should be sought. Very close (1 to 2-hourly) monitoring of plasma sodium should be performed. These patients should be admitted to a critical care unit, if such facilities are available. Some authors advocate the use of a loop diuretic in combination with hypertonic saline in order to enhance free water clearance; however, extreme caution is required as this may lead to too rapid a rise in sodium.[40]

Management of chronic hyponatraemia

It is widely accepted that patients with chronic hyponatraemia are susceptible to adverse neurological outcomes when sodium levels are rapidly corrected due to iatrogenic brain damage.[12,29,33,34,38,41–43] Current guidance suggests the desired increase in serum sodium in chronic hyponatraemia should be 4–8 mmol L^{-1} day^{-1} for those at low risk of osmotic demyelination syndrome.[12] In patient groups where the risk of osmotic demyelination syndrome is high, it has been suggested that an even lower goal of 4–6 mmol L^{-1} day^{-1} be targeted.[12] For patients with severe symptoms, the entire 6 mmol L^{-1} can be achieved during the first 6 hours of therapy, with subsequent treatment delayed until the next day. Sterns and Hix[44] have described a rule of sixes that some may find helpful: six a day makes sense for safety; so six in 6 hours for severe symptoms and stop.

As the precise time course of the disturbance is often not clear, it is often safer to adopt slow correction for all patients unless adverse neurological symptoms and signs mandate a more rapid correction or there is absolute certainty about the time course. Specific tips for the management of the different subtypes of true hyponatraemia are given below.

Hypovolaemic hyponatraemia

In hypovolaemic hyponatraemia, the aim is to correct the volume deficit, as the relative water excess will correct itself via a water diuresis once circulating volume is restored. Fluids such as 0.9% should be administered until blood pressure is restored and the patient has clinical euvolaemia.[12] Hypovolaemic hyponatraemia is almost always an example of chronic hyponatraemia, so slow correction should be employed.

Euvolaemic hyponatraemia

In euvolaemic hyponatraemia, as with all hyponatraemia, management is dictated by the underlying cause, the chronicity or acuteness of the imbalance and the presence or absence of neurological symptoms. Water restriction of 1–1.5 litres per day may be used. Drugs that may have caused SIADH should be discontinued and any underlying causes addressed.

Hypervolaemic hyponatraemia

In hypervolaemic hyponatraemia, fluid restriction is the mainstay of treatment. Strict restriction is often necessary to achieve a negative solute-free water balance. Typical initial fluid restriction for a normal sized adult should be around 1–1.5 litres per day. Loop diuretics are sometimes used to remove excess fluid with urine usually hypotonic to plasma.[12]

CONCLUSION

Hyponatraemia is a condition associated with significant morbidity and mortality. Treatment is guided by the underlying cause, speed of onset and the presence of adverse neurological signs. In the absence of severe neurological signs, current guidance suggests that correction of serum sodium should not exceed 4–8 mmol L^{-1} day^{-1} in patients with chronic hyponatraemia. Lower rates of correction may be indicated in patients with chronic hyponatraemia who have additional risk factors for osmotic demyelination. More rapid correction should only be targeted in cases where there is certainty that the hyponatraemia is acute or if the hyponatraemia is causing severe neurological symptoms. Too rapid correction of hyponatraemia may risk permanent severe neurological damage or death.

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Update in
Anaesthesia

Maternal critical care

Vandana Girotra and Mary Mushambi

Correspondence: vandana.girotra@uhl-tr.nhs.uk

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Summary
Most women experience few significant complications during pregnancy, delivery and the postpartum period. The few who become critically ill during this time should receive the same standard of critical care as non-pregnant patients. Recent Confidential Enquiries into maternal mortality highlight a number of deaths in which prior care was considered suboptimal. There is a growing need to address the area of maternal critical care with respect to the best ways of delivering care to this vulnerable patient group.

Vandana Girotra

Mary Mushambi
University Hospitals
Leicester
UK

CONFIDENTIAL ENQUIRIES INTO MATERNAL DEATHS[1]

The UK's Confidential Enquiry into Maternal Deaths is the longest-running audit in the world and has been published every 3 years for the past 60 years. The review published in 2011, for the 2006–08 triennium, highlights the decline in the overall mortality rate of pregnant women from 13.95 per 100 000 maternities in 2003–05 to 11.39 in 2006–08 (Table 1).[1] The fall in mortality is mainly due to a decrease in the number of deaths from direct causes – conditions resulting from the pregnancy (e.g. thromboembolic disease, haemorrhage, amniotic fluid embolism). Mortality due to indirect causes (medical or mental conditions worsened by pregnancy) has either increased or remain unchanged. The report highlighted that some women died despite receiving excellent care. However, there was evidence that suboptimal care contributed to the deaths of a significant number of women. Examples of suboptimal care included delays in recognising critical illness and involving the intensive care teams.

More than 1 in 10 women aged 16–50 admitted to UK intensive care units (ICU) are obstetric patients. In addition, there are likely to be significant numbers of critically ill parturients who are cared for within the maternity unit.

A multidisciplinary Maternal Critical Care Working Group, commissioned by the Joint Standing Committee of the Royal College of Anaesthetists with representation from the Intensive Care Society, the Obstetric Anaesthetists' Association, the Royal College of Obstetricians and Gynaecologists, The Royal College of Midwives and other UK organisations, published guidance on provision of maternal critical care.[2] This document defines standards and makes recommendations to help guide maternity and critical care providers in establishing and managing a maternal critical care service.

WHAT IS MATERNAL CRITICAL CARE?

Maternal critical care, rather than obstetric critical care, describes patient-centred multidisciplinary care rather than specialty-focused care.[3] The 2000 UK Department of Health document *Comprehensive Critical Care* recommends that the terms 'high dependency' and 'intensive care' should be replaced by the term 'critical care'.[4] The document also proposes that the care required by an individual should be independent of location – the concept of 'critical care without walls'. Care is subdivided into four levels, depending on the organ support and level of monitoring required independent of diagnosis. The level of care required by pregnant or recently pregnant woman can also be classified according to the Intensive Care Society's *Level of Care* document.[5] Examples of levels of care provided within a maternity unit are described below.

Level 0 or normal ward care

Care of the low-risk woman.

Level 1 or additional monitoring or step-down from higher level of care

- Neuraxial analgesia.
- Risk of haemorrhage.
- Oxytocin infusion.
- Remifentanil infusion.
- Mild pre-eclampsia on oral antihypertensives/ fluid restriction.
- Chronic medical condition at risk of deterioration, e.g. diabetes mellitus requiring IV insulin.

Level 2 or single organ support

Basic cardiovascular support (BCVS)

- Infusion of antihypertensives (e.g. labetalol or hydralazine) to control blood patients in preeclampsia.
- Arterial line used for blood pressure monitoring and blood sampling.
- Central venous catheter for central venous pressure monitoring or vascular access.

Table 1. *Adapted from Centre for Maternal and Child Enquiries 20111 (rates shown are per 100 000 maternities)*

	2000–2002		2003–2005		2005–2008	
Cause of death	**Numbers**	**Rates**	**Numbers**	**Rates**	**Numbers**	**Rates**
Direct deaths						
Sepsis	13	0.65	18	10.85	26	1.13
Pre-eclampsia and eclampsia	14	0.70	18	0.85	19	0.83
Thrombosis and thromboembolism	30	1.50	41	1.94	18	0.79
Amniotic fluid embolism	5	0.25	17	0.80	13	10.57
Haemorrhage	17	0.85	14	0.66	9	0.39
Anaesthesia	6	10.30	6	0.28	7	0.31
Indirect deaths						
Cardiac disease	44	2.20	48	2.27	53	2.31
Neurological conditions	40	12.00	37	11.75	36	1.57
Psychiatric conditions	16	0.80	18	0.85	13	0.57

Basic respiratory support (BRS)
- Oxygen support via facemask to maintain oxygen saturation
- Non-invasive ventilation (continuous positive airway pressure (CPAP), bilevel positive airway pressure (BiPAP), etc.).

Advanced cardiovascular support (ACVS)
- Simultaneous use of at least two intravenous antihypertensive or vasoactive drugs.

Neurological support
- Use of magnesium infusion to control seizures.

Hepatic support
- Severe hepatic failure (e.g. secondary to HELLP (haemolysis, elevated liver enzymes and low platelet count) syndrome or acute fatty liver of pregnancy).

Level 3 or advanced respiratory support alone or support of two or more organ systems as above
- Advanced respiratory support – invasive mechanical ventilation.
- Support of two or more organ systems: renal support and BRS; BRS/BCVS and an additional organ supported.

WHAT GROUPS OF PREGNANT WOMEN MAY REQUIRE CRITICAL CARE?

Recent UK ICNARC data (Intensive Care National Audit and Research Centre) in 2009 showed that 11.4% of women aged 16–50 years admitted to an adult general ICU were either pregnant or had recently been pregnant.[6] A total of 513 obstetric patients admitted were to an ICU, an incidence of 260 admissions per 100 000 maternities. The majority were post partum (418 women; 81.5%), and major haemorrhage was the primary diagnosis in 34%. Other postpartum critical care admissions comprised patients with preeclampsia (7%), pneumonia (3.6%) or HELLP syndrome (2.4%). Non-obstetric pathology was the main reason for admission in 95 women (18.5%) recorded as 'currently pregnant'. The single most common diagnosis in this group was pneumonia (20%), followed by asthma (7.4%) and ectopic pregnancy (5.3%). The ICNARC data confirmed that obstetric patients admitted to the ICU had a better outcome than matched control subjects (critical care mortality 2% vs. 11% in control population).

Although the ICNARC provides valuable information about pregnancy-related ICU admissions, relatively little is known about the women who receive higher level of care on maternity units. It is estimated that as many as 5% of pregnant women require level 2 care.[3,7,8]

WHERE SHOULD MATERNAL CRITICAL CARE BE PROVIDED?

Delivering high-quality critical care or obstetric management outside designated specialty-specific areas is challenging. The UK National Service Framework for Children, Young People and Maternity Services recommends consultant-led services with adequate facilities, expertise, capacity and back-up for timely and comprehensive obstetric emergency care, including intra-hospital transfer to critical care. One of the most important recommendations by the Maternal Critical Care Working Group was that the standard of care of critically ill pregnant or postpartum women should meet both their pregnancy-related and critical care needs. Arrangement models may be developed on the basis of local configuration, size and complexity of maternity and critical care services. These may include:

- providing critical care in a designated area on, or near, the delivery suite by trained midwives, obstetricians and anaesthetists with additional training in critical care;
- importing critical care skills into the labour ward via critical care outreach.
- transferring women to a general critical care unit (in this

case obstetric and midwifery input and competencies will be imported into the critical care environment, and postpartum women should maintain direct contact with their baby wherever possible).

The above models can be implemented by maternity and critical care services depending on local pathways to ensure that women have access to high-quality services irrespective of where they have delivered.

The UK Department of Health recommends that all clinical staff caring for critically ill pregnant or recently pregnant women should be trained and competent in recognising and responding to acutely ill patients.[9]

THE MATERNITY AND GENERAL CRITICAL CARE INTERFACE

The pregnant woman being cared for in a general critical care area requires daily review by a multidisciplinary team including a named obstetric consultant and senior midwife. The multiple care providers must balance the needs of critical care with the needs of the woman with regard to obstetric care.

Important additional points for antenatal critical care

- Ensure adequate lateral maternal tilt to avoid aorto-caval compression.
- Thromboprophylaxis should be provided in line with local or national guidelines.
- Regular mid-stream urine specimens should be taken owing to the increased risk of urinary tract infections.
- Meticulous fluid balance should be maintained in women with severe preeclampsia/eclampsia and following massive haemorrhage.
- A contingency plan with detail of necessary equipment should delivery be required outside the maternity unit should be available.
- Drugs commonly used in the obstetric population, such as hydralazine, magnesium sulphate and uterotonics (e.g. oxytocin, ergometrine, prostaglandin $F_{2\alpha}$) should be available.
- Consider antenatal steroids if preterm delivery is anticipated.
- Daily communication between named obstetrician and midwife and combined ward rounds.
- Implement appropriate plans for fetal monitoring and surveillance.

Additional points for postpartum care

- No lateral tilt is required.
- Breastfeeding support should be available.
- Thromboprophylaxis measures may be necessary.
- Regular follow-up by the multidisciplinary team and usual postpartum checks should include neonatal checks, administration of anti-D immunoglobulin if required and breastfeeding support.
- Attention should be paid to drug safety in breastfeeding women.

It is vital to appreciate the physiological changes of pregnancy and how they impact on critical illness. Such changes include aorto-caval compression, reduced functional residual capacity, potentially difficult airway and intubation and increased risk of pulmonary aspiration. In the event of a maternal cardiac arrest after 20 weeks' gestation, cardiopulmonary resuscitation should be conducted in accordance with Advanced Life Support (ALS) guidelines with uterine displacement and perimortem caesarean section commenced after 4 minutes and delivery within 5 minutes of the cardiac arrest.[10]

STANDARDS FOR THE RECOGNITION AND CARE OF THE ACUTELY ILL PARTURIENT

Physiological observations should be recorded on arrival in all women admitted to the maternity unit, and a clear written plan for monitoring and management should be formulated. The plan should take into account:

- high- or low-risk pregnancy
- reason for admission
- presence of comorbidities
- the agreed treatment plan.

A physiological track and trigger system should be used to monitor all antepartum and postpartum admissions. The introduction of a national modified early obstetric warning score (MEOWS) chart for use in all pregnant and postpartum women who become unwell may aid the more timely recognition, treatment and referral of women who are becoming critically ill.[11] MEOWS charts should be used in all areas of the hospital where pregnant and recently pregnant women may present, including the emergency department. Abnormal scores should prompt an appropriate response. Education, training and assessment should be provided to ensure that staff have competencies appropriate to the level of care they are providing.

A graded response strategy for patients identified as being at risk of clinical deterioration is recommended, depending on early warning system (EWS) score.

Low-score group (EWS score = 3)

- Increased frequency of observations.
- Midwife in charge alerted.

Medium-score group (EWS score =4 or 5)

- Urgent call to personnel with core competences for acute illness, e.g. critical care outreach team, anaesthetist, obstetrician, acute medical or surgical specialties.

High-score group (EWS score > 6)

- Emergency call to team with critical care and maternity competences. The team should include a practitioner with advanced airway management and resuscitation skills.

CHALLENGES TO DEVELOPING A MATERNAL CRITICAL CARE SERVICE

Increasing workload

Many countries are experiencing an increase in the number of high-risk pregnant women on account of a rising birth rate and changes in obstetric demographics including an increase in maternal age and comorbidities, morbid obesity and assisted conception. The rise in caesarean section rate in many countries has resulted in an increase in the incidence of abnormal placentation (accreta, increta and percreta) and subsequent postpartum haemorrhage.

Training

Each hospital should establish guidelines and in-service training to suit their own local arrangements. Implementation of simulation and 'skills and drills' training has been shown to improve human factors such as leadership, teamwork and communication. Midwives looking after critically ill women should have additional training in critical care competencies.[2]

Staffing

Midwifery courses vary with respect to the amount of associated training in general nursing skills and knowledge. This, combined with midwifery recruitment shortages in some areas, make provision of adequate numbers of midwifery staff with appropriate critical care training and experience challenging.

Critical care team

The care of women with complex medical conditions mandates that obstetricians, anaesthetists, neonatologists, critical care specialists and midwives work in effective multidisciplinary teams. Early involvement of a critical care team is at times vital to avoid an adverse outcome and effective lines of communication and interdisciplinary working are essential.

SUMMARY

Standards of delivering maternal critical care have been defined.[2] The cornerstone of management should involve early multidisciplinary teamwork between clinicians and specialties with effective lines of communication. The role of MEOWS and outreach services is invaluable in early recognition and prevention of maternal morbidity and mortality. There is an increasing need to ensure that care providers on maternity units have adequate training and competencies in maternal critical care.

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Update in
Anaesthesia

Cerebral Challenge

Andrew Macalister Hall and Liz Turner

Correspondence: andrewmhall@doctors.org.uk

CASE 1

A 70-year-old man in the intensive care unit has a feeding nasogastric tube inserted. The nursing staff cannot aspirate anything from the tube in order to test for acidity and confirm gastric placement. A chest radiograph is requested to confirm its placement and you are asked if it can be used for feeding (Figure 1).

- Where does the tip of the NG tube lie?
- What would be the next most appropriate course of action?
- What tests can be used to confirm correct placement of NG tubes?

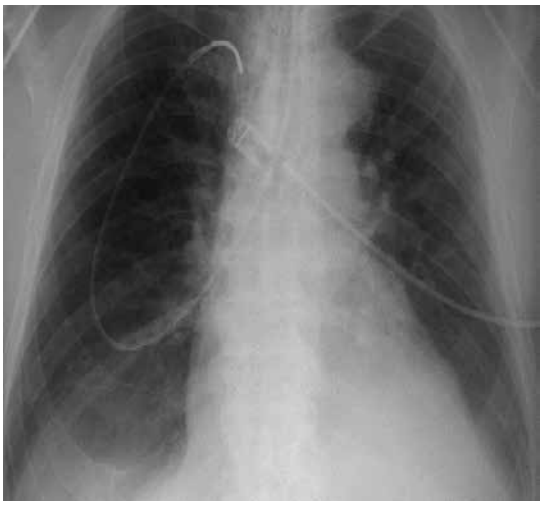

Figure 1. *Chest radiograph of patient 1*

CASE 2

You are asked to anaesthetise a 65-year-old man as a day case for inguinal hernia repair. He is otherwise well, and takes ramipril 5 mg for essential hypertension. You have asked for an ECG prior to anaesthetising him (Figure 2).

- What does the ECG show?
- What implications does this have on anaesthetising this patient?
- What is the longer term management of this condition?

CASE 3

A previously fit and well 42-year-old woman presents to the emergency department complaining of sudden-onset severe headache that occurred while she was out shopping. She describes the headache as the worst headache she has ever had. The headache started 30 minutes ago and has not improved. Her daughter reports that she appears confused. While in the emergency department her consciousness level deteriorates and she is taken for urgent computed tomography (CT) of the head (Figure 3).

- What does this CT head show?
- How would you manage this patient?

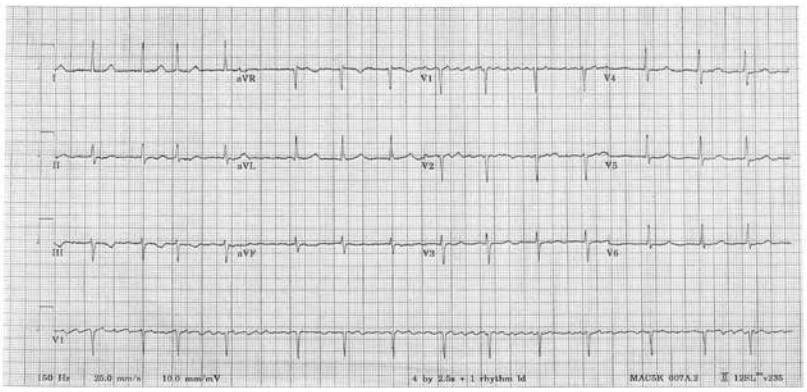

Figure 2. *ECG of patient 2*

Andrew Macalister Hall
Specialist Trainee in Anaesthesia

Liz Turner
Core Trainee in Anaesthesia
Royal Devon and Exeter NHS Foundation Trust
Exeter EX2 5DW
UK

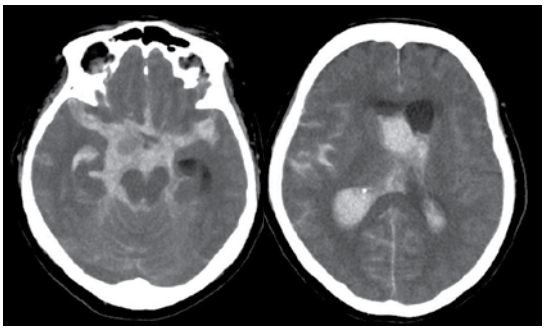

Figure 3. *CT head of patient 3*

DISCUSSION

Case 1

Guidance on confirmation of correct nasogastric tube placement

It is important to recognise correct nasogastric placement, as it is a commonly used piece of equipment with the potential to cause serious harm. In the UK alone around 170 000 tubes are supplied to the NHS each year. There is the risk of significant harm to the patient if drugs or feed are passed down a nasogastric tube that has been placed within the lungs (Figures 4 and 5). Between 2005 and 2011 the National Patient Safety Agency (NPSA) was notified of 21 deaths and 79 cases of harm due to misplaced nasogastric tubes.[1] The single greatest cause of harm was due to misinterpretation of radiographs, accounting for about half of all incidents and deaths. Misplaced nasogastric tubes have been confirmed by the Department of Health in England as a 'never event', one of a restricted list of serious avoidable events.[2] Box 1 shows an example of guidance to guide safe NG tube placement.

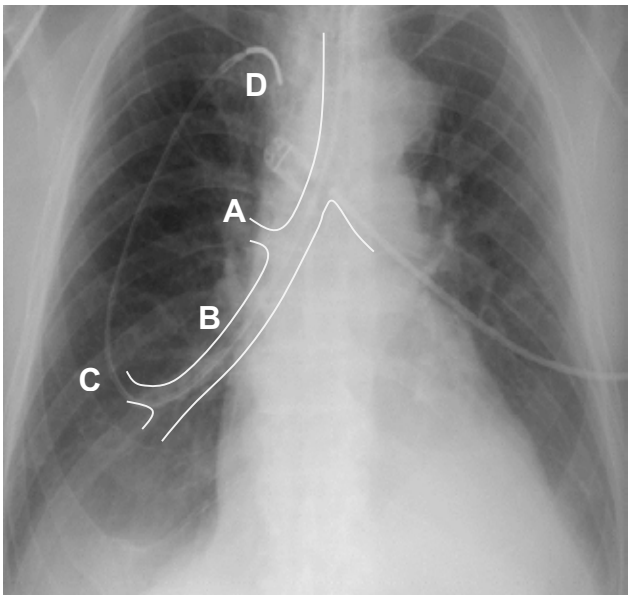

Figure 4. *Chest radiograph of patient 1. It shows that the nasogastric tube has entered the larynx rather than the oesophagus, passing down the trachea and into the right main bronchus. The right upper lobe aperture is usually within 1.5–2.5 cm from the carina (A) and the nasogastric tube has not entered this bronchus, but has continued down the bronchus intermedius (B). The nasogastric tube has probably been passed into the right middle lobe bronchus (C). After this its passage does not follow the anatomy of the bronchial tree, and to have reached its final position it must have been pushed through the bronchial wall and has entered the right pleural cavity (D). Feeding through this tube would result in accumulation of nasogastric feed within the pleural cavity ('feed-o-thorax') with respiratory compromise and other life-threatening consequences. The tube should be completely removed from the patient. As the visceral pleura has been breached there is a risk that the patient may develop a pneumothorax after the tube is withdrawn; the patient must be monitored carefully for 6 hours and the chest radiography repeated to exclude this*

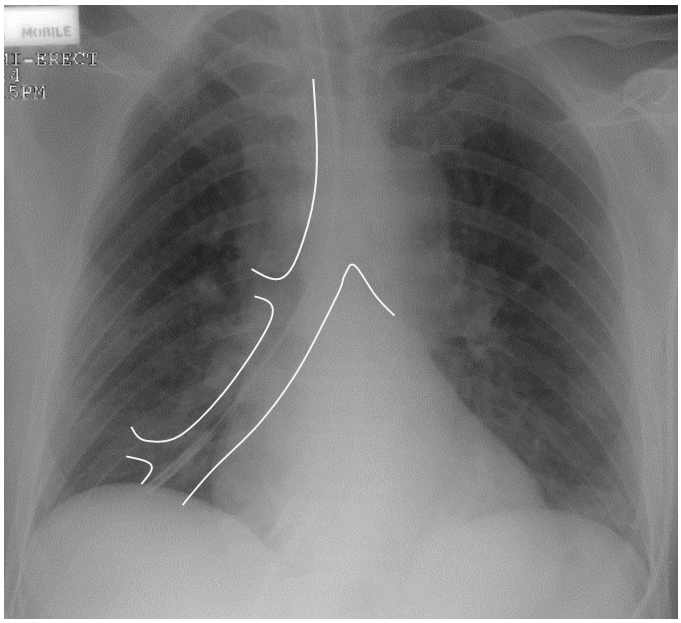

Figure 5. *Chest radiograph of a different patient. This time the nasogastric tube is still in the lungs, but has not been advanced too far and so is still within the bronchial tree, probably lying within the right lower lobe bronchus*

References

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2. Mayor S. NHS extends never events list and introduces cost penalties. *BMJ* (2011); **342**: d1263. Available at http://www.medicalprotection.org/uk/casebook/casebook-september-2012/nasogastric-tube-errors
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4. National Patient Safety Agency, UK. *Harm from Flushing of Nasogastric Tubes Before Confirmation of Placement* (March 2012). Available at http://www.nrls.npsa.nhs.uk/resources/type/alerts/?entryid45=133441

Box 1. Example of local ICU guidance on safe nasogastric tube placement[3]

A. Initial placement – pH testing of aspirate

- A pH < 5.5 indicates gastric placement.* Document tube length at nose and date and time of insertion.
- If unable to obtain an aspirate try:
  - rolling the patient onto his or her side
  - advancing the tube 10 cm
  - injecting 10–20 mL of air and re-aspirating after 10 minutes.
- If pH > 5.5, consider retesting in 1 hour provided the patient is not on acid-suppressing medication (in which case, proceed to radiological confirmation).
- If pH testing cannot confirm the correct position of the tube, placement should be confirmed by chest radiography. The only exception to this is where the nasogastric tube has been felt in the stomach by the operating surgeon at laparotomy, or the tube has been placed during upper gastrointestinal endoscopy.

B. Radiological confirmation of placement

- Radiological confirmation should be performed by suitably competent individuals – this will involve training for new staff.
- The nasogastric tube should:
  - adhere to the midline
  - bisect the carina
  - be visible throughout its length, and
  - pass beneath the diaphragm in the midline.
- The person confirming position should document this in the patient's notes (including the date and time the confirming radiograph was obtained).
- If possible, a single chest radiograph should be taken to confirm the position of an endotracheal tube, invasive lines, drains, etc.

C. Confirmation following interruptions in feeding

- Patients in the ICU experience multiple interruptions in nasogastric feeding, for example to facilitate imaging, transfer between hospital departments, administration of certain drugs, etc. In addition, there is a theoretical risk of tube migration into the oesophagus, particularly in patients who vomit or retch.
- Reconfirmation of nasogastric tube position using the methods described above leads to unnecessary delays in reintroducing feed.

Prior to interruption of feed

- Document the tube marking at the nose

Prior to restarting feed

- If the nasogastric tube position is unchanged, there has been no retching/vomiting and no evidence of coiling at the back of the throat and there is no clinical suspicion the tube has dislodged, feed can be restarted without pH testing/chest radiography. This should be documented in notes.
- If these conditions are not met, confirmation needs to be as for 'Initial placement'

*****According to the NPSA (UK) two patients have died as a result of staff flushing nasogastric tubes with water before aspirating fluid to measure pH. The mix of water and lubricant caused the pH reading to fall below 5.5, leading the staff to assume that the nasogastric tubes were correctly placed, when they were not.[4]

†In 2005 the UK's NPSA issued guidance highlighting the unreliability of the 'whoosh test' (using a stethoscope to listen for bubbling sounds over the stomach after blowing air through the nasogastric tube with a syringe). This technique should not be used.

Case 2

This 12-lead ECG shows narrow QRS complexes that are irregularly irregular that are not preceded by P waves. This patient has atrial fibrillation (AF) with a ventricular rate of 85 bpm.

Atrial fibrillation is the commonest arrhythmia and has an estimated prevalence of 1–2%.[1] It is associated with significant morbidity and mortality, including cerebrovascular events and heart failure. Atrial fibrillation is due to uncoordinated atrial electrical activity which intermittently progresses to atrioventricular node conduction, causing irregularity in ventricular depolarisation. When in sinus rhythm, atrial contraction delivers between 10% and 40% of ventricular filling;[1,2] however, this is reduced in AF due to uncoordinated atrial contractions.

Implications of AF for anaesthesia and surgery

There are many causes of AF (see Table 1). As this patient was previously unknown to have AF, further investigation may be indicated prior to proceeding with general anaesthesia. The Association of Anaesthetists of Great Britain and Ireland (AAGBI) suggests that, prior to elective surgery, routine electrocardiography (ECG) should be carried out in all patients over the age of 40 who are classified as ASA (American Society of Anesthesiologists) 2 and those who have cardiovascular disease.

Almost all anaesthetic medications are negatively ino- and chronotropic, meaning that on induction of anaesthesia the patient's cardiac output will fall as a result of a reduction in both heart rate and cardiac muscle contractility. A reduction in ventricular filling due to uncoordinated atrial contraction will cause a more profound fall in cardiac output and therefore hypotension when the patient is anaesthetised. It is essential to maintain a good cardiac output with a controlled rate, monitoring for any rate related ischaemic changes or hypotension. However, AF with a normal ventricular rate does not normally cause any major anaesthetic problems.

Assuming that further history and examination shows the patient to be otherwise fit and healthy, with no evidence of any of the conditions listed in Table 1 that would preclude safe and anaesthesia and surgery, it is reasonable to proceed. His heart rate is currently controlled with no need for rate controlling medication.

Longer-term management of AF

The long-term management of atrial fibrillation is complex and multimodal. The following factors should be considered in the management of AF.

Was the onset of AF within the last 48 hours or is it pre-existing?

It is important to establish the time of onset of atrial fibrillation because of the risk of formation of atrial thrombus due to the turbulent blood flow. This could potentially lead to clot embolism, causing a cerebrovascular event (CVE) – this is a particular risk when the rhythm changes between sinus rhythm and AF. The risk of embolism is greatly reduced if cardioversion takes place in the first 48 hours. After 48 hours, transthoracic or, preferably, transoesophageal echocardiography should be performed to look for thrombus and, if necessary, anticoagulant treatment administered for a minimum of 3 weeks prior to cardioversion.[3] Remember to look for and treat any reversible causes of AF such as electrolyte abnormalities and hyperthyroidism.

Is there evidence of cardiovascular compromise?

If the patient has adverse features related to atrial fibrillation, then urgent management is needed. Adverse features include shock (hypotension, tachycardia), myocardial ischaemia, syncope and heart failure.[4] The treatment would be assessment using the ABCDE approach and synchronised DC cardioversion with an initial energy of 120–150 J[4] to try to restore sinus rhythm and treatment of any reversible causes. DC cardioversion should not be performed on a conscious patient and so, unless the patient is unconscious, anaesthetic support should be gained in order to perform the procedure under general anaesthesia. There is no time in this situation to arrange for echocardiography or to anticoagulate the patient.

Is the aim to achieve rate control or rhythm control?

Longer-term pharmacological management includes either rate or rhythm control. Rate control is defined as a heart rate of 60–80 bpm at rest and between 90 and 115 bpm during exercise. This could be achieved by a number of drugs, including beta-blockers or cardiac glycosides (e.g. digoxin). Rhythm control (chemical cardioversion)

Table 1. *Risk factors for developing atrial fibrillation*[1]

System	Aetiology	Assessment
Cardiovascular	Underlying heart disease, valvular heart disease, cardiomyopathy, pre-existing excitatory syndromes (e.g. Wolff–Parkinson–White), sinus node disease	12-lead ECG, echocardiography, stress testing, R-tests (72-hour ECG)
Respiratory	Hypoxia, pneumonia, effusions, thromboembolic disease	Pulse oximetry, arterial blood gas, chest radiography
Electrolyte	Low or high potassium, low magnesium, low calcium	Serum biochemistry
Metabolic	Acidosis, alcohol excess, thyrotoxicosis, diabetes mellitus	Arterial blood gases, thyroid function tests, liver function tests, blood glucose levels, toxicology screen
Others	Increasing age, hypovolaemia	Fluid status assessment

can be achieved by medications such as sotalol, flecainide or amiodarone, but should be attempted only after anticoagulation because of the risk of embolism.

Does the patient need anticoagulation?

Patients who have persistent, permanent or paroxysmal AF need to be considered for anticoagulation therapy because of the increased risk of clot formation and stroke. Patients can be risk stratified using the CHADS2-VASc score (Table 2) to estimate their risk of stroke and decide if they need anticoagulation therapy.

References

1. Sokhi J, Kinnear J. Atrial fibrillation: peri-operative management in non-cardiac surgery. *Anaesthesia Tutorial of the Week* 307 (2014). Available at http://www.wfsahq.org/components/com_virtual_library/media/e12b5079331ce4d1108a2e9f38294fd0–48ca68dafce920f3e467801da9d65b06–307-Atrial-Fibrillation--AF-Peri-operative-management-for-non-cardiac-surgery.pdf.
2. Hutchins D. Peri-operative cardiac arrhythmias. Part 1: Supraventricular arrhythmias. *Anaesthesia Tutorial of the Week* 279 (2013). Available at http://www.wfsahq.org/components/com_virtual_library/media/35c9e1ade52a269fd099ffe2b2ab694c-d4034c3630abc0a887ecd5ff9087854c-279-Peri-operative-Cardiac-Arrhythmias---Part-1.pdf.
3. National Institute for Health and Care Excellence.. *Atrial Fibrillation: Management*. Clinical guideline 180. 2014. https://www.nice.org.uk/guidance/cg180/resources/atrial-fibrillation-management-35109805981381.
4. Resuscitation Council UK. *Peri-arrest Arrhythmias: Tachycardia* (2015). Available at https://www.resus.org.uk/resuscitation-guidelines/peri-arrest-arrhythmias/#tachycardia.

Table 2. *CHA2DS2-VASc score*

Congestive heart failure	1
Hypertension	1
Age (years)	
< 65	0
65–74	1
≥ 75	2
Diabetes	1
Stroke/transient ischaemic attack/ thromboembolism	2
Vascular disease	1
Sex	
Male	0
Female	1
Score of 0 is low risk	No anticoagulation
Score of 1 is low–moderate risk	Consider anticoagulation
Score ≥ 2 is moderate–high risk	Advise anticoagulation

Case 3

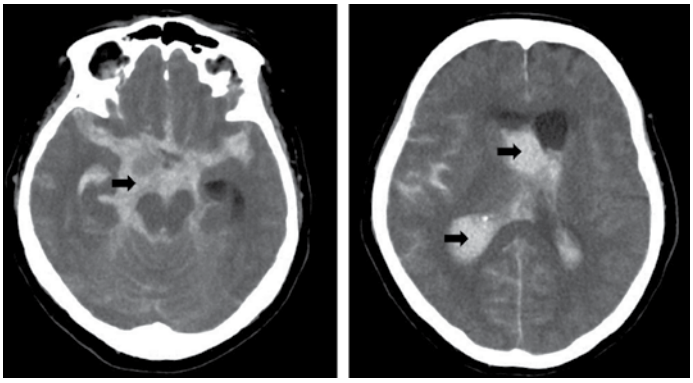

Figure 6. *Head of patient 3. The left-hand image shows a large amount of blood around the base of the brain (arrow). The right-hand image is several slices further up, showing blood within the lateral ventricles (arrow). This is a massive subarachnoid haemorrhage (SAH), with intraventricular haemorrhage.*

Epidemiology of SAH

The incidence of SAH is 6–9 per 100 000 per year and it accounts for 6% of first strokes. Approximately 85% of patients with non-traumatic SAH bleed from intracranial arterial aneurysms, with the remainder due to arteriovenous malformations (AVMs). The mean age at presentation is 50 years, and women have a higher risk than men. Traumatic brain injury is another more common cause of blood in the subarachnoid space.

The hallmark of an SAH in an alert patient is the complaint that this is 'the worst headache of my life', which is reported by approximately 80% of patients who can give a history. It is typically a 'thunder-clap' headache, describing a sudden onset, severe, 'pressure'-type headache starting in the occipital region. Other symptoms and signs include vomiting, confusion and decreased level of consciousness or seizures.

On examination patients may have normal neurology or have signs of meningism such as neck stiffness and photophobia. They may also have signs of increased intracranial pressure (ICP) or focal neurology such as third cranial nerve palsy (indicating a possible posterior communicating artery aneurysm).

Investigations include urgent CT of the head (Figure 6) to make the diagnosis and CT angiography to investigate the underlying cause (Figure 7). CT has a sensitivity of greater than 90% for SAH within the first 48 hours. If it is negative and there are no contraindications, then a lumbar puncture is performed looking for xanthochromia (degraded haem molecules). Importantly, lumbar puncture should not be done within 12 hours of symptom onset as it takes this length of time for the red blood cells to break down in the cerebrospinal fluid.

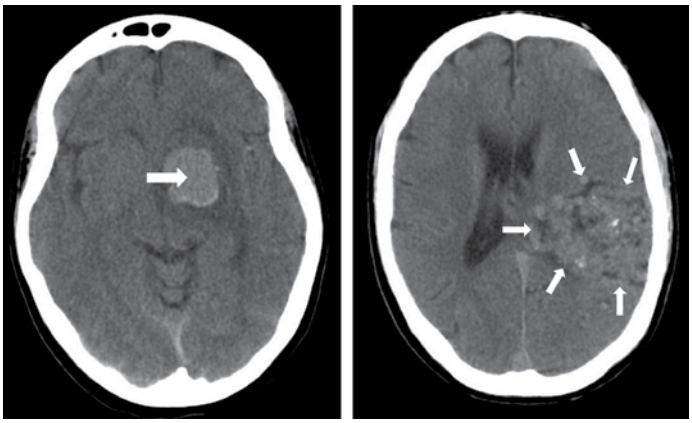

Figure 7. *(A) A large left cerebral artery aneurysm (arrow). (B) A giant left cerebral artery AVM (arrows).*

Grading of SAH

SAH is classified into five grades (Table 3).[3]

Patients with SAH grades I and II will initially require diagnosis and supportive therapy, including close monitoring of vital signs and neurological status, whilst seeking advice from a neurosurgical team.

SAH grade III, IV or V results in altered neurology and so necessitates more extensive initial therapy.

Management of confirmed subarachnoid haemorrhage

The initial management of SAH is aimed at patient stabilisation with a focus on maintaining cerebral perfusion and oxygenation.

Initial management

- In patients with a decreased level of consciousness or who are unable to maintain their own airway or show signs of raised ICP, elective intubation should be performed. This will help protect the patient from aspiration caused by reduced airway reflexes. Ideally, rapid sequence induction should be performed, avoiding hypotension and employing agents to blunt any increase in ICP.
- The patient should then be ventilated with the aim of achieving normocapnia.

Table 3. *Features of the five grades of SAH*

Grade	Clinical features
I	Mild headache with or without meningeal irritation
II	Severe headache and a non-focal examination, with or without mydriasis
III	Mild alteration in neurological examination, including mental status
IV	Obviously depressed level of consciousness or focal deficit
V	Patient either posturing or comatose

- IV access including central and arterial line, for invasive blood pressure monitoring, should be established.

Monitoring

- Intensive continuous observation is required until several days after occlusion of the aneurysm.
- Implement continuous ECG monitoring.
- Measure Glasgow Coma Scale (GCS) score, focal deficits, blood pressure and temperature at least every hour

Blood pressure

- Stop any of the patient's own anti-hypertensive medication.
- Treat hypotension with isotonic IV fluids aiming for euvolaemia and maintenance of sufficient mean arterial pressure to achieve cerebral perfusion pressure of > 70 mmHg. Aggressive treatment of hypotension is crucial in the management of SAH to maintain cerebral perfusion pressure.
- The use of vasopressors may be indicated to keep the systolic blood pressure > 120 mmHg, which would avoid the central nervous system damage as a result of the reactive vasospasm seen in SAH.
- Do not treat hypertension unless it is extreme; limits for extreme blood pressures should be set on an individual basis, taking into account age of the patient, pre-SAH blood pressures and cardiac history.
- Systolic blood pressure should be kept below 180 mmHg only until coiling or clipping of ruptured aneurysm, to reduce the risk of rebleeding.
- Start nimodipine 60 mg 4 hourly orally or 1 mg h^{-1} IV infusion to reduce vasospasm. Nimodipine substantially decreases the risk of cerebral infarction and poor outcome after SAH.
- Insert an indwelling urethral catheter and monitor fluid balance.

Seizures

- Treat seizures with benzodiazepines if required and load with phenytoin. Use only if required as the prophylactic use of anticonvulsants has been associated with a worse outcome.

Temperature

- Increased temperature should be treated both medically and physically. There is currently no evidence for therapeutic hypothermia in SAH patients.

Blood sugar management

- Routinely monitor serum blood glucose as one-third of SAH patients develop hyperglycaemia. A level over 10 mmol L^{-1} should be treated.

Pain/anxiety

- Treat pain and anxiety. Start with regular paracetamol and for severe pain use codeine or tramadol.

Intracranial pressure

- Avoid situations that will increase intracranial pressure.
- Keep the patient in bed with head elevated to 30°.

- Use laxatives and antiemetics as required.
  - If the patient is intubated, ensure that method of securing the endotracheal tube does not obstruct venous drainage (endotracheal tubes are normally taped rather than tied).
  - If possible, avoid positive end-expiratory pressure (PEEP) to minimise intrathoracic pressures.
  - Hypertonic solutions and mannitol will increase plasma osmolality and so decrease the water content of the brain tissue (the blood–brain barrier will act as a semipermeable membrane), thereby decreasing ICP.

Thromboprophylaxis

- Patients with SAH may be given thromboprophylaxis with pneumatic devices and/or compression stockings before occlusion of the aneurysm.
- If deep vein thrombosis prevention is indicated, low-molecular-weight heparin should be applied not earlier than 12 hours after surgical occlusion of the aneurysm and immediately after coiling.

Steroids

- There is no proof that steroids are effective in the management of SAH.

Definitive treatment

- This patient should be discussed with the tertiary neurosurgical referral centre regarding transfer for monitoring of ICP and/or insertion of external ventricular drain.
- Definitive management, in order to prevent re-bleeding, is by radiological coil insertion (Figure 8) or clipping of the underlying pathology at craniotomy.

Ongoing management

- The patient should be cared for in a high-dependency environment with ongoing monitoring for the common sequelae of SAH (see Figure 9). These include:
  - hydrocephalus
  - vasospasm
  - ischaemia
  - infarction
  - rebleeding.

Further reading

- van Gijn J, Rinkel GJ. Subarachnoid haemorrhage: diagnosis, causes and management. *Brain* 2001; **124**: 249–78.

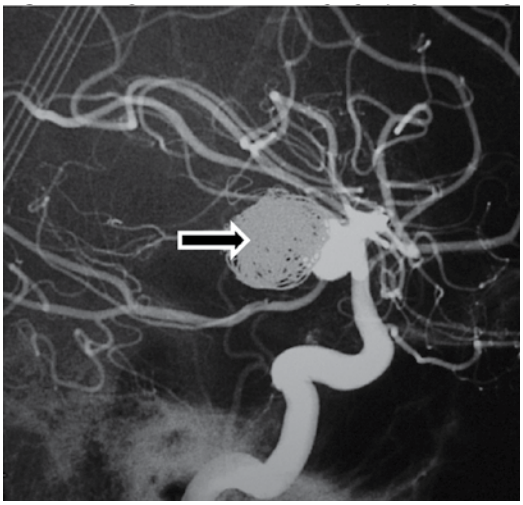

Figure 8. *Digital subtraction angiography of a large intracerebral AVM containing coils (arrow).*

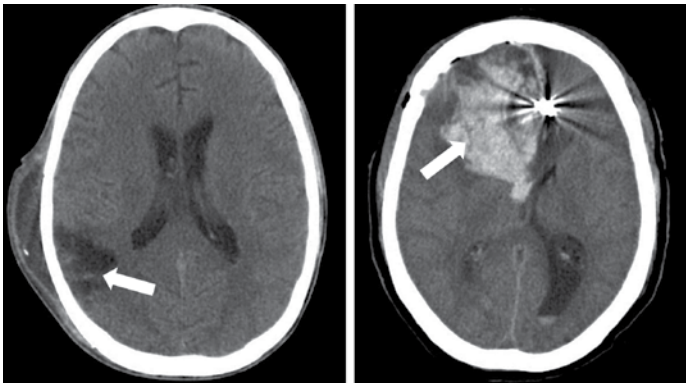

Figure 9. *Complications of clipping of aneurysms following SAH. (A) Right occipito-parietal infarction. (B) Bleeding after aneurysm clipping.*

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2. European Stroke Organisation. Guidelines for the management of intracranial aneurysms and subarachnoid haemorrhage. *Cerebrovasc Dis* 2013; **35**: 93–112.
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From the Journals

Matthew Everson and Adam Green

Correspondence: matthew.everson@nhs.net

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

Matthew Everson
Acute Care Common Stem Trainee in Anaesthesia

Adam Green
Core Anaesthetic Trainee
Royal Devon and Exeter NHS Foundation Trust
Barrack Road
Exeter EX2 5DW
UK

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.

Guide for contributors

MISSION OF UIA

Update in Anaesthesia (*UIA*) is an official journal of the World Federation of Societies of Anaesthesiologists (WFSA). *UIA*'s primary goal is to provide high-calibre, peer-reviewed, clinically relevant educational articles aimed at improving the quality and safety of anaesthesia care around the world.

UIA welcomes manuscripts focused on, and not limited to, anaesthesia that is relevant to resource-limited settings. *UIA* also serves to share knowledge from affiliated associations such as the World Health Organization (WHO) and surgical societies and educators that recognise safe anaesthesia as an essential part of safe surgery.

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Aim to include the full range of therapies available worldwide. Provide detailed descriptions of therapies available in resource-limited settings. When appropriate, discuss older medications, such as halothane and thiopentone, that may still be used around the world.

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As an official journal of the WFSA, *UIA* is the appropriate forum for publication of articles describing anaesthesia patient care, original research and audit conducted in, and specifically relevant to, low resource settings.

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- Review of Books or other Educational Materials (e.g. web app) (750 words maximum)
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This should include:

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Tables, figures, graphs and illustrations should be submitted as electronic versions of drawings (black on white) or as black and white or colour picture files in JPEG format. If computer or internet access is unavailable, print versions may be submitted. If facilities to produce drawings are unavailable, contact the Editor-in-Chief for assistance. All tables, figures, graphs and illustrations should be cited in the text and accompanied by a brief legend, which should be included along with the main text.

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Examples of the recommended format for references are noted below and can be found at https://www.nlm.nih.gov/bsd/uniform_requirements.html.

1. Reynolds F, O 'Sullivan G. Lumbar puncture and headache. 'Atraumatic needle' is a better term than 'blunt needle'. *Br Med J* 1998; **316**: 1018.
2. Costigan SN, Sprigge JS. Dural puncture: the patients' perspective. A patient survey of cases at a DGH maternity unit 1983–1993. *Acta Anaesthesiol Scand* 1996; **40**: 710–14.
3. Spriggs DA, Burn DJ, French J, Cartlidge NE, Bates D. Is bedrest useful after diagnostic lumbar puncture? *Postgrad Med J* 1992; **68**: 581–3.

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Alan Jay Schwartz, MD MSEd
Editor-in-Chief, Update in Anaesthesia
Director of Education
Department of Anesthesiology and Critical Care Medicine
The Children's Hospital of Philadelphia
34th St & Civic Center Blvd
Room 9327
Philadelphia, PA 19104-4399
Professor of Clinical Anesthesiology and Critical Care
Perelman School of Medicine
University of Pennsylvania

215-590-1885 Office
215-590-1415 Fax
schwartza@email.chop.edu

Update in
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Update contacts

Russian Edition
Vsevolod V. Kuzkov
Northern State Medical University,
Anaesthesiology Department,
Troitsky Prospekt 51
163000 Arkhangelsk
Russian Federation
Email: v_kuzkov@mail.ru
Website: http://nsmu.ru/nauka_sgmu/Update_in_Anaesthesia/

Mandarin Edition
Jing Zhao
Department of Anaesthesia
Peking Union Medical College Hospital
No 1 Shuai Fu Yuan
Beijing 100730
Peoples Republic of China
Email: zhaojing@hotmail.com

Spanish Edition
Gustavo Adolfo Elena
Pellegrini 947
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Argentina
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