

## LETTERS TO THE EDITOR

### Prostacyclin concentrations in haemolytic uraemic syndrome after acute shigellosis

SIR,—We read with interest the report of Alam and colleagues implicating prostacyclin (PGI<sub>2</sub>) in the pathogenesis of haemolytic uraemic syndrome after acute shigellosis.<sup>1</sup> However, we were confused by the methodology that they used to establish the PGI<sub>2</sub> concentrations in the plasma from their patients.

The authors state their intention to measure PGI<sub>2</sub> by firstly incubating rabbit aortic rings with their patients' plasma, and then subsequently assaying 6-keto-PGF<sub>1α</sub> in the incubation fluid, a method described by Moncada *et al.*<sup>2</sup> We have used a similar technique to investigate the role of PGI<sub>2</sub> in the pathogenesis of meningococcal shock, in which patients' serum was incubated with human umbilical vein endothelial cells.<sup>3</sup> Both of these methods have been established to assess endothelial PGI<sub>2</sub> production in vitro in response to exogenous stimuli, and not, as suggested in this paper, to measure the concentration of PGI<sub>2</sub> directly in serum or plasma.

The distinction between direct measurement of PGI<sub>2</sub> and the effect of these patient samples on PGI<sub>2</sub> production by aortic rings is important in determining the significance of the results presented by Alam *et al.* A depression of PGI<sub>2</sub> synthesis in vitro in response to plasmas from patients with haemolytic uraemic syndrome suggests that there is either a deficiency of a factor necessary for PGI<sub>2</sub> synthesis, or that there is a circulating inhibitor. We have recently suggested that the former mechanism is the most likely explanation for the observed decrease in PGI<sub>2</sub> production by endothelial cells when incubated with the sera from

children with meningococcal shock.<sup>3</sup> It is interesting that the PGI<sub>2</sub> concentrations reported by Alam and colleagues took a long time to recover. We have observed a defect in the serum of patients with meningococcal shock persisting for days, and sometimes weeks before normal endothelial PGI<sub>2</sub> synthesis can be demonstrated (unpublished results).

The authors conclude that the diminished PGI<sub>2</sub> concentrations reported in their study may be occur as a result of endothelial damage by endotoxin. However, the majority of in vitro, animal and human studies, to date, show that endothelial PGI<sub>2</sub> synthesis is stimulated rather than diminished by endotoxin.<sup>4-5</sup> This may occur as a direct response to endotoxin or following the elaboration of cytokines such as tumour necrosis factor and interleukin-1.<sup>5-6</sup> It would therefore seem unlikely that the action of endotoxin alone could adequately explain the depression of PGI<sub>2</sub> concentrations observed in haemolytic uraemic syndrome associated with shigellosis.

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### Diazoxide—an orphan drug?

SIR,—In the article on surgical treatment of hyperinsulinaemic hypoglycaemia in infancy and childhood the authors state that diazoxide, which inhibits glucose stimulated insulin secretion, is still the mainstay of medical management.<sup>1</sup> However, they fail to mention that, in its oral form, this drug is no longer readily available as the manufacture of this therapeutically desirable but commercially non-viable product has ceased and, thus, satisfies the definition of an orphan drug.<sup>2</sup>

This problem applies to other essential drugs and compounds used in paediatric practice, particularly for the treatment of inborn errors of metabolism. There is a clear need for the drug industry to be supported (by government subsidies if necessary) to maintain production of such essential drugs. Patients need orphan drugs and this must be the overriding consideration. Consequently, paediatricians, through the British Paediatric Association and the Royal Colleges should encourage the Department of Health to provide such direction to the drug industry, perhaps through the establishment of an orphan drug regulatory body under the auspices of the Medicine Control Agency.

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