

**CEFTRIAXONE** (Comment)**Co-infusion with any solution containing calcium**

Concern about the co-administration of ceftriaxone and any IV fluid containing calcium was first voiced by the French Health Products Safety Agency in November 2006 four years after they had first been alerted to one well documented death in 2002. Then in August 2007, after collating further information, Roche Pharmaceuticals modified their information leaflet and issued a warning that chelation *in vivo* (i.e. binding to calcium with the formation of an insoluble complex) made it potentially dangerous to give IV ceftriaxone to any child who was also receiving an IV infusion containing calcium at the same time. The company, in a display of possibly excessive caution, said it was also probably unwise to give ceftriaxone to any child who had been so treated in the past 48 hours, and the company's warning also applies, by implication, to almost any product used to provide parenteral nutrition.

The US Food and Drug Administration (FDA) issued their own warning about this on 11<sup>th</sup> September 2007, and an analysis of the 9 cases that came to the attention of the FDA was eventually made public in an article in *Pediatrics* in April 2009. In fact it became clear while this article was in press that one child had actually been reported twice, so the published analysis is actually based on just 8 voluntarily reported cases. In 7 of these 8 cases there was reasonably convincing evidence that the event report was a genuine adverse drug reaction, and 6 of these 7 children died. Six of the 7 babies were also being given 10% calcium gluconate at the time – the other was receiving calcium-containing hyperalimentation, and this was the one child who did not die. Six of the 7 children were less than 2 months old and at least 5 had received a higher dose than would normally be recommended (since 50 mg/kg once a day generally seems adequate unless there is meningitis). Two of the children who died had been given a 200 mg/kg IV dose. In all the cases where a full autopsy was done death seems to have been caused by pulmonary embolism and an unidentified 'white precipitate' or 'crystalline material' was reported as having been seen in the lungs.

Cefotaxime (q.v.), rather than ceftriaxone, would normally seem to be the better antibiotic to use in this situation, but some would question whether there was any strong reason for giving any of these children calcium gluconate. It is also worth remarking that there is, as yet, no evidence that the IM administration of ceftriaxone had ever proved hazardous. Neither have any serious adverse reactions yet been reported in children given IV ceftriaxone when more than a few months old.

Bradley JS, Wassel RT, Lee L, *et al.* Intravenous ceftriaxone and calcium in the neonate: assessing the risk for cardiopulmonary adverse events. *Pediatrics* 2009;**123**:e609–13.

Comment posted February 2008

Updated April 2009