Detailed contents

Chapter 1

System-based anatomy and physiology

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CHAPTER 1 System-based anatomy and physiology

Overview

- Children have an increased perioperative morbidity and mortality compared with adults.
- Provision of safe perioperative care therefore requires an understanding of neonatal and paediatric anatomy and physiology in addition to other aspects covered elsewhere.
- This chapter outlines major differences in the respiratory, cardiovascular, central nervous, and hepatorenal systems and in thermoregulation.

Airway and respiratory system

Upper airway

- Perioperative airway problems frequently result in significant morbidity and mortality.
- The airway undergoes significant changes from birth to adulthood. These changes affect the development of the skull, the oral cavity, the larynx, and the trachea. Facial structures are small and paranasal sinuses absent.
- The small oral cavity is easily compressed during mask ventilation, resulting in upper airway obstruction.
- The tongue has a flat surface with limited lateral mobility in neonates, complicating direct laryngoscopy unless a retromolar approach is used.
- Neonates are obligate nose breathers owing to the relatively large tongue; 50% of airway resistance is secondary to nasal passages.
- The large head and prominent occiput produce a cephalad (anterior) view of the larynx during direct laryngoscopy. There is a loosely embedded 'anterior' larynx at C2/3, moving to C5/6 in later life
- The epiglottis (long, narrow, U- or Ω-shaped) obscures the laryngeal inlet if not 'picked up' by the laryngoscopy blade.
- Vocal cords are shorter in neonates.
- The ETT is commonly directed against the anterior wall of the trachea, creating an impression that the ETT is too wide to pass through the cricoid ring (ellipsoid, does not expand).
- The ETT must be narrow enough not to exert pressure on the mucosa of the cricoid cartilage, but large enough to provide an adequate seal for ventilation.
- Cuffed ETTs are now considered safe provided cuff pressures are continuously monitored and maintained <20 cmH_2O.

Lower airway

- The tracheal length is measured from the cricoid to the carina and is related to age and height but not weight.
- Unintentional bronchial intubation and extubation are a constant threat during positioning. (For ETT sizing, ➔ Chapter 6.)
- A small internal tracheal diameter leads to a significant ↑ in airway resistance, particularly following mucosal injury.
- The alveoli are thick-walled in neonates and amount to only 10% of the adult total. The single terminal bronchiole opens into a single alveolus instead of a fully developed cluster.
- The chest wall of small infants and neonates is primarily cartilaginous and highly compliant. Horizontal alignment of the soft and pliable ribs prevents the 'bucket-handle' action of the adult thoracic cage.
- Weak intercostal and diaphragmatic muscles (due to a lack of type I fibres) with a more horizontal attachment and a protuberant abdomen predispose to fatigue. Sedation, GA and illness ↓ tonic muscular contraction, resulting in a diminished FRC. The latter can be reversed by CPAP or IPPV.

- Chest wall specific compliance is higher in neonates and infants (0.06 mL/cmH_2O) than in adults (0.04 mL/cmH_2O). Therefore, intercostal recession and sternal recession occur readily in neonates and young infants with increased respiratory effort and during episodes of airway obstruction.
- Upper and lower airways are susceptible to a large ↑ in airway resistance (and the work of breathing) in the event of an obstruction.

Respiratory physiology

- Respiratory complications related to GA are highest in infants owing to differences in respiratory physiology (Table 1.1).
- There is a similar V_T per kg in all age groups. The higher RR produces higher alveolar minute ventilation (MV).
- The ratio of alveolar ventilation to FRC is 5:1 in neonates and infants (2:1 in adults), resulting in rapid uptake of volatile agents.
- Changes in the concentration of inspired gases are more rapidly reflected in alveolar and arterial values.
- Risk of atelectasis and tendency for V/Q mismatch is due to closing volume encroaching FRC, resulting in a fall in arterial O_2 tension. The small available intrapulmonary O_2 reservoir (relative to O_2 consumption) can lead to rapid desaturation in the event of airway obstruction or apnoea and is measured in seconds.
- FRC is reduced further during and for a period after GA. Physiological mechanisms to maintain FRC in neonates include partial adduction of the vocal cords during expiration (laryngeal braking), early termination of expiration (tachypnoea), and inspiratory muscle activity during expiration.
- These mechanisms are abolished by GA, sedation, or illness, when FRC falls markedly when compared with awake. This further reduces the O_2 reserves and contributes to the rapid onset of hypoxia in infants and neonates in the event of an airway obstruction.
- The anteroposterior and lateral thoracic diameters are not significantly increased in neonates and infants during deep inspiration.

Table 1.1 Differences in respiratory parameters with age

Parameter	Neonate	Child	Adult
RR (breaths/min)	40–60	20–30	16–24
V_T (mL/kg)	7–8	7–8	7–8
Alveolar ventilation (mL/kg/min)	100–150		60
FRC (mL/kg)	30	30	30
Dead space (mL/kg)	2	2	2
O_2 consumption (mL/kg/min)	6–9		2–3
Airway resistance (cmH_2O/L/s)	40	20	2
Airway compliance (mL/cmH_2O)	5		100

- As the child grows (spending time in an upright position), the chest wall compliance ↓ and FRC is maintained above closing volume (6–12 months onwards).
- The work of breathing is reduced by CPAP and improves oxygenation.
- The anatomical dead space is fixed in humans (2 mL/kg). However, the dead space in anaesthetic equipment is more significant in relation to the small V_T of neonates and infants.
- Neonates and infants rely primarily on diaphragmatic movements. This tonic muscular contraction is lost during GA and hence positive pressure ventilation and PEEP during GA are the norm.
- An ETT reduces the airway diameter more in smaller airways and hence significantly increases the airway resistance, leading to an increased work of breathing. Spontaneous ventilation through a small ETT may therefore be impossible.
- Immature respiratory control: the peripheral chemoreceptor response to hypoxia is weak and the central chemoreceptor response to CO_2 is blunted in premature infants. Neonates are prone to periodic breathing with apnoeic phases (2–10 s). The apnoeic periods in the premature neonate are prolonged, especially after GA.
- Cold and dry gases lead to heat and insensible fluid losses from the lungs (15–20 mL/kg/day).

Cardiovascular system

Fetal circulation

- Fetal gas exchange occurs in the placenta.
- There is preferential streaming of oxygenated blood to the brain and myocardium due to the presence of intracardiac and extracardiac shunts (Fig. 1.1).
- The fetal circulation is said to be 'shunt-dependent'.

Fetal blood flow

- Deoxygenated blood reaches the placenta in the umbilical arteries and returns to the fetus in the umbilical vein.
- pO_2 in the umbilical vein is approximately 4.5–5.0 kPa and fetal blood is 80–90% saturated.
- In the inferior vena cava (IVC), oxygenated blood from the placenta mixes with desaturated blood from the lower body.
- In the right atrium (RA), oxygenated blood from the IVC is directed across the foramen ovale into the left atrium (LA). In the LA, the SpO_2 is around 65%.

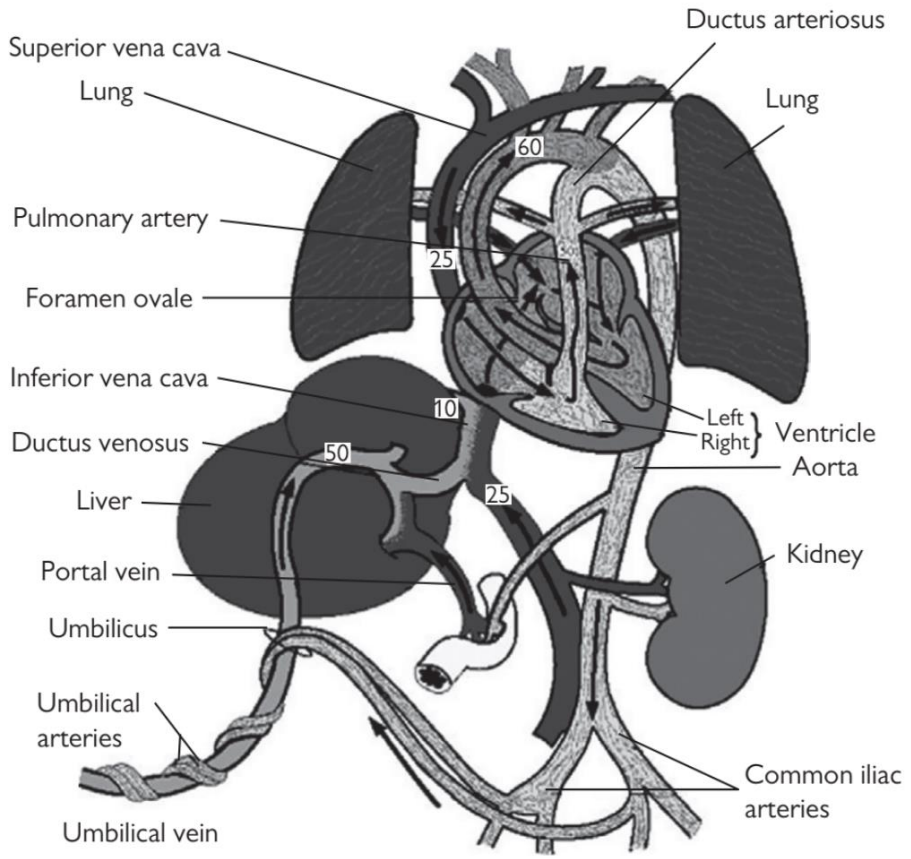

Fig. 1.1 Fetal circulation.

- This well-oxygenated blood enters the left ventricle (LV) and is ejected into the ascending aorta. The majority of the LV blood is delivered to the brain and coronary circulation.
- Desaturated blood from the IVC, SVC, and coronary sinus is directed across the tricuspid valve and into the right ventricle (RV). This blood is then pumped into the pulmonary artery (PA).
- Because of the high pulmonary vascular resistance (PVR) in utero, only about 12% of the RV output enters the pulmonary circulation. The remaining 88% passes through the ductus arteriosus into the descending aorta and the lower half of the body; it is relatively desaturated blood (pO_2 2.5–3.0 kPa).
- O_2 delivery in the relatively hypoxic fetus is maximized by:
  - A high haemoglobin concentration, around 16 g/dL at term
  - A high cardiac output (CO), 250–400 mL/kg/min at term.

The presence of fetal haemoglobin (HbF) leads to a lower concentration of 2,3-diphosphoglycerate (2,3-DPG) than HbA and shifts the haemoglobin–oxygen dissociation curve to the left (P_{50} 3.6 kPa).

Changes at birth

- Gas exchange is transferred from the placenta to the lungs, the fetal circulatory shunts close, and the LV output increases.
- With the onset of respiration:
  - pH and arterial O_2 tension ↑.
  - PVR falls by 80% from prenatal levels within a few minutes of commencing ventilation.
  - Blood flow through the lungs and the LA ↑.
  - LA pressure rises above RA pressure closing the foramen ovale.
- With removal of the placenta and closure of the umbilical artery:
  - A large low-resistance vascular bed is excluded from the systemic circulation.
  - SVR ↑ while pressure in the IVC and flow through the RA both ↓.
  - The fall in flow through the IVC and RA reduces RA pressure below that in the LA and contributes to functional closure of the foramen ovale.
- The ↑ SVR and simultaneous ↓ PVR with increasing flow in the pulmonary vascular bed lead to an aortic pressure above that in the PA. The blood flow through the ductus arteriosus reverses direction and now goes from left to right, filling it with oxygenated blood. The ↑ local arterial O_2 tension and lack of prostaglandin E_2 from the placenta cause the muscular tissue of the ductus arteriosus to constrict, leading to functional closure.
- Prostaglandin is used to open the ductus arteriosus in neonates with CHD where the systemic perfusion or the pulmonary blood flow depend on an open ductus arteriosus, e.g. coarctation of the aorta or pulmonary atresia. Conversely, the closure of the duct can be achieved by administration of prostaglandin inhibitors, e.g. indometacin.

Transitional circulation

- The PVR remains high for the first weeks, and the ductus arteriosus may be open for first few days of life. Under some circumstances, a normal

neonatal circulation may revert to a fetal circulatory pattern (persistent fetal circulation).

- This is associated with congenital diaphragmatic hernia, meconium aspiration, and significant respiratory distress of any cause.
- Main stimuli: hypoxia, hypercarbia, acidosis, and hypothermia.
- The pulmonary arterioles constrict in response to these stimuli. PVR rises and right-to-left flow through the functionally closed but anatomically patent foramen ovale and ductus arteriosus may resume. This worsens hypoxia and acidosis (for treatment, ➔ Chapter 13).

Neonatal and infant circulation

- The myocardium contains fewer contractile elements (30% vs 60% in adults) and more supporting tissue. The ventricles are less compliant when relaxed and can generate less tension during contraction. This limits the stroke volume (SV). Therefore, in neonates, LV end-diastolic volume is relatively fixed and CO is largely dependent on heart rate (HR).
- Reduced compliance and contractility of the ventricles lead to heart failure with increasing volume load. Distension of either ventricle results in compression and dysfunction of the contralateral ventricle.
- The neonatal myocardium has a reduced Frank–Starling response. Afterload compensation is finite.
- Bradycardia is not well tolerated and a neonatal HR < 60 beats/min does not provide adequate CO; CPR should be initiated.
- Asystole is the commonest terminal rhythm. VF is rare.
- Tachycardia is well tolerated and the neonate can cope with rates of up to 200 beats/min.
- Sinus arrhythmia is common, but other irregular rhythms are abnormal.
- Term neonates have functional autonomic and baroreceptor control mechanisms. However, the parasympathetic tone mediated by the vagus nerve predisposes them to bradycardia during vagal stimulation, e.g. hypoxia.
- A rough rule of thumb: neonatal MAP in mmHg = gestational age in weeks (Table 1.2).

Table 1.2 Normal cardiovascular parameters for different age groups

Age	Systolic BP (mmHg)	Diastolic BP (mmHg)	Mean BP (mmHg)	HR (beats/min)	CO (mL/kg/min)
Neonate (<1 kg)	40–60	15–35	25–45	80–200	400
Neonate (3 kg)	50–70	25–45	35–55	80–200	200–250
Infant (6 months)	85–105	55–65	65–80	80–140	
Child (2 years)	95–105	55–65	65–80	80–120	
Child (7 years)	100–110	55–70	70–85	80–120	
Adolescent	110–130	65–80	80–95	50–90	80

Central nervous system

Anatomy

- The neonatal CNS is immature and differs from the adult and older child. These differences are relevant to GA and regional techniques.
- At birth the brain weighs approximately 330–350g (10–15% of body weight). Adult proportions (1200–1400 g or 2% of body weight) are obtained at around 12 years of age.
- The cerebral cortex is underdeveloped and synaptic connections are immature. Myelination and dendritic proliferation progress in the last 3 months of pregnancy and during the first years of life.
- The cranial sutures are open, with a large anterior fontanelle that closes by 20 months of age. Palpation of the anterior fontanelle can be used to evaluate ICP in neonates and infants. The posterior fontanelle closes by 3 months of age.
- Increasing ICP is partly relieved by expansion of the fontanelles and separation of the suture lines, so head size ↑ before ICP rises.
- The blood–brain barrier is anatomically and functionally incomplete. Bilirubin, opioids, and barbiturates cross freely.
- In the preterm neonate, cerebral vessels are at risk of rupture, especially in the region of the germinal matrix close to the nucleus caudatus. The germinal matrix has a rich blood supply, scarce vascular supporting tissue, and thin vessel walls, leading to a high chance of intracerebral and intraventricular haemorrhage. With increasing gestational age, the germinal matrix involutes and the risk of bleeding ↓.
- The spinal cord of the fetus initially occupies the entire length of the spinal canal. Differential growth of the canal and spinal cord causes the termination of the cord to move cephalad relative to the vertebral canal: S1 at 28 weeks' gestation, L3 at term, L2/3 at 1 year, and the adult level of L1/L2 around the age of 8 years.
- The intercristal line in neonates is at L5–S1, compared with L4 in adults, and LP is performed below this line. Ossification of the sacral vertebrae is not complete, making a sacral epidural possible.
- The epidural space in the infant contains fat that is loculated, with distinct spaces between individual lobules. A catheter introduced into the epidural space via the sacral hiatus can be threaded to thoracic level to provide epidural analgesia for thoracic dermatomes.
- The sacral hiatus is relatively large compared with later life and is not ossified, allowing easy access to the lower epidural space.
- The volume of CSF is proportionately greater in neonates/infants/adults (10 vs 4 vs 2 mL/kg) and there is a higher relative volume of CSF in the spinal canal (50% in children vs 33% in adults). The pia mater is highly vascular. Therefore, spinal anaesthesia requires a higher dose of LA; and is of shorter duration.
- The cervical and lumbar curves in neonates are undeveloped. The ligamentum flavum is thin compared with that in adults.

Physiology

- Cerebral metabolic rate, blood flow, O_2 requirements, and glucose consumption are all higher in small children than older children and

adults (Table 1.3). This makes them vulnerable to any interruption in cerebral perfusion during GA or at other times.

- The global cerebral blood flow (CBF) between 6 months to 4 years of age is twice that of an adult, secondary to the accelerated cerebral development during this period. The low cerebral mass and metabolism in the preterm neonate is reflected in the low CBF.
- Cerebral perfusion pressure (CPP) equals mean arterial pressure (MAP) less central venous pressure (CVP) or intracranial pressure (ICP) (whichever is greater):

$$CPP = MAP - ICP\,(\text{or } CVP)$$

- Autoregulation maintains constant CBF despite changes in CPP within an adult range of 60–150 mmHg. The thresholds of CPP autoregulation in the infant and young child are unknown. Animal models suggest that the limits of autoregulation are lower than those in adults.
- Cerebral autoregulation might be compromised in severely ill children when CBF becomes pressure-dependent. Hypotension may induce cerebral ischemia.
- ICP in neonates and infants (2–5 mmHg) is lower than in older children and adults (8–18 mmHg). Chronic ICP ↑ are compensated to some extent by expansion of sutures and fontanelles (hydrocephalus). Acute ↑ cannot be compensated for in this way.
- Incomplete myelination of nerve tissue in neonates and infants allows effective blockade with low concentrations of LA solution.
- The sympathetic nervous system is not fully developed until the age of 6 years. Central neuraxial blocks (spinal or epidural anaesthesia), therefore, causes little change in HR or BP.
- The baroreceptor reflex is poorly developed in premature neonates and hypovolaemia does not result in tachycardia.

Table 1.3 Cerebral metabolism in children and adults

Age	CBF	O_2 consumption	Glucose requirement
Premature	**40** mL/min/100 g		
Neonate	40–50 mL/min/100 g	2.3mL/min/100g	
Child	**100** mL/min/100 g	**5.8** mL/min/100 g	**6.8** mg/min/100 g
Adult	**50** mL/min/100 g	**3.5** mL/min/100 g	**5.5** mg/min/100 g

Liver

- Hepatic phase I and II reactions are not fully functional in neonates and premature infants. However, function matures rapidly, reaching adult values at 2–3 months of age (often exceeding that of adults).
- Phase I reactions (cytochrome-dependent) include oxidation, reduction, and hydrolysis. These reactions primarily produce less-active or inactive compounds. These compounds undergo phase II reactions (conjugations), e.g. glucuronidation (opioids) or sulfation (paracetamol) to produce polar compounds; which are eliminated in urine or via the GIT.
- Phase I reactions are catalysed by the cytochrome P450 mixed function oxidase system, which in neonates has about 28% of adult activity.
- Deficient phase I activity is also present for other systems e.g. alcohol dehydrogenase (chloral hydrate metabolism), plasma esterase (amino-ester LA metabolism), and *N*-acetyltransferase (isoniazid and hydralazine metabolism).
- The phase II reactions acetylation, glycination, and glucuronidation are very deficient at birth, but sulfation is highly active. This pathway can metabolize opioids before glucuronidation matures and is also responsible for paracetamol metabolism in neonates.
- Bilirubin is produced from the breakdown of erythrocytes (80%) and from ineffective erythropoiesis (20%). The enzyme that catalyses the transfer of glucuronic acid to bilirubin (uridine diphospho-glucuronosyltransferase) to form glucuronides and allow excretion in bile has only 1% of adult values at term (adult values are reached at 3–4 months of age).
- Physiological jaundice occurs from the second or third day of life, lasting for about 10 days, when most term and virtually all premature infants experience a period of unconjugated hyperbilirubinaemia. This is a consequence of high production (100–140 mcg/kg/day compared with 50–70 mcg/kg/day in adults) from erythrocyte breakdown (neonates are relatively polycythaemic), limited metabolism and excretion, and ↑ enterohepatic recirculation of bilirubin (due to a limited capacity to form urobilinogen and urobilin).
- Kernicterus occurs if plasma bilirubin concentration > 200 micromol/L, resulting in damage to basal ganglia, cerebellum, and hippocampus. Reduced albumin concentration, neonatal infection/sepsis, and haemolysis are risk factors. Phototherapy converts unconjugated bilirubin to photoisomer products, which are excreted in bile or urine without the need for glucuronidation.
- Vitamin K-dependent clotting factors (II, VII, IX, and X) are low in the term neonate. Vitamin K is given to most neonates to prevent haemorrhagic disease of the newborn, and administration is vital preoperatively.
- The ductus venosus (a connection between the IVC, portal vein, and umbilical veins) remains patent for 7–10 days after birth. This shunt bypasses the hepatic vessel bed and decreases hepatic clearance. The effects of drugs with hepatic metabolism are prolonged.

- Hepatic glucose storage is low and activity of the rate-limiting enzyme in gluconeogenesis (phosphoenolpyruvate carboxykinase) is around 10% of adult values. The neonate who is not feeding is prone to develop hypoglycaemia. A glucose infusion is necessary until there is enteral feeding.
- The limited hepatic metabolism in the infant has a limited intraoperative impact. However, the reduced hepatic metabolism is relevant postoperatively with drugs requiring dose modification.