Developmental physiology encompasses the bodily changes taking place after birth that affect clinical anesthetic management. This chapter covers the basic principles of these changes, including cardiac, respiratory, neurologic, hematologic, and renal physiology. In addition, principles of developmental pharmacology as they pertain to the administration of intravenous and inhalational anesthetic agents are reviewed.

**RESPIRATORY PHYSIOLOGY**

The normal newborn achieves almost full functionality of the lungs within several hours after birth. The full-term newborn lung contains approximately 50 million alveoli, which proliferate during early childhood until reaching the adult level of 300 million by about age 4 years.

The biochemical and reflex control of ventilation is well developed in the healthy full-term neonate. Periodic breathing is common in full-term newborns, with episodes of central apnea lasting 5 seconds or more.

In healthy infants, these episodes of central apnea are self-limited and are not associated with significant or prolonged bradycardia, as often occurs in preterm infants. In most healthy full-term infants, periodic breathing no longer exists after the first month of life.

Newborns exhibit a relatively normal ventilatory increase in response to inhaled carbon dioxide (CO₂), albeit to a smaller degree. The ventilatory response to hypoxia is characterized by an immediate increase in ventilation that lasts about 1 minute, followed by a decrease in ventilation that lasts about 5 minutes. This differs from older children in whom the initial protective phase of ventilatory stimulation has a substantially longer duration. This phase of ventilatory depression is even more prominent during concomitant hypercarbia, acidosis, or hypothermia.

Newborns demonstrate maladaptive respiratory depression (including apnea) in response to certain provocations that would normally result in stimulation of respiratory function in older infants. These include lung inflation (Hering–Breuer reflex), stimulation of the carina or superior laryngeal nerve, and upper-airway obstruction.

The most important differences in respiratory physiology between children and adults are related to the growth and maturity of the chest wall within the first 2 years of life. These differences directly influence the mechanism by which the functional residual capacity (FRC) is maintained. The newborn infant’s FRC is established in the first several breaths after birth. In conscious subjects, it is estimated that the FRC of the newborn infant is about 300 ml, which is about 15% of total lung capacity. However, this difference is that it imparts such substantial effects on anesthetic practice.

In neonates and small infants, the orientation of the ribs is more parallel than angled, which predisposes to inefficiency of movement, since the volume of the rib...
cage is not increased by raising the ribs, as in older children and adults (Fig. 2-1). The infant’s chest wall does not become more adult-like until the second year of age, when the child assumes an upright posture, and the effect of gravity causes the ribs to be angled downward. At about the same time, the structure of the ribs becomes less cartilaginous and more bony, conferring an inherent stiffness to the thoracic cavity. This stiffness imparts a tendency for the chest wall to expand outward, at the same time that the lungs tend to collapse inward. These opposing pressures generate the slightly negative intrapleural pressure at the end of exhalation, and serve to maintain FRC.

The chest wall of neonates and small infants has not yet developed its bony frame; so it is highly compliant and tends to collapse inward. As a consequence, young children must maintain a negative intrathoracic pressure by active recruitment of accessory muscles of respiration, such as intercostal muscles. In addition, the adductor muscles of the larynx of the young infant act as an expiratory “valve,” serving to restrict exhalation in order to maintain positive end-expiratory pressure, and contribute to the maintenance of the FRC. This is often referred to as “laryngeal braking.” Prominent abdominal excursions during normal breathing are common in newborns because of their reliance on diaphragmatic contraction for development of a sufficiently negative intrapleural pressure to initiate inspiration. Neonates may even exhibit small-airway collapse during normal tidal breathing.

These differences explain the marked changes in FRC in infants after the onset of general anesthesia that is normally not observed to a great extent in older children and adults. Because of the bony make-up of their rib cage, and noncompliant chest wall, older children and adults tend to maintain FRC when muscle tone is decreased following the administration of sedatives, anesthetics, or neuromuscular blockers. Infants and small children will respond to the administration of these agents by losing the FRC that depends on tonic muscular contraction, and thus rapidly develop hypoxemia. This effect can be overcome by application of continuous positive airway pressure (CPAP) or institution of positive-pressure breathing.

Differences in the anatomy of the infant diaphragm affect respiratory function. Prior to inspiration, the newborn diaphragm is relatively flat. Its anterior insertion onto the internal surface of the rib cage confers a mechanical disadvantage during inspiration when compared with the high-domed structure of the adult diaphragm (see Fig. 2-1). The muscular composition of the newborn’s diaphragm is also unique. In contrast to the adult diaphragm, which has a high proportion (50–60%) of slow-twitch, high-oxidative, fatigue-resistant fibers (type 1), the newborn diaphragm is made up of only 10–30% of type 1 fibers. This characteristic predisposes the newborn diaphragm to fatigue, and may contribute to the inherent instability of the chest wall, as well as apnea and respiratory failure in the face of increased ventilatory demands or work of breathing.

The relatively compliant chest wall plays a role in determining the work of breathing, and thus the respiratory rate. Respiratory rates normally range between 30 and 70 breaths per minute in full-term newborns; this declines gradually throughout childhood, and reflects the optimal rate at which work of breathing is minimized.

On a per-kilogram basis, tidal volume is the same for both neonates and adults, and ranges from 7 to 10 mL/kg. Since oxygen consumption is relatively high in neonates and small infants (6–7 mL/kg versus 3 mL/kg for the adult), minute ventilation must be increased to deliver a sufficient amount of oxygen into the lungs (nearly three times that of the adult). As a consequence, small children have a relatively increased ratio of minute volume to FRC. This results in more rapid oxyhemoglobin desaturation during ventilatory depression or apnea.

**Figure 2-1** Developmental changes of the rib cage and diaphragm from birth to adulthood. Adults can increase lung volume by raising the ribs and contracting the diaphragm. Early in development, the configuration of the rib cage and muscular attachments of the diaphragm place the newborn at a mechanical disadvantage because the ribs are already “raised,” and contraction of the diaphragm results in a relatively small increase in thoracic cavity volume. (Reproduced with permission from Devlieger H, Daniels H, Marchal G et al: The diaphragm of the newborn infant: anatomical and ultrasonographic studies. J Dev Physiol 16:321–329, 1991.)

**HEMATOLOGIC PHYSIOLOGY**

The hemoglobin concentration at birth is approximately 19 g/dL, of which about 70% is fetal hemoglobin (Hgb F). This relatively high concentration is a consequence of the requirement for an increased oxygen delivery in utero, when the oxyhemoglobin dissociation curve is shifted to the left, and oxygen is held tightly by Hgb F. Hgb F is progressively replaced by adult hemoglobin...
(Hgb A) during the first year of life. Production of erythropoietin is absent until hemoglobin levels drop to the physiologic nadir of about 9 or 10 g/dL at between 6 and 10 weeks of age. This is often referred to as the “physiologic anemia of infancy.” Although this relative anemia may decrease oxygen delivery to the peripheral tissues, it is offset by the increased production of Hgb A and increase in red-cell 2,3-diphosphoglycerate, both of which shift the oxyhemoglobin dissociation curve to the right, and facilitate unloading of oxygen to the peripheral tissues.

Coagulation factors are relatively low at birth and normalize within the first year of life (Table 2-1).

### CARDIOVASCULAR PHYSIOLOGY

Substantial cellular and structural changes occur in the heart in the first several months of life. Neonatal cardiac muscle cells contain all the normal structural elements of the adult heart, but are qualitatively and quantitatively different. The pattern of myofilaments is described as chaotic, compared to the long parallel rows of the mature heart. More specifically, the elements of the myocyte that are responsible for contraction are less able to function properly when challenged with a resistive load. Thus, force development is impaired when compared to the adult heart, and cardiac output is relatively less in response to changes in preload and afterload. This makes intuitive sense when one considers that during fetal life the left side of the heart has little responsibility against a low-pressure systemic circuit, but in the postnatal period must adapt to a higher stroke volume and increased wall tension.

The postnatal left ventricle develops into a thicker organ capable of contracting against higher systemic pressures by increasing the size and number of myocytes. In addition, the shape of the myocyte changes from spheroidal to one with more tapered edges, to increase efficiency of contraction. Factors that increase systemic vascular resistance (e.g., acidosis, cold, pain) in the newborn may lead to a decrease in cardiac output.

Therefore, it is possible that intraoperative cardiovascular stability can be enhanced in the newborn by preventing hypothermia and adequately blunting the stress response by titration of opioids. Indeed, studies in newborn cardiac anesthesia have suggested that a primarily opioid-based anesthetic technique is associated with improved postoperative cardiac function.

One of the most important clinical correlations of these morphological differences in the neonate is the decrease in compliance of the left ventricle. The newborn, therefore, is more prone to development of congestive heart failure during periods of fluid overload, as the left ventricle is less able to stretch in response to this increase in stroke volume. Also, because of this stiffness, distension of either ventricle will result in compression and dysfunction of the contralateral ventricle, thus further decreasing cardiac function. Newborns with respiratory disease who require high inspiratory pressures may develop left ventricular dysfunction with right ventricular overload. Perhaps more importantly, the newborn left ventricle is unable to shorten normally, and the heart is less able to increase left ventricular stroke volume during periods of hypovolemia or bradycardia. Thus, episodes of hypovolemia or bradycardia can drastically decrease cardiac output in the neonate, and will endanger end-organ perfusion.

These deficits in neonatal cardiac function are often misinterpreted to mean that the only method with which to increase cardiac output is by increasing the heart rate. However, cardiac output will fail to increase substantially by increasing the heart rate to levels significantly above normal. Volume expansion remains an effective method, albeit possibly less effective than in an older child, to increase blood pressure and cardiac output, especially during periods of hypovolemia.

Sympathetic innervation of the heart and production of catecholamines, which are not fully developed at birth, increase during postnatal maturation. In contrast, the parasympathetic system appears to be fully functional at birth. Thus, neonates and small infants will demonstrate an imbalance, such that seemingly minor

### Table 2-1 Effect of Age on Coagulation Tests

<table>
<thead>
<tr>
<th>Test</th>
<th>28–31 Weeks' Gestation</th>
<th>30–36 Weeks' Gestation</th>
<th>Full-term Newborn</th>
<th>1–10 Years</th>
<th>11–18 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prothrombin time (s)</td>
<td>15.4 (15–17)</td>
<td>13 (11–16)</td>
<td>13 (10–16)</td>
<td>11 (10–12)</td>
<td>11 (10–12)</td>
</tr>
<tr>
<td>Partial thromboplastin time (s)</td>
<td>108 (80–168)</td>
<td>54 (28–79)</td>
<td>43 (51–54)</td>
<td>30 (24–36)</td>
<td>32 (26–37)</td>
</tr>
<tr>
<td>Bleeding time (min)</td>
<td>≥</td>
<td>≥</td>
<td>≥</td>
<td>7 (3–15)</td>
<td>5 (3–8)</td>
</tr>
</tbody>
</table>

*a* Values are mean (normal range in parentheses).

*b* Unknown.
stimuli (suctioning of the pharynx) will result in an exaggerated parasympathetic or vagal response that results in bradycardia. For this reason, many pediatric anesthesiologists will routinely administer atropine prior to airway manipulation in small infants.

These structural and physiologic differences explain why neonates and infants under 6 months of age appear to be more sensitive to the depressant effects of volatile anesthetics, especially halothane. Isoflurane, sevoflurane, and desflurane depress myocardial contractility equally, though less than halothane.

The normal heart rate of the newborn ranges from 120 to 160 beats per minute (bpm), although lower rates (e.g., 70 bpm) are frequently observed during sleep, and higher rates (>200 bpm) are common during anxiety or pain. Heart rates tend to decrease with age, and parallel decreases in oxygen consumption. Many children have a noticeable variation in heart rate that varies with respiration (i.e., sinus arrhythmia).

Blood pressure increases gradually throughout childhood (Figs 2-2 and 2-3) and is also dependent on the height of the child such that taller children will demonstrate a higher blood pressure. Blood pressure ranges in premature infants have been defined (Table 2-2) and will vary depending on the health status of the infant and mother.

In most children, careful auscultation of the heart reveals a soft, vibratory, systolic flow murmur. A heart murmur is not considered normal when it is louder than II/VI or has a diastolic component. Peripheral pulses in children of all ages should be clearly palpable. Absence of femoral pulses may indicate an aortic arch abnormality. Capillary refill in the distal extremities should be brisk (<3 seconds), but may be slightly delayed in the first few hours of life. Distal limb cyanosis (acrocyanosis) is normal in the first few hours of life.

As described in Chapter 1, the fetal heart is characterized by right-sided dominance that gradually abates in the first few months of life as pulmonary pressures decrease toward normal adult values. The normal newborn electrocardiograph (Fig. 2-4) demonstrates a preponderance of right-sided forces with a mean QRS axis of +110 degrees (range +30 to +180 degrees), and decreasing R wave size from leads V1 to V6. T waves are normally inverted in lead AVR and the right-sided precordial leads. This gradually shifts to left-sided dominance during early
childhood as the left ventricle hypertrophies to its normal size and the electrocardiograph becomes more like that of an adult.

The newborn cardiac output (about 350 mL/kg/min) falls over the first 2 months of life to about 150 mL/kg/min and then more gradually to the normal adult cardiac output of about 75 mL/kg/min.

**Table 2-2** Blood Pressure Ranges in Healthy Premature Infants (birthweight 501–2000 g)*

<table>
<thead>
<tr>
<th>Age (days)</th>
<th>Systolic (mmHg)</th>
<th>Diastolic (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Minimum</td>
<td>Maximum</td>
</tr>
<tr>
<td>1</td>
<td>48±9</td>
<td>65±12</td>
</tr>
<tr>
<td>2</td>
<td>54±10</td>
<td>65±12</td>
</tr>
<tr>
<td>3</td>
<td>55±9</td>
<td>67±10</td>
</tr>
<tr>
<td>4</td>
<td>57±10</td>
<td>71±11</td>
</tr>
<tr>
<td>5</td>
<td>56±9</td>
<td>72±14</td>
</tr>
<tr>
<td>6</td>
<td>57±9</td>
<td>71±11</td>
</tr>
</tbody>
</table>

*Values are mean ± standard deviation.


**Figure 2-3** Age-specific percentiles for blood pressure measurements in boys, from 1 to 13 years of age. Values for girls are slightly lower. (From National Heart, Lung, and Blood Institute, Bethesda, MD: Report of the Second Task Force on Blood Pressure Control in Children, 1987. Reproduced with permission from *Pediatrics* 79:1. Copyright 1987.)

**RENAL PHYSIOLOGY**

By the 36th week of gestation, the formation of nephrons in the kidney is complete. However, the nephrons are small, and the glomerular filtration rate (GFR) is only 25% of adult values at birth. GFR reaches adult levels over the first several weeks of life. Tubular function is also immature - the ability to concentrate and dilute the urine is impaired in the immediate newborn period. The maximal concentrating ability of the full-term newborn is 700 mOsm/L; the adult value of
1200 mOsm/L is attained within the first several months of life. Therefore, intraoperative evaporative fluid losses may result in development of hypernatremia in the neonate.

In newborn infants, daily fluid intake is gradually increased from 80 mL/kg on the first day of life to 150 mL/kg by the third or fourth day of life, and is adjusted based on additional factors, such as extreme prematurity or use of a radiant warmer, in which evaporative losses from the skin are increased. Neonates who are unable to ingest enteral feeds will receive supplementation of electrolytes (sodium, potassium, and calcium) on the second day of life (Table 2-3). Normal daily sodium requirement is 2-3 mEq/kg.

### Table 2-3 Normal Newborn Daily Electrolyte Requirements

| Electrolyte | Average Daily Requirement *
|-------------|------------------------
| Sodium      | 2–3 mEq/kg             
| Potassium   | 1–2 mEq/kg             
| Calcium     | 150–200 mg/kg          

*Adjusted to normal values on a daily basis.

**CENTRAL NERVOUS SYSTEM (CNS) PHYSIOLOGY**

The skull and central nervous system undergo a substantial amount of postnatal maturation. At birth, the brain is encased within several pieces of the skull that are separated by strong, fibrous, elastic tissues called “cranial sutures” (Fig. 2-5). The anterior fontanel, located at the junction of the frontal and parietal bones, is formed by the intersection of the metopic, coronal, and sagittal sutures; it normally closes by 20 months of age. The posterior fontanel, located at the junction of the parietal and occipital bones, is formed by the intersection of the lambdoid and sagittal sutures; it usually closes by 3 months of age.

The metabolic demand of the brain increases throughout the first year of life and then decreases gradually throughout childhood. The average cerebral metabolic rate of oxygen consumption (CMRO₂) of the child’s brain (5.2 mL/min of oxygen per 100 g of brain tissue) is greater than in the adult’s brain (3.5 mL/min/100 g) and greater than that of anesthetized newborns and infants (2.3 mL/min/100 g).

Cerebral blood flow (CBF) is closely coupled to the CMRO₂. Whereas in adults the CBF is 50–60 mL/min per 100 g of brain tissue, the CBF of premature and term...
newborns is approximately 40 mL/min/100 g; in older children the CBF may reach 100 mL/min/100 g. Autoregulation of CBF is based on systemic blood pressure and is thought to occur in newborns, but the limits are unknown. Extrapolation from animal studies indicates an approximate range of 20–80 mmHg, in contrast to the adult whose autoregulatory limits lie between 60 and 150 mmHg.

**DEVELOPMENTAL PHARMACOLOGY**

The broad subject of pharmacology encompasses the study of **pharmacokinetics**, the body’s influence on the drug, and **pharmacodynamics**, the drug’s influence on the body. Each of these two components is influenced by age, especially during the first few weeks of life. Thus the major differences in pharmacology between adults and children occur in early life, when the factors of body composition that influence pharmacokinetics and pharmacodynamics are decidedly different. This section will review the ways in which these factors influence the pharmacology of intravenous and inhalational anesthetics in children.

**Pharmacokinetics of Intravenous Drugs**

The term “pharmacokinetics” describes the physiological processes that alter a drug’s disposition after entering the body. Pharmacokinetic processes determine the amount of drug that arrives at the effect site (usually the central nervous system for general anesthetic agents) at a given point in time (i.e. the “effect site” concentration), and the speed at which it arrives. The two general pharmacokinetic processes of interest are those that determine the rate and amount of drug that initially reaches the effect site, and those that determine the rate and amount of drug that leaves the effect site. These two processes, which are of prime importance to anesthesiologists, are determined by a drug’s unique combination of pharmacokinetic parameters: volume of distribution, distribution clearance, protein binding, and elimination clearance (metabolism and excretion). Each of these parameters will be discussed, with an emphasis on the changes that occur during development.

**Volume of Distribution**

The total (or steady-state) volume of distribution is the calculated amount of plasma into which the drug appears to have distributed at some specified interval after intravenous administration. The volume of distribution is not a discrete body compartment, but rather is calculated by dividing the dose administered by the plasma concentration. Put another way, the dose of an intravenously administered drug is determined by multiplying the volume of distribution and the desired effect site concentration:

\[
\text{Dose (mg/kg)} = \text{volume of distribution (L/kg)} \times \text{desired effect site concentration (mg/L)}
\]

The relative percentage of extracellular and total body water is greatest at birth and declines with advancing age during childhood (Fig. 2-6). Since younger children have a relatively greater amount of extracellular body water, and possess adipose stores with a relatively higher ratio
of water to lipid than adults, the volume of distribution for water-soluble drugs, such as neuromuscular blockers, will be greater. A larger volume of distribution will be reflected as a larger loading (bolus) dose to achieve the desired plasma concentration and, if clearance is unchanged, a longer half-life.

**Protein Binding**

Parenterally administered medications are bound primarily to two proteins that are manufactured in the liver: albumin and α1-acid-glycoprotein. Albumin binds weak acids (e.g., aspirin), while α1-acid-glycoprotein binds weak bases (e.g., local anesthetics). Albumin levels are only slightly reduced in the newborn period but may have some qualitative immaturity. Alpha1-acid-glycoprotein is not fully produced until some time in the first year of life. Therefore, drugs such as local anesthetics that are normally bound to α1-acid-glycoprotein may have a larger free fraction in the blood of young infants, which predisposes to systemic toxicity.

**Metabolism**

Most intravenously administered anesthetic-related drugs are lipid soluble and, therefore, are metabolized in the liver or in the bloodstream. In general, children have more rapid clearance of drugs because of the relatively high proportion of blood traversing the liver. However, in neonates, the phase I (cytochrome-dependent) reactions - oxidation, reduction, and hydrolysis - are not fully developed. Therefore, some anesthetic-related drugs that rely on hepatic metabolism for termination of their action (e.g., vecuronium) may last longer than anticipated. These processes are usually fully functional within the first week after birth. However, the activity of some cytochromes, such as CYP3A4 and CYP3A5, which metabolize intravenous midazolam, continue to increase during the first 3 months of life. It appears that chronological age, not postconceptional age, is important for development of these metabolic pathways.

The phase II reactions consist primarily of conjugation with sulfate, acetate, glucuronic acids, and amino acids. These reactions convert the parent drug to a more polar metabolite by introducing or unmasking a functional group (-OH, NH2, -SH). These reactions are limited at birth but mature within the first few weeks of age, and may differ between classes of drugs.

**Excretion**

Excretion of intravenously administered anesthetic-related drugs is primarily via the kidney. In the first several weeks of life, especially in infants born at less than 34 weeks’ gestation, GFR is below normal values, so excretion of drugs may be delayed. After the first several weeks of life, GFR and tubular secretion rise steadily until adult values are reached at 8–12 months of age.

**Elimination Clearance**

Clearance is the volume of drug removed by metabolism or excretion per unit of time. Like the volume of distribution, it is a calculated value that is obtained by dividing the continuous infusion dose of a drug by the resulting plasma concentration:

\[
\text{Clearance (L/kg/h)} = \frac{\text{dose (mg/kg/h)}}{\text{plasma concentration (mg/L)}}
\]

Infants and children tend to have a more rapid clearance of drugs than adults, and for drugs metabolized in the liver, there is an age-dependent increase in plasma clearance up to approximately 10 years of age. The mechanism of this is largely unknown, but it may be related to the fact that the liver receives a proportionately higher fraction of cardiac output in children than in adults.

**Pharmacodynamics of Intravenous Anesthetic Agents**

Pharmacodynamics refers to the processes that affect the drug’s action at a given plasma (or effect site) concentration. Developmental pharmacodynamic differences for most intravenously administered anesthetic agents are not well studied. However, it appears that neonates may be more sensitive to drugs that act in the central nervous system. This may be due, in part, to an age-dependency for passive diffusion into the brain (i.e., an immature blood–brain barrier), and relatively greater central nervous system blood flow in neonates and small infants.

**Pharmacokinetics of Inhalational Anesthetics**

A variety of pharmacokinetic factors can influence the concentration of inhalational anesthetics in the brain and the speed at which this process occurs (i.e., uptake and distribution). The rate of rise of inhalational anesthesia into the lungs is determined by the delivered concentration of the anesthetic and the minute ventilation of the patient, and is quantitatively described as the alveolar to inspired concentration ratio \(F_{al}/F_{in}\). Compared with adults, children demonstrate a higher minute ventilation per bodyweight and a higher tidal volume to FRC ratio, so the \(F_{al}/F_{in}\) ratio rises faster during an inhalational induction.

Once in the lungs, uptake of the anesthetic into the bloodstream is determined by the cardiac output, the blood-gas coefficient of the anesthetic agent, and the arterial-to-venous \((A-V)\) concentration difference. All of these factors are influenced by the developmental age of the child.

Cardiac output per bodyweight is relatively higher in children than in adults. A higher cardiac output will tend to slow inhalational induction of anesthesia by removing anesthetic from the alveoli at a more rapid rate.
The blood-gas partition coefficient will determine the speed at which the inhalational anesthetic equilibrates between the alveolar gas and the blood. Although blood-gas partition coefficients have been shown to be lower in small children, it is to an insignificant degree and without clinical importance.

Anesthetic breathed into the alveoli moves into the bloodstream based on the concentration gradient difference between the alveolus and the blood in the pulmonary artery. Therefore, the larger the pulmonary A-V concentration difference, the more rapid the anesthetic will leave the alveoli, and thus the speed of induction is slowed. Upon initial uptake of inhalational anesthetic from the alveoli into the bloodstream, the anesthetic will be distributed to the various body tissues. As anesthetic partial pressures in tissues equilibrate with those in the blood, the concentration of the agent that returns to the lungs in the pulmonary artery increases. Consequently, the A-V difference decreases, which reduces the amount of anesthetic agent that is removed from the alveoli. This increases the partial pressure of the anesthetic agent in the alveolus and speeds loss of consciousness. Children demonstrate a faster decrease in the A-V difference because of their proportionately larger vessel-rich group that equilibrates anesthetic relatively faster than in adults (Table 2-4). As children grow, they increase their content of muscle and fat and take longer to equilibrate inhalational anesthetic.

The combination of these differences in factors that affect uptake and distribution of inhalational anesthetics results in children demonstrating a more rapid induction of inhalational anesthesia when compared with adults.

### Pharmacodynamics of Inhalational Agents

The relative potency of inhalational anesthetics, which is quantitatively described as the minimum alveolar concentration (MAC), changes with age (Fig. 2-7). MAC is relatively low for premature infants and gradually increases with age until approximately 6 months of age, after which it tends to decrease with advancing age. The reasons for these changes in anesthetic potency with age are unknown.

<table>
<thead>
<tr>
<th>Table 2-4</th>
<th>Effect of Age on Body Compartments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Group</td>
<td>Vessel-rich Group</td>
</tr>
<tr>
<td>Newborn</td>
<td>22.0%</td>
</tr>
<tr>
<td>1 year</td>
<td>17.3%</td>
</tr>
<tr>
<td>4 years</td>
<td>16.6%</td>
</tr>
<tr>
<td>8 years</td>
<td>13.2%</td>
</tr>
<tr>
<td>Adult</td>
<td>10.2%</td>
</tr>
</tbody>
</table>

**Figure 2-7** Changes in MAC with age. (Reproduced with permission from Miller RD: *Anesthesia*, 5th edn, Churchill-Livingstone, Edinburgh, 2000.)

**ARTICLES TO KNOW**


