

The prematurely born infant and anaesthesia

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One in 13 babies in the UK (50 000 per annum) is born prematurely.¹ Although advances in neonatal intensive care have improved survival, mortality is still 42 per 1000 live births compared with 1.8 per 1000 in term babies.¹ However, survivors can have a host of complications related to the underdeveloped organ systems and may present for a variety of surgical procedures (Table 1). They present enormous challenges during anaesthesia, surgery, and postoperative care.

A live infant delivered before 37 weeks from the first day of the last menstrual period is defined as premature. The degree of prematurity is further categorized by the gestational age (GA) or birth weight (Table 2).

Physiological considerations

GA determines the extent of physiological immaturity. Application of knowledge of developmental physiology is vital to improving the outcome of anaesthesia and surgery.

Respiratory system

Alveoli form at 17–28 weeks and pulmonary capillaries at 28–36 weeks GA. Post-natally, alveoli number 20 million at birth and 300 million at 8 months. Before 32–34 weeks, surfactant production is inadequate, predisposing to respiratory distress syndrome. Preterm infants exposed to mechanical ventilation and more than 28 days of oxygen supplementation are likely to develop bronchopulmonary dysplasia (BPD). This is classified as mild, moderate, or severe according to the degree of ventilatory support and oxygen they require.² Symptoms of BPD such as increased oxygen requirements, reduced lung compliance, and reversible airway obstruction may persist for many months or even years.

Control of respiration and apnoea

Chemoreceptor responses are blunted in preterm babies. The normal biphasic response

to hypoxaemia (hyperventilation followed by hypoventilation or apnoea) is replaced by apnoea only.

The incidence of apnoea varies from 25% in the low birth weight (LBW) premature to 84% in the extremely LBW (ELBW) group³ (Table 2). Central apnoeas are attributed to diminished hypercapnic response, hypoxic ventilatory depression, and active inhibitory reflexes. Obstructive apnoea follows opposition of hypopharyngeal soft tissues or nasal occlusion. Mixed apnoeas (obstruction followed by central pauses) are the most frequent. Apnoea is pathological when >20 s alone, or <20 s with bradycardia (30 beats min⁻¹ decline from resting heart rate), or with cyanosis, pallor, or hypotonia.³

The preterm diaphragm contains only 10% of type I fibres compared with 25% at term, contributing to apnoeas at times of physiological stress.⁴ Hypoglycaemia, hypoxia, anaemia, hypothermia, and sepsis also contribute. After operation, apnoeas are frequent in the first 12 h and can continue until 48–72 h.

Cardiovascular system

The change from fetal to neonatal circulation results normally in closure of the foramen ovale and the ductus arteriosus. In prematurity, the ductus arteriosus often remains patent (PDA). This and other atrial or ventricular septal defects can cause significant left-to-right shunting, progressively increased pulmonary flow, and congestive cardiac failure.

Hypoxia is a potent pulmonary vasoconstrictor. Raised pulmonary vascular resistance (PVR) in response to hypoxia or excessive airway pressures can lead to right-to-left shunting, exacerbating hypoxia, and acidosis. Prolonged raised PVR may lead to poor right ventricular function, impaired cardiac output, limited oxygen delivery, pulmonary oedema, and sudden death.

Key points

During anaesthesia in the premature infant, provision of a thermoneutral ambient temperature is essential to prevent excessive heat loss.

High airway pressures and pulmonary hypertension can lead to reversion to the fetal circulation with right-to-left shunting.

Apnoea tolerance is greatly reduced in small infants and the use of classical rapid sequence induction has been questioned.

Acetaminophen and regional anaesthetic techniques must be utilized fully to reduce opioid usage.

Newer volatile agents with caudal analgesia can be used successfully for inguinal herniotomy in ex-premature babies.

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Table 1 Surgical conditions requiring anaesthesia in the premature baby

PDA ligation (20–30% incidence in moderately premature neonates)
Laparotomy for NEC or spontaneous bowel perforation
Laparotomy for re-anastomosis of bowel or relief of adhesions
Inguinal hernia repair (2% incidence in females and 7–30% incidence in males with 60% risk of incarceration)
Fundoplication for unresolving and symptomatic oesophageal reflux
Vascular access under X-ray control
Vitrectomy or laser surgery for retinopathy of prematurity
CSF drainage or ventriculoperitoneal shunt insertion for obstructive hydrocephalus after intraventricular haemorrhage
CT and MRI scanning to evaluate cerebral damage

Table 2 Categorization of prematurity by GA and birth weight

Gestational age	Birth weight		
36–37 weeks	Borderline/near term	<2500 g	LBW
31–36 weeks	Moderately premature	<1500 g	VLBW
24–30 weeks	Severely premature	<1000 g	ELBW

Haematology

A term baby has 18–20 g dl⁻¹ of haemoglobin (Hb); in prematurity, this can be 13–15 g dl⁻¹, 70–80% of which is HbF. Fetal Hb has a reduced ability to release oxygen; however, at term, the relatively high blood volume, Hb concentration, and cardiac output compensate. This compensation is much less in the preterm baby. A target haematocrit of 40–45% facilitates oxygen delivery; this may necessitate earlier perioperative blood transfusion.

Renal function

Functional capacity is related to GA. The limited capacity of renal tubules to reabsorb bicarbonate accounts for the ‘normal’ acidosis seen in newborns. The ability to retain sodium effectively does not develop until 32 weeks. The distal tubular response to aldosterone is low until 34 weeks and antidiuretic hormone levels in the premature neonate are high.⁴ These factors predispose to hyponatraemia.

Total body water in the preterm infant is 75–85% of body weight and is inversely related to the GA. The marked trans-epidermal permeability and a relatively large body surface area accelerate water loss. Evaporative water loss is increased 15-fold during the first few days of life compared with term babies.⁴

Temperature regulation

The high surface area to body weight ratio, decreased brown fat stores, and the non-keratinized skin render the preterm neonate extremely susceptible to heat loss. A thermoneutral environment for an unclothed preterm baby is 34°C. At this temperature, oxygen demand is minimal, and temperature regulation is achieved via non-evaporative physical processes alone. Hypothermia-induced stress can lead to hypoglycaemia, apnoea, and metabolic acidosis.

Glucose homeostasis

Preterm babies have fewer glycogen stores and underdeveloped gluconeogenesis pathways. Routine glucose monitoring is important. Hypoglycaemia is treated when blood glucose is <2.5 mmol litre⁻¹ with a 2 ml kg⁻¹ bolus of dextrose 10% followed by an infusion of dextrose at 4–6 mg kg⁻¹ min⁻¹. Hyperglycaemia should be avoided as a hyperosmolar state can lead to intraventricular haemorrhage (IVH), osmotic diuresis, and dehydration.

Gastrointestinal system

Necrotizing enterocolitis (NEC) with bowel wall necrosis and possible perforation can lead to systemic sepsis. Bowel perforation without NEC may be associated with administration of indomethacin and corticosteroids. Gastro-oesophageal reflux is common, resulting from an underdeveloped and incompetent lower oesophageal sphincter leading to laryngospasm, laryngitis, tracheitis, apnoea, chronic cough, otitis media, and asthma. Post-premature infants may present for fundoplication after exhaustive medical management.

Nervous system

Cutaneous nociceptors are complete at about 20 weeks GA. By 26 weeks, even very LBW (VLBW) infants show a measurable flexion withdrawal reflex to noxious stimulation suggesting that the spinal cord neural connections are present.⁵ Moreover, descending inhibitory pathways are immature leading to greater pain sensitivity. The incidence and severity of IVH is inversely related to GA. Disturbed vascular autoregulation from hypoxia, pneumothorax, or rapid fluid shifts can result in IVH. Retinopathy of prematurity affects the partially vascularized retina. Changes in oxygen exposure have been postulated to cause disruption of the natural course of retinal vascularization.

Pre-anaesthetic assessment

Preoperative assessment should include parental consultation with a realistic description of a likely deterioration in pulmonary function necessitating postoperative ventilatory support.

Respiratory factors including $F_{I_{O_2}}$, the need for respiratory support, ventilator parameters, and baseline arterial gas values must be noted. The $P_{a_{O_2}}$ often lies on the steep part of the oxyHb dissociation curve, and short periods of apnoea can lead to marked desaturation. If spontaneously breathing, the extent of any respiratory distress can be assessed by intercostal retraction, ventilatory frequency, and upper airway appearance. The anatomy of the head, neck, and the upper airway may provide crucial warnings about likely difficult intubation. Nursing observations can inform of apnoeic episodes and possible triggers. Apnoea could indicate the presence of underlying metabolic derangements. If intubated, the size and length of the tracheal tube (TT) should be noted. Chest auscultation is performed to check for tube placement and for

added or reduced breath sounds. A recent chest X-ray may be useful.

All premature babies will have an echocardiogram performed before surgery. Clinical signs of congestive cardiac failure include delayed capillary refill and hepatomegaly. Rates of inotrope infusions and their concentrations should be noted.

Hb, haematocrit, platelets, and the coagulation profile should be within acceptable limits before surgery. All babies should receive vitamin K before operation. Cross-matched blood must be available for transfusion where blood loss exceeds 10% of blood volume (i.e. 9 ml for a 1000 g baby). Preoperative serum electrolyte and glucose levels and hourly i.v. replacements will help guide requirements in theatre. Periods of starvation must be taken into account to calculate fluid deficits that need replacement intraoperatively. Some babies may be receiving total parenteral nutrition to provide their maintenance fluid, glucose, and electrolyte requirements.

Premedication is not required. However, atropine (10–20 $\mu\text{g kg}^{-1}$) should be considered to pre-empt transient bradycardia, although these are less frequent during anaesthesia with newer inhalation agents.

Intraoperative management

Operating theatre and equipment

Heat loss is a major potential stress in prematurity. The ambient temperature of the theatre must be raised to a minimum of 27°C for reception of the baby. Once the waterproof surgical drape is applied to non-involved areas and surgical preparation is complete, the ambient temperature is less relevant. However, there must be an effective warming device on the operating table, such as a warming mattress and a warm air blanket device. Inspired gases should be heated and humidified with a paediatric heat-moisture exchanger. I.V. fluids, blood, and blood products should be warmed. Irrigation fluid must be warmed. In the smallest of neonates and especially when 360° access to the patient is required by the surgeon (e.g. laser surgery for retinopathy), access can be improved by removing the head and foot ends of the operating table.

Anaesthetizing a preterm neonate requires constant vigilance, rapid recognition of events and trends, and swift intervention. Extra personnel may be required. An experienced operating department practitioner is essential.

All equipment including the anaesthetic machine, ventilator, breathing circuits, infusion pumps, and laryngoscopes should be pre-checked. Electrical supply for infusion pumps must be assured, especially if inotropic support is to be continued. A pressure-controlled ventilator capable of delivering small tidal volumes with PEEP is essential. Some may prefer hand ventilation via a Mapleson F circuit for the smallest babies provided the procedure is not prolonged. The temptation must be avoided to ventilate poorly compliant lungs with excessive pressure; high inflation

pressures in the presence of transient systemic hypotension and residual pulmonary hypertension will lead to reversion to fetal circulation and right-to-left shunting. Moderate concentrations of volatile agents as part of a balanced technique can be used to minimize increases in PVR while avoiding untoward decreases in systemic arterial pressure. Equipment may be available to use inhaled nitric oxide intraoperatively to assist this aim.

Monitoring

Routine monitors include Sa_{O_2} , ECG using neonatal electrodes, capnography, and non-invasive arterial pressure using an appropriate sized cuff. Two oximeter probes are recommended in all patients. In patients who have a PDA, one saturation probe is placed on the right hand (pre-ductal) and the other on a lower limb (post-ductal). Intra-arterial arterial pressure monitoring is recommended if possible; this also facilitates blood sampling. Intraoesophageal temperature is monitored using a combined stethoscope and temperature probe.

Anaesthesia

The majority of preterm neonates requiring emergency surgery are likely to be intubated and ventilated and transported in a dedicated transfer incubator. The baby must be carefully but expeditiously transferred to the operating table. Attention to detail and effective communication is crucial in order to avoid accidental disconnections and decannulations. If not intubated, an inhalation or an i.v. induction can be performed. Rapid sequence inductions can be challenging as even a short period of apnoea can cause detrimental desaturations, and mechanical pressure over the cricoid area can render the anatomy unrecognizable. Its use in children is questioned in contemporary practice.⁶ A range of uncuffed TTs should be available. Planned postoperative ventilation may indicate nasal intubation. The TT should allow a positive pressure breath with a small leak at 20–25 cm H_2O pressure. A neonate of <1200 g may need a 2.5 mm tube and as the weight increases 3, 3.5, and 4 mm tubes are required. The tracheal length is <4 cm in a preterm neonate; therefore, the tube length should be carefully adjusted and secured. As a guide 1, 2, 3, and 4 kg babies should have the TT positioned at the gum margin at the 7, 8, 9, and 10 cm marks. This position must be confirmed by auscultation.

Analgesia

Careful titration of anaesthetic and narcotic analgesic agents is necessary. Tachycardia and hypertension can be detrimental in the presence of underdeveloped cerebral autorogulation. For those who will be extubated after operation, minimal use of opioids combined with local anaesthetic techniques and acetaminophen is beneficial, while planned postoperative ventilation indicates an opioid-based technique. Fentanyl is advised as part of balanced anaesthesia in those with potential or overt pulmonary hypertension.⁷

The dosage of acetaminophen to achieve analgesic plasma concentrations is age-dependent.⁸ The recommended i.v. dosages of acetaminophen are: 7.5 mg kg⁻¹ 8 hourly in the 28–32 week group, 7.5 mg kg⁻¹ 6 hourly in the 33–36 week group, and 10–15 mg kg⁻¹ 6 hourly in those >37 weeks.⁸ Rectal dosing is dependent on the formulation; bioavailability of suppositories decreases with age. Suppositories of acetaminophen 30 mg are available for neonatal use. The above doses are recommended for a maximum of 3–4 days due to the unavailability of toxicity data for prolonged use.

Intraoperative fluid management

Ideally, fluid, acid–base, electrolyte, and Hb deficits should be corrected before reaching theatre. However, in certain circumstances, worsening acid–base status and cardiovascular instability precipitate the need for surgery.

The estimated maintenance fluid requirement of a preterm infant is 100 ml kg⁻¹ 24 h⁻¹. During surgery, the maintenance fluid should be isotonic (e.g. Hartmann's solution, 0.9% sodium chloride).⁹ Preterm infants often receive a glucose-containing solution to maintain normoglycaemia and this should continue during surgery. If parenteral nutrition is discontinued intraoperatively, glucose should be added to the maintenance fluid.

Estimation of blood loss can be difficult, but replacement can be guided by capillary Hb and haematocrit measurements, perceived ongoing and anticipated losses, and cardiorespiratory status. The extremely premature and those with cyanotic heart disease need a haematocrit of 35–40% to maintain oxygenation.

As a transfusion guideline, the volume of packed cells required (ml)=desired increment in Hb (g dl⁻¹)×weight (kg)×3. The required volume of platelets and fresh frozen plasma is given as 10–20 ml kg⁻¹, and cryoprecipitate as 5–10 ml kg⁻¹. Third-space losses are difficult to quantify and should be replaced with an isotonic fluid. Recommended estimates are 1–2 ml kg⁻¹ h⁻¹ for superficial surgery, 4–7 ml kg⁻¹ h⁻¹ for thoracotomy, and 5–10 ml kg⁻¹ h⁻¹ for abdominal surgery.⁹

Hypotension, diminished heart sounds, tachycardia, increased core-peripheral temperature gradient, and delayed capillary refill suggest fluid depletion. Urine output is a good indicator of fluid status and perfusion; an output of 0.5–2 ml kg⁻¹ h⁻¹ is the norm. However, monitoring such small volumes is difficult. If an arterial line is *in situ*, the position of the dirotic notch and the area under the arterial waveform can give valuable information to guide fluids.

Care must be taken during drug injections and when priming i.v. lines not to introduce air bubbles into the circulation which may traverse right-to-left shunts. As little as 0.2–0.4 ml kg⁻¹ can be hazardous.

The ex-premature surgical baby

The ex-premature baby can present for a wide range of surgery. Common procedures include herniotomy and orthopaedic procedures. The occurrence and management of postoperative apnoea

is a concern in this group. Its incidence in ex-premature babies after minor surgery is about 12%.⁴ GA is the single most important characteristic in identifying the risk. Recommendations for the risk-free period vary from 44 to 60 weeks due to inconsistencies in the studies.¹⁰ Other factors to consider are a history of apnoea at home, anaemia (Hb <10 g dl⁻¹), neurological disease, and chronic lung disease.¹⁰ Elective surgery should be delayed until these are addressed. I.V. caffeine 10 mg kg⁻¹ has been recommended to reduce the incidence of postoperative apnoea in ex-prematures but should be used with caution in this age group.

Tracheal intubation and controlled ventilation is indicated for all surgery in infants <60 weeks GA. Acetaminophen and local anaesthetic techniques should be utilized where possible to reduce opioid usage. Spinal anaesthesia alone has been used for inguinal herniotomy in this group but is associated with a significant failure rate; the short duration of the block is a disadvantage if surgery is bilateral. A subarachnoid block can be supplemented with a caudal injection of bupivacaine 0.25% with 1:200 000 epinephrine to produce anaesthesia lasting >2 h.¹¹ A Cochrane review revealed insufficient evidence to support the routine use of spinal anaesthesia for herniotomy in ex-prems.¹² The use of newer volatile agents with caudal analgesia can be equally beneficial.

Conclusion

The outlook for the premature baby is continually improving. Ongoing development of minimally invasive techniques will transform surgical outcomes further. These techniques will also impose unique physiological challenges and dictate the need for a greater understanding of preterm neonatal physiology when these babies present for anaesthesia and surgery.

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Please see multiple choice questions 1–4