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.[2] 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.[3]

It is clear that many health professionals now accept the need for 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—for example, cystic fibrosis, leukaemia, cardiac defects, etc. When seeking funding for research on the extent and risk of unlicensed and off label drug use in children[2 4] 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 off label prescribing[4 5] and the consequences of such prescribing[7] 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.

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Editors' comments

We issue press releases on articles of public interest with the aim of helping journalists 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 even greater scope for misinterpretion.

Glycosaminoglycans in neonatal urine

EDITOR,—Mucopolysaccharidoses (MPS) are a group of lysosomal storage disorders caused by deficiency of the enzymes catalysing the stepwise degradation of glycosaminoglycans (GAG). Bone marrow transplantation can slow down or reverse some of the features of these diseases. Enzyme replacement (ERT) studies in several animal models of MPS disorders have shown promising results[1–3]; human clinical trials of ERT in MPS type I have only recently become possible.[4] The clinical symptoms of MPS usually become evident only between the second and third years of life. This therefore argues for early therapeutic intervention before the development of irreversible changes.

Quantitative measurement of urinary GAG (glycosaminoglycans) can be used to diagnose MPS. We investigated the change in urinary excretion of GAG to use for early diagnosis.

Random urine samples were obtained from 570 neonates on days 2–6 of life. The samples were obtained from 320 boys and 250 girls with birthweights of mean 3137 (SD 374) g and gestational ages of 39.7 (1.1) weeks. Urine specimens were collected from 85 neonates on day 2; 254 on day 3; 92 on day 4; 65 on day 5; and 74 on day 6. The babies had been born after an uneventful pregnancy and delivery and were not known to have any specific clinical abnormalities. Urine samples were also obtained from 1328 infants aged between 1 and 12 months old who had no symptoms of MPS, and from five MPS patients aged 1 month or less (MPS type II, 15 days old, 978 mg GAG/g creatine; MPS type II, 26 days old, 940 mg GAG/g creatine; MPS type II 1 month old, 1177 mg GAG/g creatine; MPS type III, 1 month old, 1180 mg GAG/g creatine; MPS VII, 1 month old), 205 mg GAG/g creatine.

The urine collector (ATOM pediatric urine collector, ATOM medical Co, Japan) was removed as soon as it was full of urine; it was then immediately stored at −20°C until analysis. After thawing at room temperature the urine were analysed as follows. Urinary excretion of GAG was measured using the DMB method[5] and the urinary creatinine concentration was measured using the Jaffe method.[6] Both measurements were performed using an MR 5000 plate reader (Dynatech, USA). The Wilcoxon rank sum test for unpaired data was used to compare groups.

Figure 1 shows the urinary GAG:creatinine ratio for normal neonates and infants and for five MPS patients. Urinary excretion of GAG decreased each day after birth until day 5 of life. The median for the GAG:creatinine ratio was 459.0, 446.4, 400.0, 323.0, and 311.5 mg/g on days 2, 3, 4, 5 and 6, respectively. Between days 2 and day 4 of life, the decrease was significant. Urinary excretion of GAG in the normal neonates was much lower than in the five MPS patients: type II, 15 days of age, 978 mg GAG/g creatinine; type II, 26 days old, 940 mg GAG/g creatinine; type II, 1 month old, 1177 mg GAG/g creatinine; type III, 1 month old, 1180 mg GAG/g creatinine; type VII, 1 month old 1205 mg GAG/g creatinine.

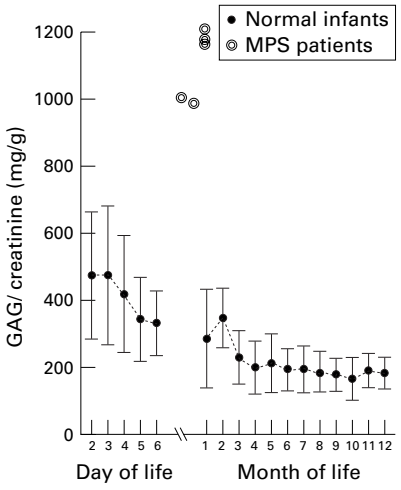

Figure 1 Urinary GAG: creatine excretion ratios for normal infants and MPS patients. Circles indicate means; bars SD.

The GAG:creatinine ratio in MPS patients was much higher than in normal infants. We conclude that these results might be useful for the early diagnosis of MPS.

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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:

2 Todd DA, Jane A, John E. Chronic oxygen dependency in infants born at 24-32 weeks' gestation: the role of antenatal and neonatal factors. *J Paediatr Child Health* 1997:**33**:402-7.

From there on all references should be renumbered accordingly.