Calculation of drug dosage and body surface area of children

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Summary
The British National Formulary and many reference textbooks recommend that drug dosages for children be calculated according to body surface area (BSA). Although many rules for drug dosage have been developed, based on age, weight and surface area, none has been accurate and simple enough for routine use. These rules are described, and one for clinical use: up to 30 kg, a child's drug dose may be \((\text{wt} \times 2)\%\) of an adult dose; over 30 kg, \((\text{wt} + 30)\%\) of an adult dose. If this percentage of an "adult" dose of a drug is used, not only is the BSA curve followed more closely than with the conventional \(\text{mg kg}^{-1}\) regimen, but fewer major errors of prescription may be expected. (Br. J. Anaesth. 1997; 78: 601–605).

Key words

The British National Formulary (BNF),\(^1\) Martindale's Pharmacopoeia\(^2\) and many other reference textbooks state that the most reliable methods for calculation of children's drug doses are those based on body surface area (BSA). This principle has been commended for nearly 90 yr, but there is still no consistency in the guidance offered, and the same BNF uses a mixture of \(\text{mg kg}^{-1}\), age and weight ranges in its recommendations.

All dosage rules based on a single physical dimension only hold good while that dimension is associated with other normal dimensions. Thus one could use an age-based rule if associated height and weight for that age were typical; however, there is substantial normal variation in height and weight with age (see below) and so weight is used more usually as the dimension for calculations. This however is still relatively unreliable, and therefore if better prediction of drug concentrations is required, a multidimensional rule is needed. Fortunately, this is usually beyond clinical needs.

The therapeutic ratio (the ratio of toxic to effective dose) for most drugs is more than 50\%, so that some approximation may usually be made with safety. It would appear that for routine practice, an “accuracy” of 10–20\% is reasonable; more than this complicates the mathematics substantially, and would not be justified because of individual differences in response. This generalization excludes those drugs which are given according to known individual requirements (e.g. insulin or digoxin), for which a prescribing rule is inappropriate.

A large number of children's drug dosage rules have been described,\(^3-5\) almost all using percentages of an adult dose to calculate an appropriate child’s dose—the notable exception being the commonly used “\(n\)” \(\text{mg kg}^{-1}\) regimen. An advantage of these rules is that modifications to adult doses to allow for sickness in adults are appropriately incorporated into calculations for children. An obvious requirement of these percentage methods is that adult doses of the drug are known, but for the majority of anaesthetists this does not present a problem, and certainly no more difficulty than the different dosages at different ages noted in the BNF.

Reports in the literature quote many examples of prescription errors in children, of 2–10 times the recommended dose.\(^6-10\) Many believe that the great majority of these errors would have been noticed if easily calculated percentages of a normal adult dose had been used, as the prescriber may readily check his mathematics by inspection of the values involved.

Dosage rules may be described as those based on age, weight or body surface area.

Age-based rules
The earliest rules used age as the base. Augsberger\(^3\) referred to Dilling’s rule (age/20) as dating back to...
the 8th century. Those most commonly used: 
age/20, (4 x age) + 20 and age/(age + 12)
are shown in figure 1, plotted using weights for ages
obtained from standard tables.11 12 The normal
variation of weight with age (from 3rd to 97th
percentiles) is considerable, being least at 1 yr
(+25% to -20% at 10 kg), and reaching a maxi-
mum at about 13 yr (+45% to -26% at 40 kg). The
consequence is that these rules are highly unreliable.

If weight is unavailable, then (4 x age) + 20 pro-
vides the best fit to the BSA curve for normal sized
children.

Weight-based rules

Professor A. J. Clark of Edinburgh is said to have
been the first to propose a weight proportional
regimen for drug therapy.13 His first rule was:

\[(\text{wt (lb})/150)\text{ fraction of an adult dose.}\]

This was improved in accuracy by Augsberger,3
who substituted multiplication for division and
added 10, suggesting:

\[((1.5 \times \text{wt (kg)}) + 10)\text{ percent of an adult dose.}\]

However, this made it difficult to calculate, and
this rule is not quoted widely. It is as good a linear fit
as can be made to the BSA curve, reaching 100% at
60 kg (fig. 2).

The most common regimen, mg kg\(^{-1}\) dosages, has
an attractive simplicity which has given it widespre-
ded popularity despite its disadvantages, namely: (a) it
requires a complete set of drug dosages (\(n \text{ mg kg}^{-1}\))
to be learned for its purpose, and indeed different
doses at different ages; (b) the mathematics may not
be as easy as a bedside rule demands, the decimal
point sometimes being misplaced when tenths or
hundredths of a mg kg\(^{-1}\) are being multiplied; (c) it
does not immediately relate to adult doses, so that
inappropriate prescriptions are not immediately
obvious; (d) assays of drug concentrations show that
its use “under doses” for much of its range14, this
varies from approximately -45% at 15 kg to -20%
at 40 kg compared with the BSA graph (fig. 5).

Body surface area calculation

Body surface area is recommended as the principal
basis for drug dosage\(^{15,16}\) as the rate of metabolism or
redistribution of a drug is proportional to metabolic
rate, which in turn reflects heat losses which, as for
any warm object, are generally proportional to
surface area. Many measurements of organ size,
fluid compartment volumes and assays of blood
concentrations of drugs correlate well with
BSA.\(^{13,17-20}\)

While this is valid for most ages, some decrease
below the BSA proportional dose is in fact approp-
riate when prescribing for children of less than
approximately 18 months, typically 10 kg, as below
that age there are differences other than size that
should be borne in mind, that is: in the neonate,
many enzyme systems are immature; neonatal renal
clearance is approximately 50% of adults, reaching
adult values at approximately 6 months; the half-life
for many drugs is therefore longer in neonates and
infants; and children have a higher total body water
percentage than adults (80% at birth, 70% at 3
months and 60% at 1 year, compared with approxi-
ately 55% for adults). This is important when con-
sidering the distribution volumes of drugs; in
children less than 1 yr of age, distribution volume is
relatively large for drugs that are water soluble, and
small for those that are fat soluble.\(^{14,21-23}\)

Moore, in 1909,19 was the first to recognize the
importance of BSA, saying that: “stating dosage in
reference to body weight is not only inaccurate, but
rests entirely on a wrong principle”, and that it
should be:

“proportionately instead to the body surfaces or,
in other words, proportionately to the two thirds
powers of their weights, which leads to quite
different doses.”

(1)

Moore was using the same formula as Meeh,24
who is widely quoted. Clark gave his name to his
second rule by reporting Moore’s work in 1937,13
again recommending dosage proportional to the
two-thirds power of body weight.

The history of actual measurements of surface
area is fascinating, with examples of marvellous
ingenuity, from covering surfaces with paper, plaster
or lead, to “wrapping a human in silk tights, charg-
ing up the silk as one would a Leyden jar, and calcu-
lating the surface by applying a metal plate of known
area”.25 The power of 2/3 is the ratio of surface area
to volume of cubes, spheres and other such solid
objects, and in humans appears to be a quite reason-
able approximation (fig. 2) for those of normal build,
using a proportionality constant of approximately 12
for kilograms, that is 12 \(\times wt^{2/3}\).26 27 It is, how-
ever, unidimensional.

The first multidimensional formula for surface
area to be used widely was proposed by DuBois and
DuBois:26

\[
S = W^{0.425} \times H^{0.725} \times 71.84
\]

(2)

where \(S = \text{surface area (cm}^2\)\), \(W = \text{weight (kg)}\) and
\(H = \text{height (cm)}\).

The nomograms derived from this equation are
drawn most often, as for example in Martindale’s
Pharmacopoeia\(^{2}\) or Geigy Scientific Tables\(^{27}\) despite
the fact that the investigators only measured nine
subjects.

The definitive work on surface area is a
monograph by Edith Boyd\textsuperscript{28} who improved the formula as follows:

\[ S = 3.207W^{0.7285} - 0.0188 \log W H^{0.3} \]  

(3)

where \( W \) = weight (g). She quoted the SD in her subjects as 7%.

Gehan and George\textsuperscript{29} summarized all existing data, and suggested a further marginal improvement on the above equations, namely:

\[ S = 0.02351^{0.42246} W^{0.0235} H^{0.11005} / H^{0.11002} \]

(4)

In fact, equations (1–4) are within 5\% of each other to a value of 15 kg in subjects with a normal build. Thin subjects would appear to have approximately 10\% more surface area than predicted by equation (1), and fat subjects approximately 20\% less,\textsuperscript{25} but unfortunately the literature does not provide reliable data on variations of BSA with build.

### BSA-based rules

The nomograms constructed from these formulae provide the actual surface area, from which further mathematics provide the fraction of an adult dose, and thence the required dose, but this is hardly a bedside calculation.

The consensus has generally been that fixed tables of percentages of an adult dose derived from BSA\textsuperscript{30} are a lesser evil than calculations requiring such higher mathematical powers, although they do require interpolation and the consequent possibility of introducing further errors. This approach, first suggested by Butler and Richie\textsuperscript{17} and popularized further by Catzel and Olver as “The percentage method”\textsuperscript{31} is also difficult to use in a clinical situation: the values may be learned by heart, but this is little more use than nomograms or a calculator. They appear to be the basis of the table given in the \textit{BNF}\textsuperscript{3} (which does not quote its source) and many current textbooks: Catzel’s values (table 1, fig. 3) follow the BSA curve up to 40 kg, from which point they are 5\% higher. Differences in the percentages recommended in different sources appear to arise from a combination of approximations and differences in the size of an “adult” (whether 140 lb, 65 kg or 70 kg). Much of this work was done in the early part of the century, since when the normal adult has increased in size.

### Salisbury rule

None of the rules described above is both simple and accurate enough for clinical use. A rule is needed that allows a dosage calculation that is approximately “correct”, rather than having complicated mathematics in order to achieve academic accuracy, but getting the point wrong.

As a curve cannot be calculated easily with bedside mathematics, it was decided to use two straight lines crossing over at an appropriate point. As pointed out, the wt/70 (mg kg\textsuperscript{–1}) rule falls substantially below the BSA curve throughout its range, with consequent under dosing. Wt/50, which is the same as double the body weight as a percentage of the adult dose, makes for easier calculation and provides reasonable results up to 30 kg, although still deviating to the low side at low weights (thereby accommodating the reservations concerning infants described above). Over 30 kg, one may simply add 30 to the body weight to obtain the graph shown in figure 4, following the BSA curve closely.

The differences in the wt/70 (mg kg\textsuperscript{–1}) and Salisbury rules from the BSA curve are illustrated in figure 5.

Thus we propose the following rule in children:

less than 30 kg: weight \times 2

more than 30 kg: weight + 30

percentage of the adult dose of a drug.

Expressed colloquially, this is: “to obtain the

### Table 1

<table>
<thead>
<tr>
<th>Age</th>
<th>Weight (kg)</th>
<th>% Adult dose</th>
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<tbody>
<tr>
<td>2/52</td>
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<td>12.5</td>
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<tr>
<td>2/12</td>
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<td>15</td>
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<td>20</td>
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<td>25</td>
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<td>28</td>
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<td>20</td>
<td>65</td>
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</tr>
</tbody>
</table>

**Figure 3** Catzel’s recommended doses of drugs for children as a percentage of adult doses.

**Figure 4** The Salisbury rule for drug dosages for children compared with BSA and wt/70 (mg kg\textsuperscript{–1}).
We have been using this rule now for almost 10 yr. It has often been repeated, and in order to provide a satisfactory alternative the Salisbury rule is that children should have:

“less than 30 kg, double the body weight; more than 30 kg, add 30 to the body weight” percentage of the adult dose of a drug.

This rule gives as close adherence to fractional body surface area as is desirable, under dosing where immature development may be present, together with the added advantage of easier and more reliable calculation of the result.

**References**

18. **Crawford JD, Terry ME, Rourke GM. Simplification of drug dosage calculation by application of the surface area principle. Pediatrics 1950; 5: 783–789.**
19. **Moore B. The relationship of dosage of a drug to the size of an animal treated, especially in regard to the cause of the failures to cure trypanosomiasis, and other protozoan diseases in man and in other large animals. Biochemical Journal 1909; 4: 322–330.**


