At birth, a newborn baby must be able to function independently and adapt to a new environment in order to survive. This process involves anatomical, physiological and pharmacological changes that occur with the first breath and continue throughout early childhood. Anaesthesia for neonates and infants can only be managed safely with a thorough understanding of the developmental changes taking place in early life.

Respiratory physiology

Pulmonary development

During early fetal life, the bronchial tree grows by a process of dichomatous branching to produce 16–25 generations that will form the future airways. Structures then develop, by a process of branching and budding, to form respiratory bronchioles by 24 weeks’ gestation and extra-uterine survival of the fetus is possible at this stage. Lamellar bodies, which contain mature components of the surfactant system, increase in number and achieve a critical mass at 30–32 weeks’ gestation, thereby increasing surfactant production. From then until birth, the lungs grow peripherally by branching and growth of the peripheral ducts to fill the pleural space. At birth, the lung contains relatively few alveoli (10% of adult). The region for gas exchange is made up of a few generations of wide and smooth walled transitory ducts that open into saccules with rounded contours. Alveolar growth accelerates following birth and continues until 8 years of age.

Mechanics of respiration

In the newborn and during infancy, the ribs extend horizontally from the vertebral column and their configuration is circular, similar to the position of deep inspiration in adults. As a result, the rib cage contributes little to inspiratory volume changes. The diaphragm is flatter and less domed than the adult with limited and less efficient movement. It also contains a lower percentage of fatigue-resistant type-I muscle fibres. Tidal volume is relatively fixed and increasing respiratory rate (not tidal volume) increases alveolar minute ventilation. Chest wall compliance is high and the total compliance of the chest approximates to that of the lungs. The lungs are relatively stiff at birth, but compliance increases dramatically over the first few hours as residual lung fluid is removed. Functional residual capacity (FRC) is low in the neonate due to the elastic recoil of the lungs drawing in the compliant chest wall during expiration. Closing volume is high and often encroaches on FRC, a situation seen during anaesthesia. This results in airway closure during ventilation leading to intrapulmonary shunting and a reduction in oxygen tension. This effect can be reversed with the use of continuous positive end-expiratory pressure. Oxygen consumption is relatively high in the newborn (6–8 ml kg⁻¹ min⁻¹), approximately twice that of adult levels. As the ratio of alveolar ventilation to FRC is high in early life (5:1 compared with 1.5:1 in older children and adults), FRC is a less efficient buffer to changes in the partial pressures of the inspired gas mixture, these changes being more rapidly reflected in alveolar and arterial pressures. One result of this is that hypoxaemia develops rapidly when ventilation is interrupted. The combination of a high work of breathing, increased oxygen consumption, high alveolar ventilation compared with FRC, higher closing volume and susceptibility to diaphragmatic muscle fatigue indicates that anaesthesia in the very young is best achieved with a technique based on intubation and controlled ventilation.
Anatomical differences

Infants have a large head and a short neck, the neck muscles being insufficiently developed to maintain the head in position without support. Neonates and infants are obligatory nasal breathers, so that any obstruction of the nasal passages can significantly increase the work of breathing. A large tongue in relation to the oropharynx increases the likelihood of airway obstruction and difficulties with laryngoscopy during anaesthesia. The larynx is at a higher level (C3/4) compared with the adult airway; the narrowest part is at the level of the cricoid. The epiglottis is long, U-shaped and angled at 45°. Straight blade laryngoscopes are more useful for intubation in neonates and infants as the tip of the blade can be used to lift the long and floppy epiglottis to expose the larynx. In the newborn, the length of the trachea is only 5 cm and the tip of an endotracheal tube may easily be displaced into a bronchus during intubation.

Postoperative apnoea

Infants born prematurely are prone to develop apnoea following anaesthesia and surgery, with an incidence of 20–30% in otherwise healthy preterm infants undergoing inguinal hernia repair. Apnoeic episodes can occur up to a postconceptual age (PCA) of 60 weeks (PCA = gestational age at birth + postnatal age). However, the peak incidence occurs in infants younger than a PCA of 44 weeks. Although certain anaesthetic techniques may reduce this serious complication, all former preterm infants less than a PCA of 60 weeks should have surgical procedures carried out on an in-patient basis only.

Cardiovascular physiology

Myocardial function

Before birth, the combined ventricular output of the fetal heart is high (500 ml kg⁻¹ min⁻¹) and the left ventricle contributes only one-third to this combined output. After birth, the output from the left and right ventricles is the same (300–400 ml kg⁻¹ min⁻¹). Therefore, the output of the left ventricle increases by > 200% and determinants of myocardial performance are close to maximum. Over the next few months, cardiac output decreases to 150–200 ml kg⁻¹ min⁻¹, suggesting that the heart acquires a greater functional reserve with maturation. Right ventricular wall thickness is greater than left at birth resulting in right axis deviation on the electrocardiogram. Ventricular thickness equilibrates at 3–6 months and then becomes greater on the left. The newborn myocardium cannot generate the same force as that of an adult. This is due to a decreased density of the functional contractile units (sarcomeres) in the myofibril. Sarcomeres comprise about 60% of the adult myocardium compared with only 30% in the newborn. This results in a neonatal myocardium that is less compliant with a fixed stroke volume. Thus, cardiac output is rate dependant with normal heart rates of 130–160 beats min⁻¹ at birth.

Sympathetic innervation of the myocardium is incomplete at birth and parasympathetic tone predominates. Bradycardia is easily induced by hypoxaemia and manoeuvres that increase vagal tone. Vagal stimulation initially leads to a reduction in ventricular output with only small changes in heart rate. However, when bradycardia develops, profound decreases in cardiac output occur.

Circulating volume

Total blood volume in babies is small (Table 1) so that a modest loss of blood can give rise to significant hypovolaemia. It is, therefore, important to calculate blood volume before the start of surgery and keep an accurate measurement of blood loss. During anaesthesia, systolic arterial pressure offers an excellent guide to the blood volume status in neonates and infants; hypotension usually indicates hypovolaemia. Fluid requirements in term and preterm infants are high, reflecting high metabolic demands. However, requirements decrease during infancy. It is essential to calculate intra-operative maintenance fluid requirements for each individual child and thought needs to be given to the type of fluid used. Healthy children, who are not fasted for a prolonged period, are at little risk of developing hypoglycaemia. Hyperglycaemia is not without hazard and a non-glucose isotonic salt solution should be used for maintenance requirements. This fluid is also appropriate for replacement of third space losses and blood. If surgery is prolonged, blood sugar estimations can be carried out. However, in term and preterm babies, maintenance fluid should contain 5% glucose as these children have less carbohydrate reserve and ability to prevent hypoglycaemia. At birth, the volume of the extracellular fluid compartment

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<th>Table 1 Normal values in neonates and infants</th>
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<td>Haemoglobin (g dl⁻¹)</td>
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<tr>
<td>Blood volume (ml kg⁻¹)</td>
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<td>Total body water (% wt)</td>
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<td>ECF (% wt)</td>
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<td>ICF (% wt)</td>
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<td>Fluid requirements (ml kg⁻¹ day⁻¹)</td>
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(ECF) exceeds that of the intracellular space (ICF). However, during infancy, the ECF volume as a percentage of body weight decreases, achieving the ICF:ECF ratio normally found in older children and adults.

**The central nervous system**

The brain of a neonate weighs 350 g (25% of adult weight) and grows rapidly, doubling in size by 6 months. At birth, approximately 25% of neuronal cells are present and cellular development of the cortex and brain stem is complete at one year. The central nervous system begins to show signs of myelination prior to birth and this process continues into the third year of life. Myelination begins in the peripheral nervous system and the motor nerves myelinate before the sensory nerves. Incomplete myelination does not imply lack of function but merely a slower conduction time. This is offset by a shorter interneuron distance for the impulse to travel. There is now overwhelming evidence indicating that the neurophysiological components required for pain perception are present by mid-gestation.

Control of cerebral blood flow (CBF) involves a complex interaction of metabolic, chemical and neural factors which produce their effects by direct action on the cerebral vessels. In adults, CBF is constant over a wide range of mean arterial pressures, *i.e.* 50–150 mmHg. However, the range over which CBF remains constant in the very young has not been determined. As arterial pressure is lower in infants than in adults, the range of pressures over which CBF is auto-regulated should be lower.

In preterm infants, the thin-walled cerebral vessels are poorly supported by the surrounding connective tissue. Thus, abnormalities in CBF may lead to intraventricular haemorrhage (IVH) and periventricular haemorrhagic infarction, the incidence of which is related to the degree of prematurity. Impaired autoregulation may also occur in association with severe asphyxia, cranial trauma and hypercarbia. The occurrence of IVH during anaesthesia should largely be preventable. Abrupt fluctuations in cerebral blood flow, cerebral blood volume and cerebral venous pressure play a role in the development of IVH and values should be maintained at normal levels during anaesthesia. Therefore, arterial and venous pressures should remain constant and rapid fluid administration, hypoxaemia and hypercarbia should be avoided.

**Thermoregulation**

The maintenance of normal body temperature in neonates and infants during anaesthesia is of paramount importance. The large surface area in relation to body mass, low heat production and low tissue insulation predispose to rapid heat loss. The range of ambient temperatures that neonates can tolerate is narrow and the preterm infant is at even greater risk of developing hypothermia. Being unable to shiver, the neonate produces heat by non-shivering thermogenesis. This involves the oxidation of triglycerides located in brown fat stores. This heat production requires an increase in basal metabolic rate and oxygen consumption that may worsen any pre-existing hypoxaemia. Approximately 11% of the body fat of a term neonate is located in brown fat stores, principally found at the base of the neck, axillae, between the scapulae and in the mediastinum. The range of temperatures over which heat production is kept to a minimum is known as the neutral thermal environment. During anaesthesia, babies can be kept warm by heating the operating theatre to 25–27°C before the child arrives. A warm air convection blanket should be placed over the infant and a heater-humidifier used in the breathing circuit. Other strategies include the use of overhead heaters, heating mattresses and fluid warmers. All heating devices should be thermostatically controlled to prevent thermal injury.

**Pharmacology**

The response to drugs during early life differs in several respects from that of older children and adults. In general, uptake and distribution of drugs are increased or unchanged while elimination is reduced, leading to an increased risk of overdose and toxicity. Increased cardiac output in the neonate leads to a faster circulation time and, therefore, faster distribution of drugs to their site of action. A large percentage of a neonate’s body water is contained in the ECF compartment (Table 1). This large ECF volume influences the volume of distribution of many drugs, especially those which are highly ionised, e.g. muscle relaxants. Increases in protein binding and protein concentration occur with age and concentrations of α₁-acid glycoprotein are significantly lower in newborns than in adults.

Developmental changes in hepatic and renal physiology occur, affecting the metabolism and elimination of drugs and their metabolites. Hepatic enzymes involved with drug metabolism mature at different times. There is decreased activity and concentration of the microsomal enzymes responsible for phase I (non-synthetic) reactions involved in the metabolism of synthetic opioids. The activity of this system reaches adult levels within a few days of birth. The ability to form conjugates
Basic principles of anaesthesia for neonates and infants

Inhalational agents

The potency of an inhaled anaesthetic is determined by its minimum alveolar concentration (MAC). MAC is lower in preterm infants than in term infants and increases with PCA. MAC generally increases to a maximum level by 6 months of age in a term infant and, thereafter, decreases with increasing age. Sevoflurane is somewhat unusual in that there does not appear to be an age related difference in MAC during early infancy. After 6 months, an abrupt step down in MAC has been observed with sevoflurane, following which it remains constant during childhood. Age related changes in MAC imply that the same alveolar concentration will produce different levels of anaesthesia in children of different ages.

The rate of rise of the alveolar to inspired anaesthetic partial pressure (wash-in) is more rapid in infants and children than in adults. The more rapid rate of rise of anaesthetic partial pressures in neonates compared with adults has been related to four differences between these two age groups. The order of these four factors in Table 2 may reflect their relative importance in producing this effect.

Intravenous agents

Various intravenous agents, including barbiturates and ketamine, can be used safely for induction of anaesthesia in neonates. There is an increased sensitivity to barbiturates and opioids in the neonate and they also have prolonged effects. This has been attributed to the immaturity of the blood-brain barrier, allowing faster penetration and rise in concentration of these drugs in the brain.

| Table 2: Factors responsible for the rapid wash-in of inhalation anaesthetics in infants |
|---------------------------------|-----------------------------------------------|
| Greater alveolar ventilation in relation to FRC |
| Greater fraction of cardiac output distributed to the vessel rich group |
| Lower tissue/blood solubility |
| Lower blood/gas solubility |

Muscle relaxants

There is substantial evidence to suggest that the neuromuscular junction in neonates is 3 times more sensitive to non-depolarising muscle relaxants than that of adults. However, this sensitivity is balanced by an almost identical increase in the volume of distribution (because of a large ECF) so that the required dose is unaffected. However, as a result of the prolonged elimination time, doses of additional relaxants should be reduced and given less frequently. The recommended dose of succinylcholine is twice that of adults (approximately 2 mg kg⁻¹). Its duration of action, terminated via the action of plasma cholinesterase, is 5–8 min. The rate of succinylcholine hydrolysis may be slower in the preterm infant (immature liver) than in older child. Due to the activity of succinylcholine at muscarinic acetylcholine receptors, significant side-effects may occur. For example, the action of succinylcholine on the sino-atrial node in neonates and infants may produce severe bradycardia and asystole. This can be attenuated by the prior administration of atropine.

Key references


See multiple choice questions 79–83.