

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 $(wt \times 2)\%$ of an adult dose; over 30 kg, $(wt + 30)\%$ 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 $mg\ kg^{-1}$ regimen, but fewer major errors of prescription may be expected. (*Br. J. Anaesth.* 1997; 78: 601–605).

Key words

Anaesthesia, audit. Children. Anaesthesia, administration schedule.

The *British National Formulary (BNF)*,¹ *Martindale's Pharmacopoea*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 $mg\ kg^{-1}$, 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*" $mg\ kg^{-1}$ 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. Augsberger³ referred to Dilling's rule ($age/20$) as dating back to

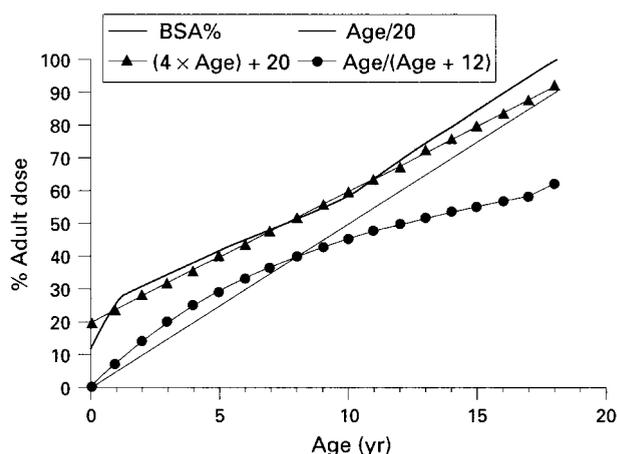


Figure 1 Age-based rules at ages shown for calculation of children's drug dosages as a percentage of adult doses plotted using weights derived from standard growth tables.

the 8th century. Those most commonly used:

$\text{age}/20$, $(4 \times \text{age}) + 20$ and $\text{age}/(\text{age} + 12)$

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 maximum at about 13 yr (+45% to -26% at 40 kg). The consequence is that these rules are highly unreliable.

If weight is unavailable, then $(4 \times \text{age}) + 20$ provides 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:

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

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

$((1.5 \times \text{wt (kg)}) + 10)$ 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).

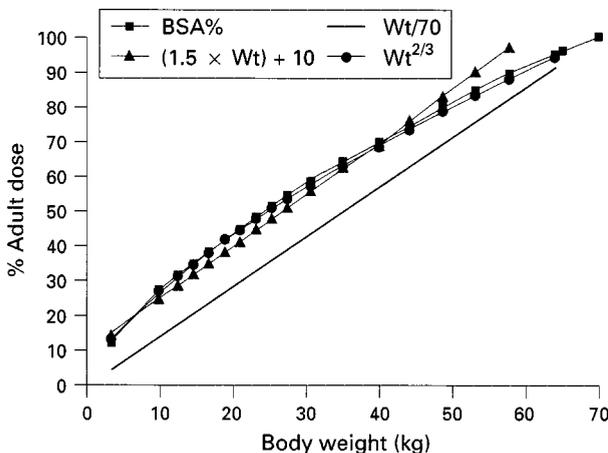


Figure 2 Weight-based rules for calculation of childrens' drug dosages as a percentage of adult doses.

The most common regimen, mg kg^{-1} dosages, has an attractive simplicity which has given it widespread 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 ages¹; (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 appropriate 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 approximately 55% for adults). This is important when considering 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, charging up the silk as one would a Leyden jar, and calculating 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 reasonable approximation (fig. 2) for those of normal build, using a proportionality constant of approximately 12 for kilograms, that is $12 \times \text{wt}^{2/3}$.²⁵ It is, however, unidimensional.

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

$$S = W^{0.425} \times H^{0.725} \times 71.84 \quad (2)$$

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

The nomograms derived from this equation are those seen most often, as for example in *Martindale's Pharmacopoea*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 Boyd²⁸ who improved the formula as follows:

$$S = 3.207W^{0.7285} - 0.0188 \log W \quad (3)$$

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

Gehan and George²⁹ summarized all existing data, and suggested a further marginal improvement on the above equations, namely:

$$S = 0.0235H^{0.42246} W^{0.51456} \quad (4)$$

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,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 $BSA^{3/20}$ 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 Richie¹⁷ and popularized further by Catzel and Olver as “The percentage method”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 *BNF*¹ (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 $wt/70$ ($mg\ kg^{-1}$) 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 $wt/70$ ($mg\ kg^{-1}$) 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 Catzel’s Recommended Doses of Drugs for Children³¹

| Age | Weight (kg) | % Adult dose |
|-------|-------------|--------------|
| 2/52 | 3.2 | 12.5 |
| 2/12 | 4.5 | 15 |
| 4/12 | 6.5 | 20 |
| 8/12 | 8.5 | 25 |
| 12/12 | 10 | 28 |
| 18/12 | 11 | 30 |
| 3 yr | 15 | 33 |
| 5 | 18 | 40 |
| 7 | 23 | 50 |
| 10 | 32 | 60 |
| 12 | 40 | 75 |
| 14 | 45 | 80 |
| 20 | 65 | 100 |

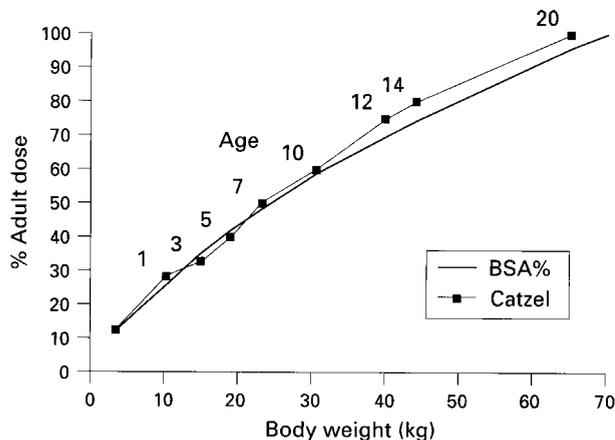


Figure 3 Catzel’s recommended doses of drugs for children as a percentage of adult doses.

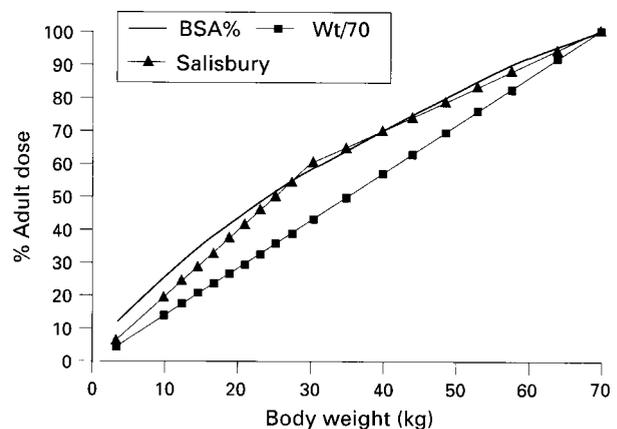


Figure 4 The Salisbury rule for drug dosages for children compared with BSA and $wt/70$ ($mg\ kg^{-1}$).

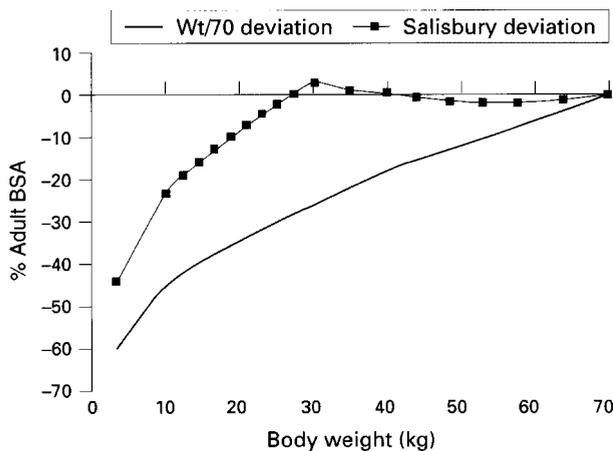


Figure 5 Deviation from BSA of the wt/70 (mg kg^{-1}) and Salisbury rules.

Table 2 Examples of drug dosage calculations using different rules. Most doses are rounded to the nearest milligram. n/r = Not recommended

| | Weight | | | |
|---------------------------------------------------------------------------------------------------------------------------|---------|---------|---------|-------|
| | 3.2 kg | 8.5 kg | 18 kg | 45 kg |
| Atracurium: "Adult" dose assumed to be 35 mg | | | | |
| 0.5 mg kg^{-1} | n/r | 4 | 9 | 23 |
| Salisbury rule | n/r | 6 | 13 | 26 |
| Catzel/ <i>BNF</i> | n/r | 9 | 14 | 28 |
| Thiopentone: "Adult" dose assumed to be 280 mg | | | | |
| 4 mg kg^{-1} | 13 | 34 | 72 | 180 |
| Salisbury rule | 18 | 48 | 101 | 252 |
| Catzel/ <i>BNF</i> | 35 | 70 | 112 | 224 |
| Morphine: "Adult" dose assumed to be 10 mg. " <i>BNF</i> " follows <i>BNF</i> guidance for different age/weight groupings | | | | |
| 0.1–0.2 mg kg^{-1} | 0.3–0.6 | 0.9–1.7 | 1.8–3.6 | 4.5–9 |
| <i>BNF</i> mg kg^{-1} | 0.5 | 1.7 | ~4 | 10 |
| Salisbury rule | 0.6 | 1.7 | 3.6 | 9 |
| Catzel | 1.25 | 2.5 | 5 | 8 |

BSA% from weight, under 30 double it, over 30, add 30".

Examples of this rule for some commonly used drugs are given in table 2. The results from the Salisbury rule fall into a safe area close to those recommended by the *BNF*. It is particularly useful that it removes the need to learn different doses at different ages. Therefore, for example, the dose for morphine is quoted in the *BNF* as: "<1 month, 150 $\mu\text{g kg}^{-1}$; 1–12 months 200 $\mu\text{g kg}^{-1}$; 1–5 yr 2.5–5 mg; 6–12 yr 5–10 mg". The Salisbury rule tracks these different doses accurately, so eliminating the need for different dosage recommendations at different ages.

We have been using this rule now for almost 10 yr. It has proved easy to use, and there has been no clinical evidence of inappropriate dosage.

Summary

Nearly 90 yr ago the following suggestion was made: "For the great majority of drugs the method of stating dosage as so much per kilogram should be abandoned".¹⁹

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.

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