Anaesthetic management for craniosynostosis repair in children

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Key points

- Craniosynostosis occurs isolated in 80% of patients.
- Syndromic craniosynostosis is often combined with midface hypoplasia, skull base, and limb abnormalities.
- Treatment is predominantly surgical and depends on the age of the child, associated complications, and the type of craniosynostosis present.
- Specific risks related to surgery include major blood loss and venous air embolism.
- Newer surgical techniques are emerging which adopt a minimally invasive approach with the intended benefits of reducing morbidity, hospital length of stay, and costs. These techniques remain controversial and are as yet not widely practiced.

Craniosynostosis is a condition in which premature fusion of one or more of the cranial sutures occurs, leading to abnormal skull development and head shape. The infant skull is made up of a series of bony plates separated by sutures that allow distortion of the head shape during birth and permit growth and development of the infant brain into adulthood. Abnormal premature fusion of one or several of these sutures results in restricted growth of the skull perpendicular to the affected suture. Compensatory bone growth occurs parallel to the affected suture in order to allow for continued brain growth and results in distinct clinical skull characteristics (Fig. 1).

Children may present with a broad range of conditions requiring correction, from otherwise well children with single suture craniosynostosis (80% of cases) to syndromic children with multiple synostoses with other cranial and extracranial anomalies. The overall incidence of craniosynostosis is about one in 2500 live births.

Correction may require extensive surgery that is commonly performed at a young age, and although the incidence of adverse events is low, potential risks and complications exist. Uncorrected craniosynostosis may result in complications that include:

- Raised intracranial pressure (ICP)—this is more common in syndromic craniosynostosis and particularly when multiple sutures are affected. Factors causing this include hydrocephalus, craniocerebral disproportion, airway obstruction, or abnormalities in the venous drainage from the brain.¹
- Cognitive and neurodevelopmental impairment—including global developmental delay, problems with speech and hearing, and poor feeding may occur.
- Psychological implications of poor self-esteem and isolation due to an abnormal appearance.

Syndromes associated with craniosynostosis

Syntheses most frequently associated with craniosynostosis include Apert, Crouzon, Pfeiffer, Saethre–Chotzen, Carpenter, and Muenke syndromes (Table 1). Most show autosomal-dominant inheritance, although they are often sporadic and may involve mutations in genes encoding for fibroblast growth-factor receptors (FGFR), leading to defective intracellular signalling, and in TWIST genes.¹ Syndromes often include midface hypoplasia, skull base, and limb abnormalities that may lead to associated problems such as raised ICP, airway obstruction, feeding difficulties, behavioural, and psychological issues (Table 1).
Surgical options

The treatment of craniosynostosis is predominantly surgical and requires a coordinated and integrated approach between a large multi-disciplinary team, including, but not limited to, combined plastics and neurosurgical teams, anaesthesia, and specialist nursing. Surgical correction is not solely cosmetic; corrective procedures are performed early in life to allow normal brain growth and cognitive development. It is important to remember that every patient is different in terms of the cosmetic appearance and functional problems faced and treatment is therefore highly individualized. For this reason, a range of procedures and techniques exist (Table 2), varying between centres across the world particularly between the UK and North America.

The timing of surgical intervention is controversial. Indications for emergency surgery include an immediate threat to the airway or eyes, or the presence of raised ICP. Advantages of early surgical intervention include increased malleability of the softer younger bone and the ongoing brain growth encouraging continued growth of the cranial vault. This comes at the cost of performing complex surgery and anaesthesia in a younger child, increased complications associated with blood loss, and the increased likelihood of the need for re-do surgery at a later date. In older children, the re-operation risk is lower and surgery and anaesthesia are potentially safer; however, surgery can be more challenging due to increasing severity of deformities and thicker, less malleable bone. There may also be reduced ability of the skull to ossify small defects necessitating the use of bone grafts. Surgery is often performed around 8–12 months of age to balance these challenges.

Surgery is often specific to the particular synostosis involved, but some general principles apply for all of the surgeries; these are to prevent progression and correct the abnormality and to reduce the risks of raised ICP that may occur without surgery. Three-dimensional CT scanning provides useful anatomical information and can clearly demonstrate the abnormally fused suture(s) and allowing surgeons to plan. There is a trend away from the more traditional invasive open surgery towards less invasive endoscopic techniques with the potential advantages of reduced morbidity and length of stay balanced against surgical outcomes and risk of re-operation rate in the less invasive surgeries.

Invasive surgery

Correction of sagittal synostosis

Surgery performed before 6 months of age

In craniosynostosis diagnosed before 6 months of age, the best cosmetic and functional results are often obtained if the surgery is performed early in the child’s life for the reasons previously discussed. This type of corrective surgery is performed at around 4–6 months of age with an extended strip craniectomy and, in some institutions, subsequent helmet moulding therapy which relies on early rapid brain growth to drive remodelling. This surgery comprises excision of the fused suture, usually sagittal, and expansion of the adjacent bone using cuts to allow brain growth. Surgical time is usually around 1–3 h and, when used, a helmet may be fitted around 7–10 days later to ensure a more symmetric skull shape and to protect from any undue pressure. This is worn for 23 h a day for usually around 4–6 months. Although early surgery may be beneficial for many reasons, it comes at the compromise of increased inherent risks of anaesthesia and surgery in a younger infant and concerns regarding restenosis rate and poorer resolution of the cephalic index compared with other more invasive surgical techniques.
<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Gene mutation and inheritance</th>
<th>Synostosis</th>
<th>Facial features</th>
<th>Extracranial features</th>
<th>Anaesthetic considerations</th>
</tr>
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<tbody>
<tr>
<td>Apert</td>
<td>FGFR-2 AD</td>
<td>Bicoronal</td>
<td>Maxillary hypoplasia</td>
<td>Complex syndactyly</td>
<td>Potentially difficult facemask ventilation and airway management</td>
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<td></td>
<td></td>
<td>Brachycephaly</td>
<td>Low set ears, cleft palate, exorbitism, hypertelorism, strabismus, hearing loss</td>
<td>Developmental delay</td>
<td></td>
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<tr>
<td>Crouzon</td>
<td>FGFR-2 AD (FGFR-3)</td>
<td>Bicoronal</td>
<td>Midface hypoplasia (less severe than Aperts, cleft palate rare) Tall flattened forehead, proptosis</td>
<td>Cervical spine abnormalities (present in 1/3rd) Normal hands and feet Normal development</td>
<td></td>
</tr>
<tr>
<td>Pfeiffer</td>
<td>FGFR-1 and 2 AD</td>
<td>Ranges—bicoronal to fusion of all sutures (cloverleaf skull) Midface hypoplasia (varying degrees)</td>
<td>Broad thumbs, wide great toes, partial syndactyly Radiohumeral synostosis of elbow, hydrocephalus, imperforate anus may occur</td>
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<tr>
<td>Muenke</td>
<td>FGFR-3 AD</td>
<td>Uni- or bicoronal</td>
<td>Midface hypoplasia—usually mild Wide set eyes Low set ears</td>
<td>Broad toes, brachydactyly Potential developmental delay</td>
<td></td>
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<tr>
<td>Carpenter</td>
<td>RAB23 AR (RAS-associated protein)</td>
<td>Coronal, sagittal, and lamboidal with brachycephaly</td>
<td>Midface hypoplasia Low set ears, high arched palate, shallow orbital ridges, flat nasal bridge</td>
<td>Limb defects—preaxial polydactyly Up to 50% have cardiac defects (ASD, VSD, PDA, PS, TToF, TGA) Hypogonadism, omphalocoele Developmental delay</td>
<td></td>
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<tr>
<td>Saethre–Chotzen</td>
<td>TWIST/FGFR-2 AD</td>
<td>Coronal, lamboidal metopic (mild)</td>
<td>Towering forehead, low set hairline, facial asymmetry with septal deviation Ptosis upper eyelid</td>
<td>Cutaneous syndactyly Normal Intelligence</td>
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</table>

OSA: Obstructive sleep apnoea

Table 1 Characteristics of syndromes associated with craniosynostosis. AD, autosomal dominant; AR, autosomal recessive.
It is commonly performed on children who have reached puberty. Later diagnosis requires more extensive surgical correction called a total cranial vault reshaping. This is a more invasive procedure and not only aims to repair the fused suture but also directly addresses the compensatory calvarial anomalies that have occurred. It involves removal and reconstruction of the bones with plates and screws and usually lasts around 4–6 h. Owing to the more invasive nature of the procedure and risks involved, it is usually performed later in life usually around 10–12 months of age, or in some centres, at around 15–18 months of age.

**Frontal advancement and posterior expansion**

Frontal advancement procedures are used to remodel abnormal frontal bone and advance the supraorbital rims, particularly in metopic and coronal synostosis. It is most commonly performed around age 12 months and involves a frontal craniotomy to release the involved sutures and elevate the forehead to provide eye protection and improved brain growth. It may be performed as a first-stage procedure when eye protection is needed, or later after another procedure such as a posterior vault expansion. Posterior cranial vault procedures aim to expand the posterior aspect of the skull and may be used in severe cases of turricephaly due to bicornal and lamboidal synostosis. It is commonly performed around age 6 months.

**Midface hypoplasia**

Midface hypoplasia is found in many forms of syndromic craniosynostosis and may be addressed at the time of cranial vault surgery or at a later time by Le Fort III advancement. The Le Fort III advancement involves repositioning the midface in the forward position and is typically performed as a single-stage procedure at around 4–8 yr, or later around 9–12 yr if the abnormality is less severe.

**Monobloc frontofacial advancement**

In some patients, it may be possible to advance the forehead and midface in one procedure rather than the above combination of fronto-orbital and subsequent Le Fort III advancements. This is usually performed at age 4–12 yr and involves a frontal craniotomy followed by osteotomies of the orbits and midface.

**Facial bipartition and box osteotomies for hypertelorism**

Facial bipartition is a technically challenging procedure. It involves the mobilization and advancement of the bony orbits, the midface, together with splitting of the midfacial segment. After this, the central nasal and ethmoid bones are removed, and the two facial partitions rotated towards each other to correct the hypertelorism. Box osteotomies involve the medial rotation of one or both orbits to correct the hypertelorism, requiring a 360° incision around the base of each orbit to release them. Box osteotomies are typically performed on children who have reached puberty.

**Minimally invasive surgery for craniosynostosis**

**Spring-assisted cranioplasty**

Spring-assisted cranioplasty is a newer minimally invasive technique in craniosynostosis surgery. It involves a sagittal strip craniectomy with placement of two springs across the defect to gradually separate the narrowing. These are then subsequently removed at a second procedure usually around 6 months or even earlier once the desired result has been achieved. Early data suggest that the clinical outcomes do not differ between different surgical techniques; however, the outcomes regarding operation time, blood loss, intensive care unit (ICU) stay, and hospital stay are in favour of the spring-assisted surgery. The quality of evidence is low, and therefore, it is not currently a widely accepted technique.

**Endoscopic suture release with helmet moulding**

Endoscopic suture release with subsequent postoperative helmet moulding is emerging as another minimally invasive alternative.
in some centres. The procedure depends on brain growth for re-modelling of the bones and uses a helmet after operation to direct this growth. Surgery is performed in the supine or modified prone position and burr holes are used to pass a rigid endoscope for visualization. When compared with more extensive surgical techniques, it promises a shorter surgical time, reduced blood loss, associated transfusions, and reduced hospital stay and costs. The ideal age for this procedure is typically <3 months, but children aged 3–6 months are good candidates. This technique may lead to a change in perioperative practice as blood transfusion is unusual; incidence of venous air embolism (VAE) is reduced compared with open surgery.

**Anaesthetic management**

**Preoperative concerns**

A thorough preoperative assessment tailored to the individual child and the proposed surgical procedure is essential. Preoperative airway assessment and cardiac evaluation are important to identify the need for specific interventions, particularly when associated with syndromes such as Aperts or Crouzons. It is important to consider the presence of intracranial hypertension and to adjust the anaesthetic technique, particularly induction, accordingly. Obstructive sleep apnoea and respiratory complications occur more frequently in these children requiring the review of sleep studies and consultation with ear, nose, and throat surgeons. In cases of severe respiratory obstruction, where extensive facial osteotomies are planned or the airway is found to be extremely challenging, a covering tracheostomy may be considered. This should be considered as part of a preoperative multi-disciplinary team discussion.

Baseline haematological, biochemical, and coagulation studies should be performed and blood products ordered. Patients who are anaemic should be considered for preoperative optimization, with iron therapy or recombinant human erythropoietin. Parents should be appropriately counselled as to the specific anaesthetic and surgical risks involved with the procedure, particularly regarding blood transfusion and the risk of VAE.

**Intraoperative concerns**

Premedication is often not necessary but when used; concerns for possible effects on raised ICP should be taken into account.

Induction of anaesthesia may be inhalational or i.v. depending on the anaesthetist’s, patients, and parents’ preference with the considerations of potential airway compromise and difficult venous access in this age group, particularly in syndromic children. Midface hypoplasia can cause difficulties with mask ventilation and appropriate airway adjuncts should be considered in advance.

The type of tracheal tube used and the route of intubation may vary between the procedure type and individual centres, anaesthetists, or surgeons; nasal intubation is often preferred in our institution due to the added stability it offers in different positions. Tube position should be checked with the head flexed and extended to avoid accidental extubation or endobronchial intubation during position changes. In our institution, the preference is for the surgeons to suture the tracheal tube to the nasal septum to prevent dislodgement. During surgery, access to the tracheal tube will be limited; therefore, it is imperative to cross-check all airway and tube connections before draping the patient and surgery commencing.

Monitoring includes standard monitors with the addition of invasive arterial pressure monitoring due to the need for repeated blood samples and rapid haemodynamic changes secondary to rapid blood loss. Two large-bore peripheral i.v. cannulae should be placed. With the advent of minimally invasive surgery, some now prefer not to place arterial access. In our institution, it is not current practice to routinely use central venous access in these cases, except if large-bore peripheral access is unobtainable, the risk of VAE is high or in patients undergoing complex major surgery. This may differ in other centres where central venous access may be considered mandatory. Temperature monitoring should be used throughout the case and methods of active warming should be used, such as forced-air warming blankets and fluid warmers from the start of the case.

Positioning must be done in conjunction with the surgeons and may be supine, prone, or a modified prone position with the head extended. Care should be taken to ensure pressure areas are protected and particular attention should be paid to the eyes to avoid direct pressure or corneal abrasion. It is important to consider the position of the surgical field relative to the heart as this may increase the risk for VAE. A compromise between this risk and reducing venous bleeding in the head-up position must be discussed as a team. Care to avoid hyperextension of the neck must be taken and attention paid to the potential for jugular venous obstruction.

Maintenance of anaesthesia with a balanced technique involving inhalational agent in an air/oxygen mix with opioid allows for manipulation of depth of anaesthesia during various different stages in the procedure. Remifentanil infusions are often used in our institution to allow titration of the arterial pressure. A total i.v. technique using propofol may be also be used in older children.

Attention should be paid to the management of raised ICP with consideration of cerebral perfusion pressure, particularly until craniectomy is performed with avoidance of factors known to increase ICP such as hypercapnia, hypoxia, and raised venous pressures.

**Intraoperative mishaps and management**

**Haemorrhage and massive blood transfusion**

Blood loss may be slow and insidious or sudden and acute. It is important that the anaesthetist is aware of the timings in surgery where blood loss is more likely and that communication is maintained between the surgical and anaesthesia teams.

Massive blood transfusion can be required in craniosynostosis surgery. Studies have shown that the average transfusion is in the region of 50 ml kg\(^{-1}\) although may be in excess of 100 ml kg\(^{-1}\). Factors that increase the likelihood of large-volume blood loss include:

- Younger age and lower weight—along with a disproportionately larger head size meaning larger surface area for blood loss and increased circulating blood volume directed to the head
- Prolonged surgery—particularly occurring in syndromic craniosynostosis where surgery may be more complex

Complications associated with massive transfusion such as hypothermia, dilutional coagulopathy, and metabolic and electrolyte disturbances (hypocalcaemia, hyperkalaemia) should be considered and managed appropriately. Consideration of the use of coagulation factors with large-volume transfusion may reduce the volume of blood needed both intraoperatively and after operation.

**Blood conservation strategies**

Preoperative optimization of haemoglobin using iron or erythropoietin remain a vital part of blood conservation. Intraoperative
blood loss management is one of the most challenging aspects of craniosynostosis surgery and estimation of blood loss can be difficult due to losses occurring into the surgical drapes and surrounding area. Elevation of the vascular perosteum is a significant source of bleeding; the dural sinuses are often the source of sudden and rapid blood loss requiring immediate resuscitation with fluids or blood products. Both insidious and rapid blood loss and electrolyte changes may occur necessitating regular point-of-care testing for haematocrit, electrolytes, and acid–base balance and allogeneic blood transfusion; blood loss may be >100% of the circulating volume.

For all but the most minor cases, blood products should be in the room and checked before surgery starts. Blood conservation strategies have been used in an attempt to reduce the amount of donor blood transfusion required (Table 3). 3–7

Preoperative autologous blood donation involves the patient donating blood in the weeks before surgery, allowing time for self-correction of the subsequent anaemia and then re-transfusing the patient’s own blood. This is sometimes combined with recombinant human erythropoietin to encourage production of red blood cells. This method does not always remove the need for allogeneic blood and still carries risks surrounding handling and storage and transfusion side-effects and requires careful coordination to prevent wastage of the blood if not used within its expiry date. Similarly, acute normovolaemic haemodilution involves collecting the patients’ own blood at the start of surgery and replacing it with crystalloid to create normovolaemia with a lower haematocrit with a view to replacing the blood once blood loss occurs. These strategies are generally not useful in this paediatric population due to a small circulating blood volume and difficulty collecting blood before operation without sedation.

Similarly, intraoperative and postoperative cell salvage can be used to collect either intraoperative blood loss from the surgical field or from postoperative losses from the surgical drains. Again, these techniques are more limited in infants and small children due to the slow processing times, high priming volumes, and limited ability to concentrate the washed shed blood, 8 but can be useful techniques to consider particularly in complex major surgery.

The use of antifibrinolytic agents, such as tranexamic acid, has been shown in some studies to reduce blood loss and the need for transfusion in children having craniosynostosis surgery. 8–12 Tranexamic acid acts to competitively block formation of plasmin from plasminogen and inhibits the proteolytic action of plasmin on fibrin clot and platelet receptors inhibiting fibrinolysis at the surgical site. The dose of tranexamic acid varies between different surgical types and populations and varies from 10 to 100 mg kg$^{-1}$ loading dose followed by an infusion of 5–10 mg kg$^{-1}$ h$^{-1}$ for the duration of the surgery.

Fibrin can be used at the site of surgery to encourage haemostasis and reduce blood loss. It is a naturally occurring substance and has been shown to reduce the need for allogeneic blood transfusions both intraoperatively and after operation.

Induced hypotension is not a widely accepted technique for blood conservation due to the increased risk of VAE with low venous pressures and the potential haemodynamic instability associated with rapid blood loss.

Current evidence related to the above strategies is limited and further trials are needed to fully assess their safety and efficacy in this population.

In our institution, preoperative optimization of nutrition and iron levels, meticulous surgical technique, positioning, arterial pressure control, and tranexamic acid are routinely used to minimize blood loss and allogeneic transfusions.

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<tr>
<th>Table 3 Blood conservation strategies in craniosynostosis</th>
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<tr>
<td>Blood conservation strategies</td>
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<tr>
<td>• Preoperative autologous blood donation</td>
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<tr>
<td>• Acute normovolemic haemodilution</td>
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<tr>
<td>• Intraoperative cell salvage</td>
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<tr>
<td>• Postoperative cell salvage</td>
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<tr>
<td>• Perioperative recombinant erythropoetin</td>
</tr>
<tr>
<td>• Antifibrinolytic drugs (tranexamic acid)</td>
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<td>• Fibrin sealants or fibrin glue</td>
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<table>
<thead>
<tr>
<th>Table 4 Intraoperative VAE</th>
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<tr>
<td>Symptoms</td>
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<tr>
<td>• Bronchoconstriction/wheezeing</td>
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<td>• Hypotension/circulatory collapse</td>
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<tr>
<td>• Hypoxaemia (V/Q mismatch)</td>
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<tr>
<td>• Dyshyrtthymias</td>
</tr>
<tr>
<td>• Myocardial ischaemia</td>
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<tr>
<td>Signs</td>
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<tr>
<td>• Abrupt decrease/loss end-tidal CO$_2$</td>
</tr>
<tr>
<td>• Turbulent flow detected on transoesophageal echo or Doppler ultrasound</td>
</tr>
<tr>
<td>Management</td>
</tr>
<tr>
<td>• Notify surgeon, call for help</td>
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<tr>
<td>• 100% oxygen</td>
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<tr>
<td>• Discontinue nitrous oxide/volatile</td>
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<tr>
<td>• Flood surgical wound with saline</td>
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<tr>
<td>• Position head below the heart</td>
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<tr>
<td>• Perform valsava with manual ventilation</td>
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<tr>
<td>• Chest compressions (even if not in cardiac arrest, these may help break up bubbles)</td>
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<tr>
<td>• Treat cardiovascular compromise with usual inotropes, e.g. epinephrine</td>
</tr>
<tr>
<td>• Standard PALS protocol if in cardiac arrest</td>
</tr>
<tr>
<td>• Call for emergent transoesophageal echocardiography to confirm diagnosis</td>
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Venous air embolism

VAE is a complication seen in craniosynostosis repair and is most likely to occur when the head is positioned above the heart and the bony venous sinuses or dural sinuses are exposed. The incidence of VAE during craniosynostosis surgery has been reported as high as 83%, 8 most without haemodynamic compromise and only about 1–2% being clinically significant. Routine precordial Doppler has been recommended to increase the chance of early diagnosis; however, most centres use capnography for detection. Rapid cardiovascular collapse can occur and treatment is predominantly supportive (Table 4). A central venous line (CVL) can be used to aspirate large volumes of air from the right ventricle; however, placement can be difficult in an emergency setting. It is recommended that a CVL is placed at induction of patients with high risk for VAE, particularly related to surgical position and technique, presence of intracardiac shunts, and volume deplete patients. A discussion should take place as to whether surgery should proceed after the event.

Postoperative concerns

Most patients are extubated at the completion of surgery. Factors that may delay extubation include a prolonged procedure, marked fluid shifts, large-volume transfusions, and effects of prolonged prone positioning and patient factors such as
preoperative obstructive sleep apnoea or airway concerns. Most patients will be cared for on the ICU or high dependency units and observed for haemodynamic and volume status changes with close monitoring of haematological and coagulation profiles. Analgesia is predominantly with i.v. opiate infusions with progression to oral regimens within 24–48 h for more complex surgery with oral regimens commenced immediately after operation for less complex surgery. The use of NSAIDs in craniosynostosis surgery remains controversial.

Careful attention should be paid to postoperative electrolyte disturbances, particularly hyponatraemia. This may be related partly to the use of crystalloid infusions intraoperatively and also to anti-diuretic hormone release (SIADH) as a result of the surgical insult. A retrospective record review of patients developing hyponatraemia post-craniosynostosis surgery suggested that patients at increased risk of this complication included those with preoperative raised ICP, increased volume blood transfusion, and female sex (regardless of ICP). The use of hyponatraemic fluids intraoperatively further increases the risk.

Summary
Craniosynostosis is a condition in which premature fusion of the bony plates of the skull leads to abnormal head shape and the potential for complications such as raised ICP. The main method of treatment is surgical and has anaesthetic concerns associated with surgery in young children with the specific risks related to blood loss and VAE. Newer techniques are emerging that may help to mitigate these risks and may change the way we manage these patients both in the operating theatre and in the immediate postoperative period. These techniques remain controversial and are as yet not widely practiced.

Declaration of interest
None declared.

MCQs
The associated MCQs (to support CME/CPD activity) can be accessed at https://access.oxfordjournals.org by subscribers to BJA Education.

References