Paediatricians tell us that infants and children are not little adults and that the manner in which medicines are absorbed, distributed and eliminated from the body is different to that of adult neonates, in particular, differ from adults in their response to medicines and special care is needed in the neonatal period (first 30 days of life). At this age, the risk of toxicity from a medicine is increased by inefficient renal function, relative enzyme deficiencies, different target organ sensitivities and inadequate detoxifying systems causing delayed excretion. Medicine doses in the neonate, therefore, should be calculated with great care.

Before discussing the treatment of some common paediatric conditions presenting in the clinic, it is of value to briefly review the basics of paediatric pharmacokinetics and dose calculation.

Pharmacokinetics in children

• Absorption
Neonates have a much lower secretion of gastric acid than adults. However, the practical importance of this with regard to the absorption of medicines and the efficacy of oral therapy has not been well documented. The oral absorption of medicines in older infants and children is similar to that in adults.

Percutaneous absorption of medicines is generally enhanced in neonates, infants and children, particularly if the skin is excoriated or burnt. Several cases of toxicity due to excessive percutaneous absorption have been reported. Examples include corticosteroid excess from ointments and creams.

• Distribution
Premature babies, neonates, infants and young children differ from adults in their distribution of body fat and water. See Table 1. Since the extent to which a medicine distributes between water and fat is related to its physicochemical properties, it would be expected that the distribution between various body compartments would be different in children, particularly in neonates. This difference is most evident for water-soluble medicines which are mainly distributed within the extracellular space. This has been well-documented for sulphonamides, whose apparent volume of distribution in the neonate is about twice that of an adult.

Plasma protein binding of medicines is reduced in the neonate, but increases with age and reaches adult values by about one year. The neonate has a lower concentration of albumin and a lower capacity of albumin to bind to medicines. This reduced protein binding is of particular importance in the infant with malnutrition and may result in toxicity of medicines at lower doses than anticipated.

The interaction of medicines with the binding of bilirubin to plasma proteins in neonates is important, since unconjugated non-protein bound bilirubin can cross the blood-brain barrier and cause kmetic. Sulpho-namides, aspirin and vitamin K can displace bilirubin from plasma binding sites, increasing the concentration of unconjugated bilirubin in blood and predispose to kmetic.

Metabolism
In general, hepatic oxidative metabolism and glucuronide conjugation are deficient in the newborn and the maturation of these drug-metabolising systems is variable. For example, the hydroxylisation of diazepam is related to age and is particularly poor in neonates. While the half-life of diazepam in the adult ranges from 24 to 48 hours, it may range from 38 to 120 hours in the premature neonate. Similarly, the half-life of theophylline in the neonate is 14 to 56 hours but in an adult ranges from 3 to 8 hours.
Continued from p26

Renal excretion

In the neonate, both the glomerular filtration rate (GFR) and renal tubular function are immature and take about six months to reach adult levels.

For example, the GFR in the neonate is about 30 to 40% of that in the adult. Therefore, medicines which are excreted in the urine tend to accumulate in neonates and young infants. Examples include the penicillins, the dosages of which need adjustment particularly in the premature neonate.

Dose calculation in children

When there is no specific paediatric dose available in the manufacturer’s prescribing information or in the published medical literature, paediatric doses may be calculated from adult doses by using age, body-weight or body-surface area, or by a combination of these factors. The most reliable methods are based on body-surface area.

However, it must be emphasized again that children are not miniature adults and that age-related differences in drug handling or drug effects may lead to different dose requirements to achieve efficacy or to avoid adverse effects. Dose calculations cannot be assumed to be as reliable as specific clinical trials in paediatric populations.

Body weight

The child’s weight may be used to calculate a dose expressed in mg/kg. In many instances, young children may require a higher dose per kilogram than adults because of their higher metabolic rates. However, in the obese child, a dose calculation based on body weight would result in much higher doses being administered than necessary and in such cases, the dose is often calculated from an ideal weight, related to height and age.

Note: The percentage method of calculating doses, should only be used if a specific dose cannot be found, since it assumes a child is average.

While the percentage method may be used to calculate paediatric doses of commonly prescribed medicines that have

### Table 1: Relative amounts of body water and fat at different ages

(Oxford Textbook of Clinical Pharmacology 2nd Ed.p139)

<table>
<thead>
<tr>
<th>Age</th>
<th>Total body water (% of weight)</th>
<th>Extracellular fluid (% of weight)</th>
<th>Intracellular fluid (% of weight)</th>
<th>Fat (% of weight)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premature baby</td>
<td>85</td>
<td>50</td>
<td>35</td>
<td>1</td>
</tr>
<tr>
<td>Full-term neonate</td>
<td>70</td>
<td>40</td>
<td>30</td>
<td>15</td>
</tr>
<tr>
<td>Infant (6 months)</td>
<td>70</td>
<td>35</td>
<td>35</td>
<td>15</td>
</tr>
<tr>
<td>Child</td>
<td>65</td>
<td>25</td>
<td>40</td>
<td>15</td>
</tr>
<tr>
<td>Young adult</td>
<td>60</td>
<td>15</td>
<td>45</td>
<td>20</td>
</tr>
<tr>
<td>Elderly adult</td>
<td>45</td>
<td>10</td>
<td>35</td>
<td>10</td>
</tr>
</tbody>
</table>

### Table 2. Percentage method of calculating doses

<table>
<thead>
<tr>
<th>Age</th>
<th>Mean weight for age (kg)</th>
<th>Mean surface area for age (m²)</th>
<th>% of adult dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>New born (full term)</td>
<td>3.5</td>
<td>0.23</td>
<td>12.5</td>
</tr>
<tr>
<td>2 months</td>
<td>4.5</td>
<td>0.27</td>
<td>15</td>
</tr>
<tr>
<td>4 months</td>
<td>6.5</td>
<td>0.34</td>
<td>20</td>
</tr>
<tr>
<td>1 year</td>
<td>10</td>
<td>0.47</td>
<td>25</td>
</tr>
<tr>
<td>3 years</td>
<td>15</td>
<td>0.62</td>
<td>33.3</td>
</tr>
<tr>
<td>7 years</td>
<td>23</td>
<td>0.88</td>
<td>50</td>
</tr>
<tr>
<td>10 years</td>
<td>30</td>
<td>1.05</td>
<td>60</td>
</tr>
<tr>
<td>12 years</td>
<td>39</td>
<td>1.25</td>
<td>75</td>
</tr>
<tr>
<td>14 years</td>
<td>50</td>
<td>1.50</td>
<td>80</td>
</tr>
<tr>
<td>16 years</td>
<td>58</td>
<td>1.65</td>
<td>90</td>
</tr>
<tr>
<td>Adult</td>
<td>68</td>
<td>1.73</td>
<td>100</td>
</tr>
</tbody>
</table>
a wide margin of safety between the therapeutic and toxic doses, more precise body-surface values may be calculated from height and weight by means of nomogram.

Refer to a nomogram in any paediatric formulary, to get the relationship between height, weight and body surface area in children and adults.

Body-surface area (BSA)

BSA estimates are more accurate than body weight since many physiological phenomena correlate better to body-surface area. The average body-surface area of a 70kg human is about 1.8m². Therefore, to calculate the dose for a child, the following formula may be used:

\[
\text{Dose} = \frac{\text{Surface area of patient (m}^2) \times \text{ADULT DOSE}}{1.8}
\]

Prescriptions for children

While there can be no substitute for carefully controlled clinical trials, ethical constraints placed upon the investigations of medicines in children often result in medicines coming onto the market without reliable information on their suitability of use in children, let alone with recommended dosage regimens for children. It is estimated that over 50% of medicines used in children may not have been studied in this age group. However, the need for specific information for children should be balanced against the ethical concerns and the usage of a particular medicine which has not been adequately tested in the paediatric patient population.

Therefore, if it is considered necessary to prescribe a medicine for a child, for which no optimal paediatric dose has been defined, careful attention to determining the correct dosage or indeed whether the medicine can be used in children at all, is essential. Remember: Prescribers take full responsibility for prescribing products outside the recommendations in the approved package insert. Furthermore, many a parent can attest that even with the best will and technique, the dosage that eventually gets into the child, after medicine drooling down the chin or being spat or vomited out is possibly not very close to the recommended or prescribed dose.

Some basic concepts for prescribing and using medicines in children include the following:

- Only recommend medicines for children, especially infants and young children if they are deemed essential.
- Prescriptions for children should indicate the child’s age and weight.
- It is important to state the strength of the medicine required, the dosage form and dosing frequency.
- Prescriptions for liquid oral preparations should be dispensed with a medicine measure if the dose is 5ml or more.
- Prescriptions for liquid oral preparations should be dispensed with an oral syringe if the dose is less than 5ml.
- Some parents find it easier to dispense all medicines using an oral syringe.
- Parents should be advised not to add medicines to the contents of the infant’s feeding bottle. If the feed is not finished, the dosage ingested may be reduced. Furthermore, the altered taste may put the child off the feed.
- Keep all medicines out of the reach of children.

**Treating common paediatric conditions**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Possible treatment*</th>
<th>Refer</th>
</tr>
</thead>
</table>
| Common cold         | If necessary, treat presenting complaint only:  
• Nasal congestion – Saline nose drops or decongestant paediatric nasal preparation (for 7 days)  
• Rhinorrhoea or nasal congestion – oral pseudo-ephedrine and/or an oral antihistamine  
• Sore throat – pastilles or lozenges | Influenza (hot and cold shivers, muscle aches and pains, high temperature). Sore throat of more than 5 days duration. |
| Constipation        | 1. Increase dietary fibre and fluid.  
2. Lactulose  
3. Bulk-forming laxative (e.g. ispaghula) for children over 6 years  
4. Single glycerine suppository | Persistent constipation  
Blood in the stool  
Abdominal pain |
| Cough (dry)         | Glycerine, lemon and honey or simple cough linctus  
Pholcodine or noscapine cough preparations administered three times a day and before bedtime | Cough of more than 2 week’s duration  
Breathing difficulties |
| Cough (productive)  | Glycerine, lemon and honey or simple cough linctus  
Guaifenesin cough preparation | Coloured sputum, blood in sputum  
Cough of more than 5 days duration. |
| Diarrhoea           | Oral fluid therapy  
Continue breast or bottle feeding in infants | Diarrhoea more than 1 day in infant and young child  
Diarrhoea more than 2-3 days in child over 5 years  
Diarrhoea associated with severe vomiting & fever  
Blood or mucus in the stools |
| Fever               | Paracetamol and/or Ibuprofen  
Fever of more than 1-2 days duration | High fever |
| Gastro-oesophageal reflux | Smaller, more frequent feeds  
Change feeding posture  
Infant alginate combinations | Infant is not gaining weight  
Simple measures are not effective |
| Pain                | Paracetamol and/or Ibuprofen  
days without a doctor’s advice | Do not use continuously for more than a few days |
| Worms               | Mebendazole or albendazole for children over 2 years | Children under 2 years |

* Please consult the product’s prescribing information for dosage recommendations.