Drugs and the elderly

Sir: I was interested to read the article by Bird1 on drugs and the elderly. I agree that a substantial proportion of doctors will not understand pharmacokinetics. Unfortunately, their level of understanding will not be helped by some of the errors that have crept into this article.

For drugs which display first order kinetics the plasma half life and clearance are constant irrespective of the amount of drug available in the body for elimination. This is in contrast with a drug which displays zero order kinetics, where the clearance falls with increasing concentration as the elimination process becomes saturated. The definition of the volume of distribution of a drug is not, as stated in this paper, the amount of drug in the body available for elimination, but is the theoretical volume of fluid in which the drug is distributed if it existed in the same concentration elsewhere as it does in the plasma. This would be given by dividing the total amount of drug in the body by the plasma concentration. It is also incorrect to state that if the volume of distribution is reduced the peak plasma concentration will increase. This will be the case if the distribution process is rapid, but another major determinant of peak plasma concentration is the rate of absorption, and for a drug which is rapidly absorbed but slowly distributed, such as digoxin, volume of distribution will have a negligible effect on peak plasma concentration.

Finally, I find the term 'accumulation', as used here, confusing. Accumulation is not a phenomenon that depends upon the property of a drug, nor are there drugs which accumulate and drugs which do not accumulate. It depends upon the relation between the half life of the drug and the dosing interval and, by definition,4 accumulation occurs if the drug is given at a dosage interval of less than 1.44 half lives. Thus, even in young patients, accumulation of piroxicam will occur and we are speaking about in elderly subjects is relatively greater accumulation. It must also be stated that accumulation is not, in itself, a bad thing but is in fact necessary to produce fairly stable plasma concentrations.

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Sirs: Dr Pullar’s points are well taken, though such a detailed pharmacokinetic exposition was not available to me within the constraints on space imposed by a brief review article. Matters were rendered more ambiguous by the incorrect positioning of the term ‘volume of distribution’ which events led to frequent transcribing errors and for which I apologise. This allowed false conclusions to be drawn.

I remain less confused than Dr Pullar by the term ‘accumulation’, though accept that this enjoys a precise definition and that ‘relatively greater accumulation’ is a more accurate description of what was being discussed. Although agreeing that accumulation may be beneficial in producing stable plasma concentrations, this benefit can only be reapplied safely if the drug is relatively free from side effects.

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Cryptosporidial enteritis complicated by conjunctivitis

Sir: Shepherd et al recently reported two children with cryptosporidial enteritis complicated by reactive arthritis.1 A 13 year old girl with a past history of epilepsy, asthma, and hypothyroidism presented with a week two history of profuse watery diarrhoea, colicky lower abdominal pains, lethargy, nausea, vomiting, scattered arthralgic and myalgic pain. She also had conjunctivitis in both eyes. The child was admitted and stool examination showed oocysts of Cryptosporidia spp. No other pathogens were uncovered, and she eventually made a spontaneous recovery; her conjunctivitis subsided.

Reiter’s syndrome may follow urethral infection or gastroenteritis, and the clinical features of the condition—namely, arthritis, conjunctivitis and urethritis, or gastroenteritis, are well known. Shepherd et al described two female paediatric cases (and referred to one adult male case described by others) where cryptosporidiosis was complicated by reactive arthritis; all these subjects were evidently immunocompetent. In addition, two potentially relevant cases positive for antibody to HIV have been described, one being a 27 year old homosexual man with diarrhoea, urethritis, conjunctivitis, arthritis, and cryptosporidial oocysts, and the other a 4 year old child (sex unknown) with cryptosporidiosis who developed conjunctivitis as part of a more profound systemic illness (which was subsequently diagnosed as measles).1

Our patient had conjunctivitis and scattered arthralgic and myalgic pains associated with her gastroenteritic illness; accordingly, although the pathogenesis of cryptosporidial enteritis in immunocompetent subjects remains poorly understood, it is feasible that Reiter’s syndrome may represent a potential clinical consequence of the condition. It may be pertinent to note that unlike the almost total male exclusivity of Reiter’s syndrome associated with urethritis, among cases of Reiter’s syndrome associated with gastroenteritis (of whatever underlying cause) a much larger proportion occur in women.1 In addition, the syndrome has been reported occurring in sexually inactive children.4

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