Adaptation for life: a review of neonatal physiology

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Abstract

The neonatal period (first 28 days of life or 44 weeks postconceptual age) contains the most dramatic and rapid physiological changes seen in humans. They vary from the immediate changes seen in the respiratory and cardiovascular systems to the slower progression seen in the hepatic, haematological and renal systems. These adaptations support life during the development from intrauterine physiology to adult physiology. This article describes neonatal physiological changes in a system-based approach, including slower changes that may extend beyond the neonatal period.

Keywords Cardiovascular changes; fetal haemoglobin; fluid balance; neonatal adaptation

The respiratory system

The fetal respiratory system

Lungs develop from the third week of gestation with completion of the terminal bronchioles by week 16. However, type I and II pneumocytes are distinguishable only by 20—22 weeks and surfactant is present only after 24 weeks, making this the watershed time for pulmonary gas exchange and therefore extra-uterine survival. Surfactant production can be increased after 24 weeks by giving betamethasone to the mother, thereby improving neonatal lung function if premature delivery is anticipated. Alveolar development continues after birth, increasing fivefold in number to 300 million by 5—6 years of age.

The first breath

Fluid is compressed from the fetal lung during vaginal delivery starting the process of establishing lung volume (Table 1). The coordinated first breath is initiated centrally secondary to arousal from sound, temperature changes and touch associated with delivery. Central chemoreceptors stimulated by hypoxia and hypercarbia further increase respiratory drive.

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Learning objectives

After reading this article, you should be able to understand the physiological changes which take place following birth and appreciate the unique aspects of neonatal physiology including:
- limited reserve capacity for temperature control, cardiovascular and respiratory function
- variable and individualized fluid requirements
- implications of hepatic and renal immaturity

The initial breaths generate high negative-inspiratory pressures to facilitate lung expansion by overcoming:
- airways resistance
- inertia of fluid in the airways
- surface tension of the air/fluid interface in the alveolus.

Alveolar distension, cortisol and epinephrine all stimulate type II pneumocytes to produce surfactant and reduce alveolar surface tension; facilitating lung expansion. Negative inspiratory

Normal pulmonary function and cardiovascular values

Measurement	Preterm neonate	Term neonate	Adult
Total lung capacity (ml/kg)	55—70	55—70	80—85
Tidal volume (ml/kg)	5—7	5—7	7
Functional residual capacity (ml/kg)	20—25	27—30	30
Vital capacity (ml/kg)	35—40	35—40	60
Respiratory rate (breaths/min)	30—50	30—50	12—16
Alveolar ventilation (ml/kg/min)		100—150	60

Measurement	Term neonate	2 year old	Adult
Heart rate (beats/min)	120—160	75—115	70—90
Systolic blood pressure (mmHg)	60	95	120
Diastolic blood pressure (mmHg)	35	60	80
Cardiac output (ml/kg/min)	200	100	70
Circulating blood volume (ml/kg)	90	80	70
Haemoglobin (g/dl)	16—18	10.5—13.5	12—17

The neonate has a reduced inspiratory reserve volume compared with adults, indicated by similar tidal volume and functional residual capacity values with a diminished total lung capacity. Significant increases in minute volume must be achieved by an increase in respiratory rate rather than tidal volume. The high cardiac output supplies the high metabolic demand of extra-uterine life. Systolic and diastolic blood pressures rise to 70/40 at the end of the first week and 90/50 by 6 months, under the control of the maturing sympathetic nervous system.

Adapted from Rennie JM, Robertson NRC, eds. A manual of neonatal intensive care, 4th edn. London: Hodder Education, 2002.

Table 1

pressures of up to 70–100 cm H_2O are initially required to expand the alveoli (LaPlace's relationship P =2 T/R; where P is the pressure across the alveolar wall, T is the tension in the alveolar wall surface fluid, and R is the radius of the alveolus).

As the alveoli expand, the alveolar radius increases and the wall tension of the alveolus falls. Exogenous surfactant is administered to preterm neonates to reduce alveolar wall tension and facilitate mechanical ventilation. Expiration is initially active, with pressures of 18–115 cm H_2O generated,[1] forcing amniotic fluid from the bronchi. Lung expansion and increased alveolar oxygen content reduce pulmonary vascular resistance, increasing blood flow and initiating the cardiovascular changes described later.

Neonatal lung mechanics

A marked imbalance exists between chest wall rigidity and elastic recoil of neonatal lungs. The chest wall is highly compliant, offering little support to the uncompliant lungs containing immature elastic fibres thus facilitating airway collapse. These two factors increase closing capacity to the point of exceeding functional residual capacity (FRC) until the age of 6. To counteract this, neonates produce positive end expiratory pressure (PEEP) via high-resistance nasal airways and partial closure of the vocal cords.

Inspiratory reserve volume is limited by a flatter diaphragm and more horizontal ribs. Therefore, an increase in minute volume must be achieved by an increase in respiratory rate. High respiratory rates of 30–50 breaths per minute reduce the workload of breathing while maintaining minute volume. However, respiratory fatigue is common in neonates because the diaphragmatic and intercostal muscles lack type 1 oxidative fibres.

Gas exchange across the alveolar membrane is immature in neonates, with a total shunt estimate of 24% of the cardiac output at birth, reducing to 10% of cardiac output at 1 week.[1] This rapid reduction in shunt fraction improves arterial oxygenation and reduces the effort of breathing. Neonatal lung mechanics have significant implications during anaesthesia. The effective FRC is reduced, as physiological PEEP and intercostal muscle tone is lost. These factors, together with an increased shunt fraction and high metabolic rate (6–8 ml of O_2/kg/minute), contribute to a potential rapid desaturation in neonates under anaesthesia.

Control of ventilation

Respiratory rhythm is generated in the venterolateral medulla, and modulated by central chemoreceptors in response to carbon dioxide, pH and oxygen content in the blood. Peripheral chemoreceptors in the aortic and carotid bodies are functional at birth but are initially silent because of high postdelivery blood oxygen content. Receptor adaptation occurs over 48 hours, permitting an appropriate response to the higher oxygen tension. The neonatal response to hypoxia is characterized by an initial increase in ventilation followed by a decrease in ventilation; reverting back to a fetal response. Ventilatory changes to hypoxia alter with neonatal temperature, level of arousal and maturity. The response to hypercarbia is the same as in adults, but is more rapid because of a lower resting carbon dioxide level.

All neonates can show a periodic breathing pattern defined as an apnoea of less than 5 seconds, often followed by tachypnoea. Premature neonates may exhibit apnoeic episodes of more than 15 seconds or a shorter period associated with a fall in heart rate.

This temporary loss of central respiratory drive improves with maturity[2] but may persist up to 60 weeks postconceptual age.

Cardiac changes

The fetal circulation

Oxygenated placental blood is preferentially delivered to the brain, myocardium and upper torso, with lower oxygen tension blood distributed to the lower body and placenta. Preferential splitting is achieved via intra- and extracardiac shunts that direct blood into two parallel circulations (Figure 1). Oxygenated blood returning from the placenta divides equally to pass either through the liver or via the ductus venosus to reach the inferior vena cava. Oxygenated blood from the ductus venosus remains on the posterior wall of the inferior vena cava, allowing it to be directed across the foramen ovale into the left atrium by the Eustachian valve. This oxygenated blood then passes through the left ventricle and aorta to supply the head and upper torso. Deoxygenated blood returning from the superior vena cava and myocardium via the coronary sinus is directed through the right ventricle and into the pulmonary artery. Most of this blood is returned to the descending aorta via the ductus arteriosus; however, approximately 8–10% of total cardiac output passes through the high-resistance pulmonary circulation. Blood in the descending aorta either supplies the umbilical artery to be re-oxygenated at the placenta or continues to supply the lower limbs. The fetal circulation therefore runs in parallel, the left ventricle providing 35% and the right 65% of cardiac output. Fetal cardiac output is therefore measured as a combined ventricular output (CVO).

At birth

Successful transition from fetal to postnatal circulation requires increased pulmonary blood flow, removal of the placenta and closure of the intracardiac (foramen ovale) and extracardiac shunts (ductus venosus and ductus arteriosus). These changes produce an adult circulation in series with right ventricular output equalling that of the left.

Shunt closure and neonatal circulation

Umbilical vessels constrict in response to stretching and increased oxygen content at delivery. The vessels are usually clamped to remove the large low-resistance placental vascular bed from the circulation and increase systemic vascular resistance. Blood passing through the ductus venosus is suddenly reduced, causing passive closure over the following 3–7 days[3] and immediately reducing blood return to the inferior vena cava. Lung expansion drops pulmonary vascular resistance, causing a marked increase in blood returning to the left atrium. These two changes reduce right atrial and increase left atrial pressures, functionally closing the foramen ovale within the first few breaths of life. A physiological reverse shunt from left to right commonly occurs. The foramen ovale is completely closed in 50% of children by 5 years. It remains probe patent in 30% of adults, which can facilitate paradoxical embolus and potential stroke.

The resultant drop in pulmonary artery pressure and increase in systemic vascular resistance reverses flow across the ductus arteriosus from left to right. Unlike the passive closure of the ductus venosus, the ductus arteriosus is affected by blood oxygen content and circulating prostaglandins. The potent dilator prostaglandin E_2 produced by the placenta is lost at birth, facilitating

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Differences between fetal and postnatal circulatory systems

a Fetal circulation

Lungs
High resistance
Low flow

Ductus arteriosus

Aorta

Foramen ovale

Right atrium

1/3

2/3

Left atrium

Left ventricle

Right ventricle

Inferior vena cava

Ductus venosus

Low peripheral resistance
High flow

The red arrows denote oxygenated blood

Placenta
Low resistance

b Postnatal circulation

Lungs
Falling resistance
Increased blood flow

Active closure of ductus arteriosus

Aorta

Increased pulmonary return to left atrium closes foramen ovale

Right atrium

Foramen ovale

Left atrium

1/2

1/2

Left ventricle

Right ventricle

Reduced vena cava blood flow

Passive ductus venosus closure

Increased peripheral resistance
Increased blood pressure

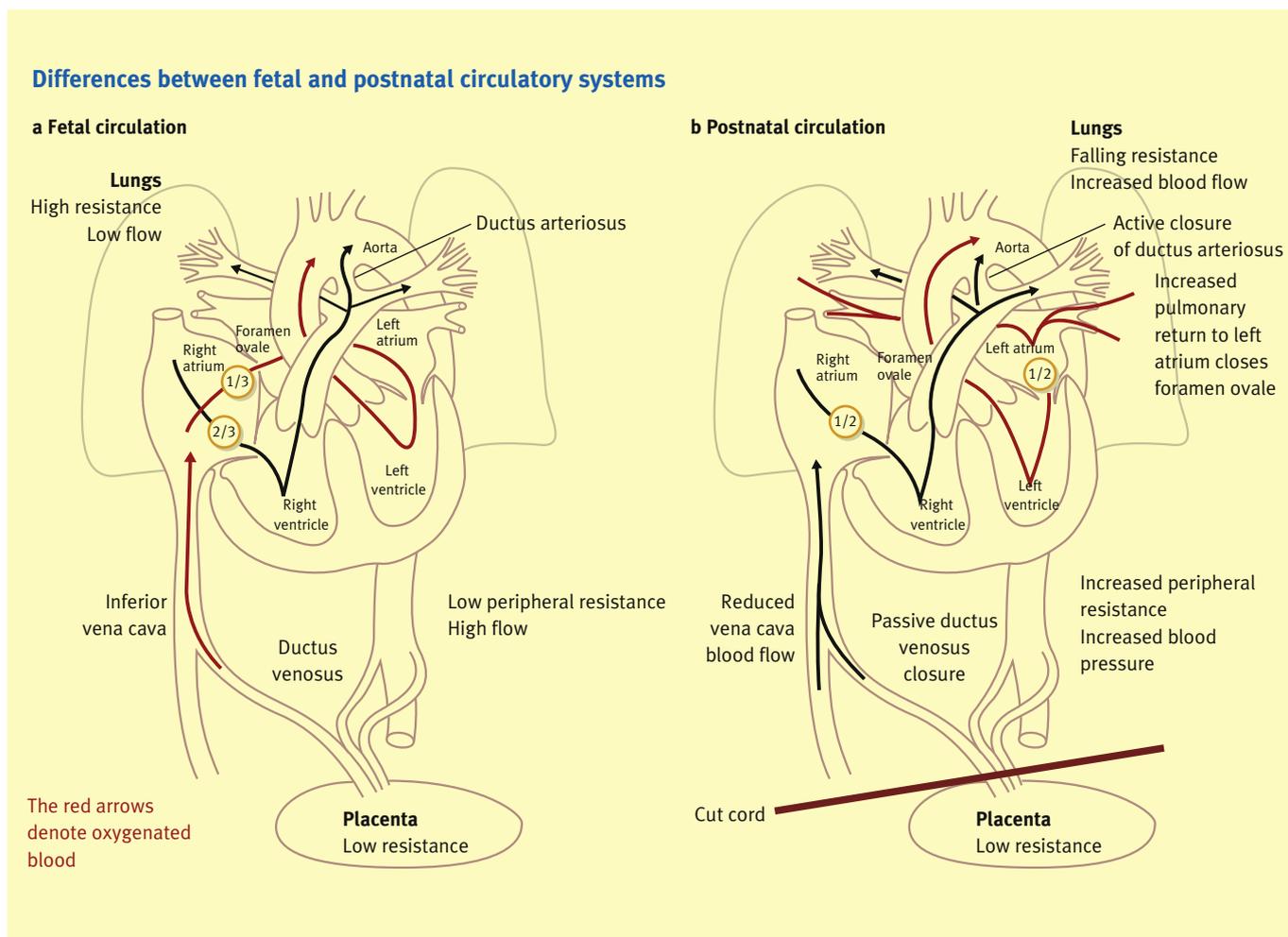Cut cord

Placenta
Low resistance

Figure 1

ductus arteriosus closure. Functional closure of the ductus arteriosus occurs by 60 hours in 93% of term infants. Over the subsequent 4–8 weeks permanent structural closure occurs via endothelial destruction and subintimal proliferation.[4] Any stimulus such as hypoxia, acidaemia or structural anomaly can increase pulmonary vascular resistance and potentially re-open the ductus arteriosus or foramen ovale. This allows a right-to-left shunt, which worsens hypoxia. This effect is seen in persistent pulmonary hypertension of the newborn.

Neonatal cardiac output
Circulating thyroid and catecholamine hormones increase myocardial maturity in late gestation, improving contractile ability in anticipation of birth. At delivery there is a large surge in circulating catecholamines, which improves myocardial function and allows output to meet the marked metabolic oxygen demand associated with spontaneous thermogenesis, feeding and breathing. At term, the neonatal cardiac output is approximately 200 ml/kg/minute,[5] more than twice that of adults (Table 1). However, the neonatal myocardium has fewer myofibrils in a disordered pattern, making the myocardium stiffer. The neonatal heart follows the Frank–Starling relationship of filling pressure to stroke volume, but on a much flatter section of the curve compared with adults. This leads to a limited increase in stroke volume for a given increase in ventricular filling volume. The neonatal myocardium is therefore more dependent on heart rate to increase cardiac output. Despite this physiological limitation cardiac output can respond to increased ventricular filling.[4]

Ventricular maturation and associated ECG changes
The fetal heart is right-side dominant, with the right ventricle responsible for 65% of cardiac output *in utero*. The neonatal ECG reflects this with right axis deviation and R wave dominance in lead V_1 and S wave dominance in lead V_6. At 3–6 months the classical left ventricular dominance pattern of adulthood is established as ventricular hypertrophy occurs in response to increased systemic vascular resistance.

Haematology

Neonatal blood contains both adult (HbA) and fetal haemoglobin (HbF). HbF is made up of the four globin chains $\alpha_2\gamma_2$ in contrast to HbA, which is made up of $\alpha_2\beta_2$. This structural difference of HbF provides a greater affinity for oxygen and helps maintain the molecular structure and function in a more acidic environment. The increased oxygen affinity of HbF facilitates oxygen transfer across the placenta from maternal HbA. Postdelivery, the high oxygen affinity of HbF becomes detrimental as oxygen is not

readily given up to the tissues. The HbF oxygen dissociation curve is moved to the left after delivery due to an increased pH and lower carbon dioxide concentration further limiting oxygen delivery to the peripheries. This inability to release oxygen to the periphery places greater demand on cardiac output to meet tissue oxygen requirements. At term, HbF makes up 70−80% of total haemoglobin; this is increased to 90% of total haemoglobin in the preterm baby. Oxygen delivery to the peripheries is facilitated by an increase in 2,3-diphosphoglycerate levels, shifting the oxygen dissociation curve to the right, thus decreasing the affinity of HbF for oxygen (Figure 2) and improving tissue supply. This adaptation sustains oxygen delivery to the peripheries until HbF is replaced with HbA at approximately 6 months of age. Haematopoiesis occurs in the liver *in utero* but is restricted to bone marrow from 6 weeks postdelivery, thus limiting potential sites for haemoglobin synthesis. HbF is lost faster than HbA is synthesized. A combination of low levels of erythropoietin due to improved tissue oxygenation after birth, decreased lifespan of HbF-laden red blood cells and a relative increase in the blood volume, contributes to the shrinking cell mass leading to the physiological anaemia of infancy which usually occurs at around 8−10 weeks of age.

Clotting

Clotting factors do not cross the placenta; however, factors V, VIII and XIII are at adult concentrations before birth. The vitamin K-dependent clotting factors (II, VII, IX, X, protein C and S) are initially low because of a lack of vitamin K stores and immature hepatocyte function causing a prolongation in prothrombin time. Breast milk is a relatively poor source of vitamin K and endogenous synthesis by the gut flora is not established for the first few weeks after birth. Therefore, vitamin K prophylaxis is administered to all newborn babies to protect against haemorrhagic disease of the newborn until normal levels of vitamin K are synthesized. Platelet function is diminished due to low levels of serotonin and adenine nucleotides, despite platelet counts in the adult range.

Thermoregulation

Heat loss

Neonates and, in particular, premature neonates are at high risk of heat loss and subsequent hypothermia. Hypothermic preterm babies have a poor outcome in the intensive care setting and therefore body temperature must be aggressively regulated. Neonates have a 2.5−3.0 times higher surface area to bodyweight ratio compared with adults, increasing the relative potential surface for heat loss. This is exacerbated by the limited insulating capacity from subcutaneous fat and the inability of neonates to generate heat by shivering until 3 months of age. Heat can be lost by radiation (39%), convection (34%), evaporation (24%) and conduction (3%). Loss of heat by radiation can be minimized by increasing the temperature of the surrounding environment. However, if the environmental temperature exceeds neonatal temperature then heat will be gained, which can be harmful as the ability to sweat is present only after 36 weeks postconceptual age. Convective heat loss from exposed surfaces to the surrounding air can be minimized by warming surrounding air and minimizing air speed across the baby's skin. Evaporation of water from body surfaces draws heat from the neonate, and is particularly important at birth when the newborn baby is covered in amniotic fluid or in the premature baby where the skin is porous to water. Evaporative heat loss is reduced by increasing ambient humidity and reducing air speed across the neonate. Insensible water loss through the skin can be minimized by putting the preterm neonate in a plastic bag or covering the body, and especially the head, with bubble wrap.

Mechanisms of thermogenesis

The neonate can produce heat by limb movement and by stimulation of brown fat (non-shivering thermogenesis). Brown fat makes up about 6% of term bodyweight and is found in the interscapular region, mediastinum, axillae, vessels of the neck and perinephric fat. It is highly vascular with sympathetic innervation and high mitochondrial content to facilitate heat generation. Norepinephrine is released from sympathetic neurons, activating protein kinases via β_3-receptors and adenylcyclase to stimulate lipases to break down triglycerides to glycerol and free fatty acids. Under the control of uncoupling, protein-1 free fatty acids undergo oxidative phosphorylation in the mitochondria to produce the required energy and heat. Non-shivering thermogenesis can double heat production, but at the expense of markedly increasing oxygen demand. This homeostatic mechanism can be impaired in the first 12 hours of life due to maternal sedation, particularly with benzodiazepines and during/after general anaesthesia, increasing the risk of hypothermia unless anticipated. The term neonate is able to vasoconstrict, diverting blood from the peripheries to the body core maintaining temperature. However, this homeostatic control mechanism is not present in the preterm neonate further increasing the risk of hypothermia in this age group.
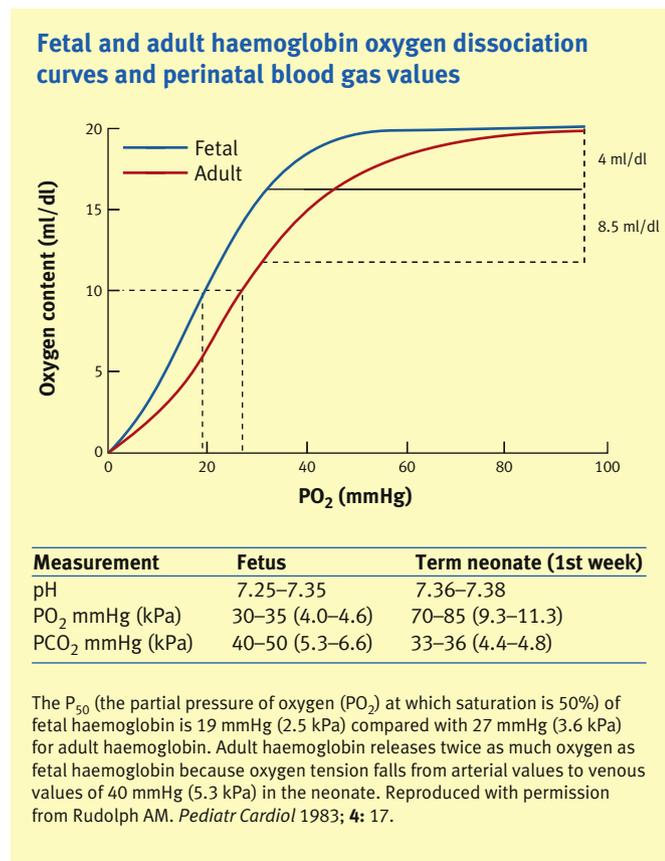

Fetal and adult haemoglobin oxygen dissociation curves and perinatal blood gas values

Measurement	Fetus	Term neonate (1st week)
pH	7.25–7.35	7.36–7.38
PO$_2$ mmHg (kPa)	30–35 (4.0–4.6)	70–85 (9.3–11.3)
PCO$_2$ mmHg (kPa)	40–50 (5.3–6.6)	33–36 (4.4–4.8)

The P$_{50}$ (the partial pressure of oxygen (PO$_2$) at which saturation is 50%) of fetal haemoglobin is 19 mmHg (2.5 kPa) compared with 27 mmHg (3.6 kPa) for adult haemoglobin. Adult haemoglobin releases twice as much oxygen as fetal haemoglobin because oxygen tension falls from arterial values to venous values of 40 mmHg (5.3 kPa) in the neonate. Reproduced with permission from Rudolph AM. *Pediatr Cardiol* 1983; **4:** 17.

Figure 2

Thermoneutral environment

Thermal stress is the extra energy required to maintain normothermia. It can occur with a normal core temperature as the neonate uses extra energy to maintain normothermia. Thermal stress can also occur if a baby is overheated because energy must be used to lose heat. The thermoneutral environment therefore minimizes neonatal energy requirements in maintaining a normal core temperature of 36.5–37.5°C rectal (axilla is 0.5–1.0°C lower). The thermoneutral temperature range varies with age and whether the baby is wearing clothes or not. The range for a naked term baby at 1 week is 32.0–33.5°C and 24.0–27.0°C when the baby is clothed. In comparison, a 30-week gestation baby's range is 34.0–35.0°C naked and 28.0–30.0°C clothed. The point at which an increase in metabolic rate is required to maintain normothermia is defined as the critical temperature.

The operating room environment must maintain neonatal thermoneutrality. Radiation heaters, increased ambient theatre temperature, warming blanket, plastic covers and head covering reduce radiation and evaporative losses. Warmed intravenous fluids and humidified warm airway gases should also be used to minimize heat loss.

Hepatic

Most enzymatic pathways are present in the neonate, but are inactive at birth and generally become fully active at 3 months postdelivery. An example of this is the conjugation pathway for bilirubin, which is inactive at birth but is fully established at 2 weeks. Unconjugated bilirubin levels rise during the first 48 hours because of the rapid breakdown of HbF and poor conjugating abilities of the immature liver. This rise can be exacerbated in the presence of haemolysis, sepsis, dehydration or excessive bruising; and if uncontrolled, pathological levels of circulating bilirubin can cross the blood–brain barrier causing kernicterus and subsequent developmental delay. Bilirubin levels gradually fall over the first 2 weeks, with jaundice in term infants being rare beyond this period.

Renal

A full complement of 1 million nephrons is present by 34 weeks' gestation. The glomeruli and nephrons are immature at birth, resulting in a reduced glomerular filtration rate (GFR) and limited concentrating ability. Lack of renal medulla osmotic gradient and absence of medullary tubules limit urinary concentrating ability. The concentrating capacity of the neonatal kidney (600 mOsm/kg) is about half that of the adult (1200–1400 mOsm/kg). GFR is gestational age related; the GFR is reduced with increasing prematurity. At 41 weeks postconceptual age the GFR is 1.5 ml/kg/minute (20–40 ml/minute/1.73 m^2), increasing to adult levels of 2.0 ml/kg/minute (120 ml/minute/1.73 m^2) by 2 years of age.[6] A limited ability to concentrate urine and the reduced GFR make the neonate susceptible to both dehydration and fluid overload.

Plasma creatinine levels at birth poorly reflect neonatal renal function. They initially mirror maternal values of 70–90 μmol/litre but rapidly fall to approximately 30 μmol/litre by week 2, where levels remain for the rest of the neonatal period. Glycosuria and aminoaciduria are commonly detected because of immature active transport pumps in the proximal tubule.

Renal immaturity also affects vitamin D formation and calcium homeostasis. The fetus and neonate have a high calcium and phosphate requirement for bone formation and growth. *In utero,* active calcium transport provides higher fetal calcium levels than maternal levels. At birth this source is removed, forcing rapid alteration in calcium homeostasis mechanisms. Levels initially fall to adult values and then climb again as parathyroid hormone and vitamin D control rapidly mature. The effect of parathyroid hormone on phosphate loss is reduced in the neonatal kidney, allowing elevated levels and thus satisfying growth requirements.

Body fluid composition

At term, 75% of neonatal bodyweight is water, which is distributed predominantly in the extracellular compartment (40%). In preterm neonates the water content is even higher at 80–85% of bodyweight, split in a ratio of 2:1, extracellular to intracellular. For the first 12–24 hours of life, urine output is limited to 0.5 ml/kg/hour due to poor renal perfusion, which improves with circulatory adaptation. Following this initial oliguric phase, a period of natriuresis ensues. Isotonic fluid is lost from extracellular compartments, accounting for the steady 1–2% bodyweight per day weight loss seen in the first 5 days. The diuresis reduces the extracelluar water content to 30% of total body water over the neonatal period. This fluid loss is an important postnatal adaptation to facilitate lung function and reduces the risks of symptomatic patent ductus arteriosus, necrotizing enterocolitis and bronchopulmonary dysplasia.[7]

Fluid requirements

Insensible fluid losses (e.g. stool, respiratory and skin evaporation) must be considered when caring for the neonate; fluid losses from the stool alone are approximately 5 ml/kg/24 hours. The 25-week neonate can lose 15 times as much transdermal fluid as the term neonate. After 32–34 weeks transdermal losses fall to 12 ml/kg/day, but can vary widely with ambient conditions. Insensible losses are replaced using weight and sodium concentration for guidance. Fluid therapy must take into account the physiological diuresis that occurs after birth and the maturation of renal solute handling. Sodium is not given in the first few days of life until the physiological diuresis is established to avoid fluid retention and overload. Because of the limited ability of the renal tubules to excrete sodium, 10% dextrose is used for maintenance fluid, which is gradually increased over the first few days of life to avoid excessive hydration. Fluid requirements are initially 60–80 ml/kg/day, increasing to 150 ml/kg/day over the first week in term infants and higher in preterm infants. Surgery and ventilation all reduce GFR and increase antidiuretic hormone production, therefore fluid intake is often restricted postoperatively.

Nutrition

The neonate must rapidly adapt from receiving all nutrient and energy requirements via the placenta to obtaining them orally. *In utero*, the gastrointestinal tract is fully formed by 25 weeks and by term provides approximately 0.3 g/kg/24 hours of protein from swallowed amniotic fluid. During the last 6 weeks of normal gestation body fat deposition almost doubles to 15% of bodyweight. Glycogen stores increase during the last 9 weeks of gestation to 2–3 times that seen in adults. These late changes store energy to meet the high metabolic demand of thermoregulation and growth. If certain energy demands are high then energy resources are limited

for growth and maturation. Nutritional requirements vary greatly with gestation, postnatal age and concomitant illness.

Carbohydrates

Under the influence of high circulating catecholamines at birth, energy stores are mobilized via glycogenolysis, lipolysis and gluconeogenesis. A physiological drop in glucose is seen for the first 2 hours postdelivery, but the above mechanisms initiate homeostasis. Glycogen stores are depleted by approximately 12 hours, after which energy requirements are supported by oxidative fat metabolism until enteral feeding is established. Neonates require carbohydrate, fat, protein, vitamins and minerals to achieve weight gain. It is important to ensure the correct balance of protein and carbohydrate intake to avoid starvation metabolic pathways from being activated, causing aminoacidaemia and potentially developmental delay. It is now well recognized that nutrition in the neonatal and infant period can programme physiological responses in later life such as blood pressure control, insulin resistance, blood lipids, obesity, atopy and cognitive function.[8]

Nervous system

The nervous system is precocious in development compared with other organ systems and accounts for 10% of total body weight at birth. This system is immature and continues to develop to achieve a full complement of cortical and brainstem cells by 1 year. The brain increases its size threefold during the first year of life, producing a high metabolic demand. This is reflected in the neonatal cerebral circulation receiving one-third of cardiac output compared with one-sixth of cardiac output in adults. Myelination and organization of the nervous system continue throughout infancy and account for the loss of primitive reflexes.

The blood−brain barrier is immature in the neonatal period, with increased permeability to fat-soluble molecules, potentially increasing the sensitivity to certain anaesthetic drugs. Blood−brain barrier maturity is not attained until 6 months of age. Cerebral autoregulation is fully developed at term, maintaining cerebral perfusion down to a mean arterial pressure of 30 mmHg, reflecting the lower blood pressures found in neonates. The autonomic responses of the neonate are better developed to protect against hypertension than hypotension because the parasympathetic system predominates. This is reflected in the propensity of neonates to bradycardia and relative vasodilation.

Nociception

Nociceptive pathways are developed by 24−28 weeks' gestation, but still require further maturation through the neonatal period. The concept of neonatal nociception is now widely accepted, with adult-like physiological stress and behavioural responses to a noxious stimulus. Neonates undergoing awake nasal intubation increase mean arterial pressure by 57% and intracranial pressure by a similar amount.[9] Noxious stimulus exposure in the neonatal period can also affect behavioural patterns in later childhood, suggesting adaptive behaviour and memory for previous experience. ◆

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