Controversies in Vaccination with Measles, Mumps, Rubella (MMR) Vaccine

To the Editor,

Many people remember the extensive adverse publicity surrounding pertussis vaccine in the 1970s which led to public concern about the safety of vaccines. Subsequently, follow-up indicated no causal link between pertussis vaccination and brain damage although the risk of recurrent collapse (shock-like syndrome or so-called hypotonic-hyporesponsive episode) with a benign outcome, after such vaccination is higher than the background rate.[1,2]

Anti-vaccine movements became more assertive after the 1970s and, by discouraging pertussis vaccination, had a pronounced impact on increasing the incidence of pertussis in Europe, Australia, USA, and the former Eastern European Block.[3] Pertussis remains a greater risk than collapse after vaccination.[1] Estimates of the incidence of collapse vary widely. In the United Kingdom from 1976-88 there were three major pertussis epidemics accounting for over 300 000 notifications and at least 70 deaths.[4]

A recent 'early report' linked MMR vaccination with non-specific colitis and pervasive developmental disorder in children.[5] The suggestion that measles infection is causally linked to Crohn's disease had been disproved already[6] but there has since been a decrease in MMR vaccination uptake with the potential for future morbidity.[7]

The basis for the early report was 12 children whose parents had reported the onset of bowel disease and autism soon after MMR vaccination.[5] The age when these conditions first appear however, is also the age for MMR vaccination. This association does not confer causation.

Similarly, in the link between infantile spasms and pertussis vaccination, the vaccine unmasks rather than causes the syndrome.[8] Tragedy may occur when the media and the public confuse association with causality and shun immunisation.[9]

As vaccination has been so successful, many parents have forgotten the dangers of measles, mumps and rubella. If all other children are immunised, but theirs are not, their children have a low risk which encourages them to avoid what they perceive as hazards of vaccination.

Publicity has further dented confidence in MMR vaccine.[7] Although some reports have been alarmist, there have been at least two balanced media reports.[10,11]

The publication of the 'early report' based on only 12 patients resulted in a prodigious correspondence which canvassed the rift which can exist between clinical medicine and public health,[12] and the inadequacy of evidence related to problems of methodology.[11-21]

The controversy in that correspondence was whether or not the paper by Wakefield[5] should have been accepted for publication. It attracted mass media attention and generated considerable public concern despite the lack of evidence linking MMR vaccination with the conditions suffered by the 12 children.

It is now accepted that all risks and benefits concerning vaccination should be carefully explained to parents rather than attempting to persuade them that the procedure is totally without risk. The most common MMR adverse reactions reported are local reactions (pain, erythema and induration), but less frequent systemic reactions (headache, myalgia, arthralgia and pyrexia) have been reported.[22]

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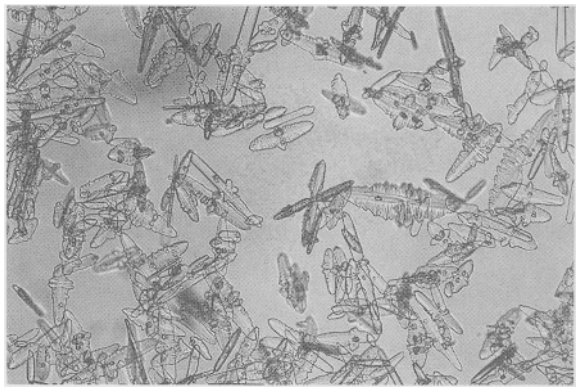
Precipitation of Potassium Sulphate During TPN Solution Admixture

To the Editor,

Total parenteral nutrition (TPN) solutions are diverse multicomponent pharmaceuticals of variable content with a considerable potential for physicochemical interaction between additives.[1] Monovalent cations do not usually lead to incompatibilities,[2] unless the solubility product of a salt is exceeded then precipitation will occur.

We have noticed the formation of translucent off-white needle-shaped crystals (Figure 1) in and around the injection port when potassium acetate 25 mmol/5 mL injection is added immediately after magnesium sulphate 10 mmol/5 mL injection during TPN solution admixture. The precipitate dissolves readily with adequate mixing.

The incompatibility was reproduced by drawing up 5 mL of each injection into a 10 mL luer lock syringe resulting in the formation of numerous crystals. Qualitative analysis of the precipitate revealed the presence of both potassium and sulphate.[3] This was further verified using electron probe energy dispersive X-ray microanalysis (EDX) which exhibited large spectral peaks for both potassium and sulphur, positively identifying the crystals as those of potassium sulphate.



500 μm

Figure 1. Micrograph of potassium sulphate crystals (magnification 20x)

The addition of potassium chloride 26.8 mmol/10 mL injection directly after magnesium sulphate 10 mmol/5 mL injection does not result in a precipitate; however, its presence in TPN solutions can decrease the solubility of potassium sulphate promoting crystal formation.[4]

The potential for potassium sulphate precipitation during compounding of TPN solutions highlights the importance of visual inspection and avoidance of local concentration gradients. TPN solution admixtures should be mixed well after each additive and on completion to stop incompatibilities which may not usually occur due to dilution and ion-shielding factors.

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First-Aid Treatment of Dermal Exposure to Hydrofluoric Acid

To the Editor,

Hydrofluoric acid (HF) is a highly toxic acid that is widely used in industry (in cleaning and etching of glass, metal, silicone, stone and porcelain; in the production of fluorides, plastics, germicides and insecticides; and in enamelling and galvanising iron, pickling stainless steel, analytical and dye chemistry, brewing, etc.) as well as in household products (alloy wheel cleaners, rust- and water-stain removers).

HF is highly corrosive and can penetrate deep into the skin causing severe tissue destruction and severe pain. The severity and time to onset of symptoms depends on the HF concentration, the duration of exposure and penetrability of the exposed tissue. In low concentration exposures (<10%), there may be a delay of several hours before symptoms are evident, whereas higher concentrations will cause quicker onset and more severe symptoms.[1]

Toxicity from HF is not limited to its acidity. Systemic fluoride toxicity may result from HF exposure by any route. The fluoride ions bind to calcium and magnesium ions in the tissue, resulting in hypocalcaemia and hypomagnesaemia, which subsequently may cause QT prolongation, ventricular arrhythmias, cardiac arrest and death.[1]

The accepted first-aid treatment of dermal exposure to HF in concentrations less than 20% is to remove any clothing from the affected area, irrigate the area with copious amounts of water and apply calcium gluconate gel.[1-4]

The Victorian Poisons Information Centre (VPIC) has become aware of recent instances where patients have presented to hospital for treatment of dermal HF exposures but calcium gluconate gel was not available from the hospital pharmacy. The VPIC is concerned that a standard antidote was not available to treat these patients and that this may have compromised their care.

There is a calcium gluconate 2.5% gel commercially available (Orion Laboratories Pty Ltd, 50 g tube), specifically developed to treat HF dermal exposures. In the absence of the proprietary product, there are several formulations for extemporaneous preparation of suitable calcium-containing gels (see Appendix 1); however, in the absence of stability data these would need to be prepared on demand.

In a review of 237 cases of dermal exposure to dilute HF (6-11%), there was some indication that calcium gluconate gel was more effective the sooner it was applied. The authors concluded that having the gel readily available in pharmacies and healthcare facilities might lead to earlier application and could lead to more rapid clinical improvement.[2]

Some authors are of the opinion that topical treatment alone may be sufficient for burns from HF in concentrations of less than 20%, but that more invasive therapy may be required if there is a significant delay in commencing treatment.[2] Patient wellbeing may be compromised if there are delays resulting from seeking the necessary components for gel preparation so, ideally, the ready-to-use gel should be available.

Exposures to HF are not uncommon; in 1996, the VPIC received 24 calls about HF exposures, 16 were to the skin, and in 1997 we received 22 calls with 17 involving the skin. As HF is present in a wide array of products for both household and industrial use, it is not only those hospitals with industrial catchment areas that need to be prepared to treat HF exposures.

The VPIC recommends that calcium gluconate gel be available in all emergency departments so that prompt, appropriate and effective treatment of dermal HF exposures can be given.

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Appendix 1. Calcium gel formulations[1]

Calcium gluconate powder method

Add calcium gluconate powder or ground tablets to water-soluble surgical lubricant (e.g. KY Jelly) to make a concentration of 2.5% w/w calcium gluconate.

Calcium carbonate tablets/powder method

Make a 32.5% w/w calcium carbonate slurry using calcium carbonate powder or ground tablets mixed into water-soluble surgical lubricant (e.g. KY Jelly).

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