Editors' view

Littluns and biguns

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Littluns

'Them kids. The littluns.
Who took any notice of 'em?'
William Golding, Lord of the Flies

It is hard to establish how to give children adequate drug therapy. Defining drug pharmacokinetics and pharmacodynamics in children is a difficult affair; determining suitable age- and weight-related doses lacks a sound scientific basis; and randomized controlled trials in children are relatively few. Thus, licensed indications and recommended dosage schedules often do not encompass the young. Off-label use is therefore common, and one suspects that the balance of benefit to harm in drug therapy in children must be generally less favourable than it is in adults, although the evidence that that is so is still limited.

Part of the problem has been that paediatric clinical pharmacology is a relatively neglected subspecialty. It is encouraging therefore that there are now three paediatric clinical pharmacologists in the UK and three others in training. It would be interesting to know what the position is in other countries. In this issue of the *Journal* Choonara *et al.* (pp. 217–18) announce the formal training programme for paediatric clinical pharmacologists that has been developed under the auspices of the Royal College of Paediatrics and Child Health. The programme is encouragingly eclectic, and it is good to see that it includes population pharmacokinetics, which, although an arcane and difficult subject, is important in studying children, in whom blood samples are often sparse. The requirement that each trainee will be responsible for a paediatric trial is also welcome. How many trainees the subspecialty will attract remains to be seen; training involves triple accredita-

tion (in general medicine, paediatrics, and clinical pharmacology) and the going must be tough. But the challenge will be a stimulating one and the rewards worth striving for.

In a parallel initiative, the *British National Formulary* is currently working on a children's BNF, in collaboration with the Royal College of Paediatrics and Child Health and the Neonatal and Paediatric Pharmacists Group. And granting extended exclusivity rights to pharmaceutical companies during drug development may encourage more premarketing studies in children.

Biguns

'Though there was a dubious region, . . . nevertheless
no one had any difficulty in recognizing biguns at one
end and littluns at the other'
William Golding, Lord of the Flies

There is, we are told, a current epidemic of obesity. Perhaps pandemic would be a better word for it. The problems that it brings in its wake – which include hypertension, diabetes, dyslipidaemias, and osteoarthritis – are well known. Less well appreciated is the problem of deciding drug doses that are suitable for overweight people. And here the old adage 'one for a man, two for a horse' breaks down; where obesity is concerned twice the size does not mean twice the dose. In this issue of the *Journal* Green and Duffull (pp. 119–33) review in detail the several different types of calculation that have been used to estimate the fraction of total body weight to which the pharmacokinetics of a drug, and hence by implication drug doses, should be related. They are the ideal body weight, fat-free mass, lean body weight, adjusted body weight, and predicted normal weight; as well as the Body Mass Index (the

WHO's standard for defining obesity). Most of them take into account total body weight, height, and sex. And none of them is satisfactory. For predicting clearance it seems that estimated lean body weight is the best predictor, but even that was the best of the bunch in only one-third of the studies in which it was used. Total body weight was as good as anything else (and better than most) in predicting volume of distribution, but was only best in 40% of the studies in which it was used. Disappointingly, the authors do not tell us how often these measures were second-best or third-best; nor do they try to calculate the best overall using the single transferable vote method. However, the results show that there is no one measure that is really good at predicting either clearance or volume.

This is not perhaps surprising. We cannot expect equations that have been based on relatively small numbers of individuals in the population to predict precisely and accurately what they purport to predict in all individuals across all the range of body weights. Furthermore, there is no reason to expect that people who are overweight are otherwise homogeneous in all other respects. Other forms of physiological variability, comorbidities, and comedications will muddy the waters.

Nevertheless, until we have a better method of calculating doses of drugs that require long-term therapy on a milligram per kilogram basis, and until we know more about the nature of the relations between different estimates of body weight for different drugs, we could do worse than using the estimated lean body weight as a guide.

But how can the clinician calculate lean body weight? It involves two complicated equations, since you first have to calculate Body Mass Index, which is then fed into another equation, and is only accessible at the bedside to those who have programmed the equations into

their palm-top computers. No doubt when we have fully implemented electronic patient records and electronic prescribing, the computer will do the calculations for us. For the moment, my own simple bedside approach is to use instead what I call the Tupman scale, in homage to the character of that name in Dickens's *Posthumous Papers of the Pickwick Club*: 'Time and feeding had expanded that once romantic form; the black silk waistcoat had become more and more developed; and gradually had the capacious chin encroached upon the borders of the white cravat'. For each level of fatness subtract the indicated percentage from the total body weight to calculate the lean Tupman weight.

Pleasantly plump	5%
Portly	10%
Suety	15%
Tubby	20%
Rolypoly	25%
Blubbery	30%
Gross	35%
Indescribable	40%

Like other scales of this sort, such as the Beaufort scale of wind speeds (from calm to hurricane) or the Mohs scale of hardness (from talc to diamond), the Tupman scale is a touch impressionistic. But I know what I mean by portly and tubby, and it works well enough for a first approximation. Perhaps I should test it against estimated lean body weight.

However, I confess myself puzzled as to how to approach the problem of the littlun who is also a bigun – the obese child. The problem reminds me of another Pickwickian character, Joe the fat boy, and what he said to Mrs Wardle when about to inform her about Mr Tupman's dalliance with her daughter: 'I wants to make your flesh creep.