OUTCOME IN ANTENATALLY DIAGNOSED RENAL PELVIS DILATATION

EDITOR,—Dr Nicholl raises some pertinent points in his letter regarding our paper.1 The nub of the matter is whether antenatal diagnosis in fetal uro-ureteric reflux (VUR), detected as a result of antenatal ultrasound findings is clinically important or not. The answer to this question is not yet known and will require a trial that looks at what, if any, difference treatment makes to outcome, as judged by the development of renal scars.

Until this matter is resolved, however, we feel it appropriate to look for VUR when there has been antenatal renal pelvis dilatation, and treat accordingly. As stated in our study,1 this judgement is partly based on the fact that the prevalence of asymptomatic VUR is around 1%, as described by Bailey, in contrast to an incidence of 20% in our study, implying that our findings were significant.

We accept that in a review of the published findings, from which Bailey acquired his data, the radiological techniques used may have differed from those currently in use, but as can be imagined, it is not easy to acquire information about the incidence of VUR in healthy children, and Bailey’s work is, to our knowledge, the currently accepted reference.2

With regard to the specific points raised by Nicholl around 50% of the babies with VUR in our study, have now undergone further imaging at the age of 3 years. Their reflux had resolved and, more importantly, no renal scar had been incurred. In those babies where both postnatal ultrasonography and the mic- turating cystogram were normal, the infants were discharged from further follow up, as we saw no further indication for continuing their surveillance.

The fact that only one baby required surgical intervention reflects that VUR, which is generally treated medically, was the most important finding. In those babies where amikacin was prescribed for 4 out of 455 involved the use of a drug in a way that the manufacturers had no license to recommend. The authors do not say what should be done about it.

They note that 84 prescriptions for vitamins and 77 for penicillin or an aminoglycoside used a dose other than the one mentioned in the drug data sheet. But they must be aware, surely, that doctors have to be shown the way in nature. Secondly, an immense amount of information has been published on these issues since the data sheets were first prepared.

What was the intended message when arranging a criticism of data sheets in the news media to latch on to this report before most clinicians had had their chance to read the paper for themselves? Were headlines such as “Doctors raise alarm over drugs given to babies,” and “Babies used as drug guinea pigs” really what you hoped to generate? Coming only a week after an article in the New Scientist,3 inspired by a steer from the Derby clinicians, the journal article led the BBC to report that “Doctors are calling for stricter controls to ensure children are not given dangerous doses of adult drugs.” Such manipulation of the news media does a serious disservice to a serious subject. Professor Anyesly-Green’s subsequent letter,4 contrasting the lack of support for paediatric pharmacology in the UK with the establishment of 13 such centres in North America, rather suggests that it was a simple bid for money.

Readers who turned to Professor Sir David Hull’s commentary in the same issue will have found little enlightenment. His main message seemed to be that children should buy Medicines for Children. However, any suggestion that this would be the first reference text to clearly identify unlicensed and off label paediatric drug use in the UK would be misleading. Even should that be the case, it wouldn’t get us very far: the new consensus driven text may tell us what most people currently do, but what most do is not necessarily right.

The neonatal use of gentamicin typifies some of the key issues, as Conroy has herself highlighted.5 The drug has been in neonatal use for over 30 years, but the best dose is still a matter for debate. High trough concentra- tions frequently cause concern, but there are actually very few reports of neonatal renal or ototoxicity. Low peak concentrations, on the other hand, often go unremarked.

Six separate papers have been published over the past year, which show that a therapeutic peak concentration will not be achieved for 12 to 24 hours using any standard policy, unless an initial loading dose is given—the volume of distribution being particularly high at birth—but such a strategy is still only recommended in a few reference texts.

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This is not an area where more money is needed for research. More than 100 papers have already been published on this topic over the past decade. There is no commercial pres- sure on the manufacturer to modify the data sheet: they are generic products unprotected by patents. Nor does the MRC or the Medicines Control Agency believe that it should take the initiative over this, although it would be very willing to review the case for voluntary modification with manufacturers if it is appropriate and responsible professional body. Why, then, does the Royal College of Paediatrics and Child Health not do this?

For most of the drugs listed by Conroy, there no need for further papers since other papers stating that drug data sheets are out of step with current practice. Nor do “they” need to tighten the prescribing rules and restrict what “we” can do. What is needed is sensible, sustained, and constructive dialogue between the profession, the licensing authorities, and the manufacturers, to get drug sheets revised at regular intervals, so that they reflect all the additional information that becomes available in the years after the product has entered the market. My message is, that it is up to the profession to start the ball rolling.

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have many other potentially contributory problems. Research is needed to establish the dose and frequency required to provide therapeutic, non-toxic serum concentrations of this drug for babies of all gestations.1

We were surprised by the media interest in our paper and responded to requests for interviews accordingly. Unfortunately, we cannot be held responsible for the headlines or tone of the published newspaper reports.

The extent of drug toxicity from unlicensed and off label drug use in neonates is unknown. We know that severe adverse drug reactions in children are more likely to occur with unlicensed and off label treatment than licensed drugs. The scientific study of drug treatment in neonates has been relatively neglected by both doctors and pharmacists in the UK and Europe. However, there are positive developments: the British Forum for the Use of Medicines in Children and the European Network for Drug Investigation in Children are trying to both encourage and coordinate clinical trials in this area.2

It is clear that many health professionals now have an interest in research in paediatric therapeutics. We are not simply bidding for money but trying to raise the profile of a neglected area of research. Historically, research has been centred on disease in specific areas such as cancer, cystic fibrosis, leukaemia, cardiac defects, etc. When seeking funding for research on the extent and risk of unlicensed and off label drug use in children3 we were told by a major children’s charity that they did not consider it an appropriate area for research and that they would not even consider an application for funding. We hope that the studies documenting the extent of unlicensed and offlabel prescribing4 and the consequences of such prescribing5 will convince the Department of Health and the major charities that this is an important area of research, and that the use of drugs in the neonate should be evidence based.


Editors’ comments

We issue press releases on articles of public interest with the aim of helping journalists to understand the material. The press releases are seen in advance by authors who have an opportunity to make changes, and are issued with an embargo date, to avoid media publicity before the Journal's publication date. However, we have no control over how the media choose to headline this information. The public and the media have access to articles in scientific journals once they are published and if we did not issue press releases we believe there would be evidence of scope for misinterpretation.

Glycosaminoglycans in neonatal urine

Editor,—Mucopolysaccharidoses (MPS) are a group of lysosomal storage disorders caused by deficiency of the enzymes catalysing the

[Graph not shown]

Figure 1 Uribary GAG:creatinine excretion ratio for normal infants and MPS patients. Circles indicate means; bars SD.

CORRECTION

Please note that the authors of Gilbert et al (Role of Ureaplasma urealyticum in lung disease of prematurity: 1999;81:F162-7) have noted a discrepancy in the reference list for this article. Reference 2 should read: