Essentials of Paediatric Intensive Care

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Children are not just small adults. Various anatomical, physiological and pharmacological differences occur. The differences are significant and there is a continuous and variable change from the neonate onwards. This chapter covers the relevant differences between neonates and adults.

Anatomy and physiology

Airway

Neonates have relative to adults:
- the cricoid ring which is the narrowest part of the airway in the child; the vocal cords are in the adult
- the cricoid cartilage which is a full ring of cartilage
- large tongue
- large omega shaped epiglottis
- anterior larynx which is at a higher level
- large head
- short trachea, greater angle of carina; left main bronchus more horizontal
- the nasal passage which is approximately the same size as the cricoid ring in children
- obligate nose breathers

Problems/relevance
- for basic airway management the head needs to be in the neutral position
- tend to be more difficult to intubate than older child or adult
- a straight bladed laryngoscope is needed to lift the epiglottis in children up to about 2 years of age to give a better view of the vocal cords
- uncuffed endotracheal tubes are used up to about 10 years of age to reduce the risk of sub-glottic oedema and long-term sub-glottic stenosis
- risk of endobronchial intubation (tubes too long)

Breathing
- alveoli increase mainly in number in infants and in size in older children
- bronchi have relatively more cartilage, less muscle and more glands
- small airway obstruction is more likely to be due to inflammation and oedema in infants and muscle spasm in older children

- ribs more horizontal
- breathing is diaphragmatic
- greater elasticity of chest wall
- the diaphragm and intercostal muscles have fewer Type I muscle fibres which are adapted for sustained activity
- leads to relatively earlier tiring of these muscles
- faster respiratory rate 30–40 bpm at birth (Table 1.1)
- respiration often irregular with apnoeas particularly in premature infants
- similar tidal volume, compliance per kg compared to adults
- neonates have higher oxygen consumption, higher closing volumes and increased V/Q mismatch leading to lower PaO$_2$
- reduced oxygen reserve
- chemoreceptors have a more effective response to CO$_2$ rise than oxygen fall
- fall in oxygen tension stimulates respiration but only briefly in neonates
- surfactant production is reduced in premature babies, infant respiratory distress syndrome, bronchiolitis, adult respiratory distress syndrome (ARDS), pulmonary oedema and pneumonia
- more likely to have respiratory rather than cardiac arrest

**Problems/relevance**

Signs of increased work of breathing include:
- increased respiratory rate
- intercostal, subcostal recession due to the elastic chest wall
- use of accessory muscles, nasal flaring, grunting
- sweating and anxiety
- diaphragmatic splinting (e.g. air in stomach) may compromise respiration
- 50% of airway resistance is in the nasal passages
- tendency to have respiratory failure/arrest when critically ill

**Table 1.1** Respiratory rates in children by age

<table>
<thead>
<tr>
<th>Age</th>
<th>Rate (breaths/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>30–40</td>
</tr>
<tr>
<td>1–2</td>
<td>25–35</td>
</tr>
<tr>
<td>2–5</td>
<td>25–30</td>
</tr>
<tr>
<td>5–12</td>
<td>20–25</td>
</tr>
<tr>
<td>&gt;12</td>
<td>15–20</td>
</tr>
<tr>
<td>Adult</td>
<td>12–15</td>
</tr>
</tbody>
</table>

• in particular ex-premature neonates are prone to apnoeas
• bradycardia occurs often with hypoxia

Cardiovascular
• cardiac output is heart rate dependent in neonates
• stroke volume is fixed due to less compliant left ventricle
• relatively less intracellular calcium in neonates
• the myocardium is therefore more sensitive to parenterally administered calcium
• closure of foramen ovale and ductus arteriosus normally occurs during first 48h of life with pulmonary vascular resistance and arterial pressure falling to normal by 2–4 weeks of age
• assessment in the child includes central capillary refill time (normal less than 2 s) or core-peripheral temperature difference (less than 2°C). Beware cold peripheries leading to a longer capillary refill time.
• palpation of the fontanelle can assist in assessment of fluid status in infants
• systolic blood pressure can be estimated by the formula:
  \[80 + (\text{age in years} \times 2)\] (Table 1.2)

Problems/relevance
• hypotension is a pre-terminal sign
• response to fluid loss is tachycardia and vasoconstriction, leading to increased capillary refill time and sometimes mottling and air hunger
• transitional circulation can persist precipitated by cold, hypoxia or acidosis. This leads to worsening hypoxia. Treatment is by hyperventilation with 100% oxygen, correction of precipitating factors, inotropes or vasodilators may be required.

CNS
• relatively larger brain in newborn and infants
• larger proportion of cardiac output goes to the brain
• myelination increases during first 2 years of life

<table>
<thead>
<tr>
<th>Age</th>
<th>Heart rate (bpm)</th>
<th>Systolic blood pressure (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>110–160</td>
<td>70–90</td>
</tr>
<tr>
<td>1–2</td>
<td>100–150</td>
<td>80–95</td>
</tr>
<tr>
<td>2–5</td>
<td>95–140</td>
<td>80–100</td>
</tr>
<tr>
<td>5–12</td>
<td>80–120</td>
<td>90–110</td>
</tr>
<tr>
<td>&gt;12</td>
<td>60–100</td>
<td>100–120</td>
</tr>
</tbody>
</table>

Table 1.2 Pulse rate and blood pressure by age
ESSENTIALS OF PÆDIATRIC INTENSIVE CARE

• low myelin sheath thickness leads to slower nerve conduction
• blood-brain barrier is less well formed

Problems/relevance
• greater passage of some drugs especially opiates and barbiturates across blood-brain barrier
• more sensitive to sedative and analgesic drugs

Neuro-muscular junction
• formation of motor end plates is not complete at birth
• takes longer to recover after stimulation than in adults
• in the first few days of life, the immature neuro-muscular junction leads to greater sensitivity to non-depolarising muscle relaxants and relative resistance to depolarising relaxants (suxamethonium)

Renal
• immature at birth. Rapid improvement occurs after birth but the kidney is less efficient in premature infants.
• the proportion of cardiac output to the kidneys increases from 4–6% at birth to 20–25% when mature
• more flow to medulla and juxta-medullary apparatus than cortex in the newborn
• leads to difficulty in excreting sodium
• the low blood flow is the cause of low glomerular filtration rate (about one third that of adults) and therefore reduced excretion of some drugs
• difficult to cope with water load
• unable to concentrate urine as efficiently
• ability to excrete acid reduced in first week of life

Temperature control
• skin fully developed by 32 weeks gestation
• greater surface area to volume ratio than in adults
• head has a greater surface area leading to heat loss
• also fluid losses greater in premature infants compared to term infants. In addition the greater surface area to weight ratio of infants over children leads to greater fluid loss.
• main heat production is by non-shivering thermogenesis by increasing brown fat metabolism in the first few hours of life. This leads to increased oxygen consumption.
• sweat glands more inefficient and therefore easier for the infant to become hyperthermic
• in colder environmental temperatures, heat loss occurs by radiation, conduction and convection
Prematurity increases heat losses for the same environmental temperature compared to term infant

Problems/relevance
- quickly cool down if left exposed
- need to keep warm either by wrapping or heating devices
- increased fluid requirements in neonates relative to older children

Blood
- Blood volume is increased in neonates (90 ml/kg)
- Haemoglobin F (HbF) predominant at birth. Only small amounts remain by 6 months of age.
- HbF has a greater affinity for oxygen than haemoglobin A
- Oxygen dissociation curve is shifted to the left
- Therefore oxygen is less readily given up to tissues
- Physiological anaemia is maximal at 3 months and tends to be lower the smaller the infant at birth

Pharmacology
Pharmacokinetics is the quantitative assessment of absorption, distribution, metabolism and excretion of a drug. Also described as how the body deals with a drug.

Pharmacodynamics is the biochemical and physiological effects of drugs or what the drug does to the body.

- To produce a predictable and safe pharmacological response it is important to understand the physiological differences that occur as neonates evolve to children and then adults.
- In general for many drugs, there is a period of sensitivity in neonates followed by a relative resistance in infants and young children and then tending towards adult doses in adolescence.
- Remember that ill children are likely to be generally more sensitive to most drugs.

Pharmacokinetics
Absorption
- The intravenous route avoids problems with variability in drug absorption.
- Inhalation: The combination of a higher alveolar ventilation and relatively large cardiac output of the neonate causes a quicker equilibration of alveolar to tissue concentration of drug than in adulthood.
- Oral/nasogastric routes: The rate-limiting step for absorption for the upper gastrointestinal tract is the speed of gastric emptying. This is altered in patients who are ill, have suffered trauma or received drugs
that reduce gastric mobility such as morphine. The acidity of the stomach is lower in the newborn infant (higher pH).

- Rectal routes: The rectal route can be useful. Absorption can vary with pH (normal 7–12).
- Intramuscular: Children have a lower muscle mass as compared with adults but a higher cardiac output which ensures a reliable and rapid onset of action of intramuscular drugs. In conditions with a reduced cardiac output, onset may be delayed. The intramuscular route should be avoided as much as possible due to the dislike of painful injections.

**Distribution**

- When a drug is absorbed it will be distributed according to blood flow and the drug’s solubility in that tissue.
- Neonates differ considerably from adults in that as the cardiac output is double that of adults, the circulating volume is relatively less leading to a much more rapid circulation time.
- The relative volumes of body compartments are also very different. The extracellular space in a neonate is 45% of body weight compared with only 20% in adults. Total body water is 80% in the neonate dropping to 55% in the adult.
- It would be expected that neonates would need a larger loading dose but due to the increased sensitivity at receptor level this is not the case.

**Protein binding**

- Infants have lower levels of proteins such as albumin, and binding sites are occupied by endogenous substances such as bilirubin. Drugs with a high affinity for albumin may displace bilirubin.
- Basic drugs such as opioids and local anaesthetics are bound to α1-glycoprotein which only reaches adult levels at about 6 months of age. Hence in early life these drugs will have a much more potent effect due to the higher free fraction in the plasma.

**Elimination**

- Most drugs are metabolised by the liver to a more water soluble form and excreted by the kidneys.
- The liver is relatively large at birth, thus Phase I reactions in the liver (oxidation, hydrolysis and reduction) are relatively mature early on in life while Phase II reactions (mainly conjugation) develop more slowly.
- The kidney is immature at birth and takes up to 2 years to develop fully and this may delay excretion. Glomerular filtration rate is about one third that of adults at birth. Secretion and absorption within the tubule is less leading to reduced elimination of drugs such as penicillin and gentamicin.
Pharmacodynamics
Receptors: The differential maturity and numbers of receptors may explain some of the differences in dose requirements in neonates. For example neonates are particularly sensitive to non-depolarising neuromuscular agents and resistant to depolarising neuro-muscular agents.