Hypoglycaemia and hypothermia due to nimesulide overdose

Editor—Although toxicity due to chronic administration of nimesulide has been reported,1,2 to the best of our knowledge there is no report about poisoning due to a single ingestion. We report a 20 month old boy who accidentally took a high dose of nimesulide; 40 mg/kg, 8 times the recommended daily dose.

Physical examination was unremarkable. Laboratory findings, including hepatic and renal function, were normal, except for low to moderate acidosis (pH 7.35, bicarbonate 40 mg/kg, 8 times the recommended daily dose.

The most striking events in our patient were the development of hypotension and hypothermia. Hypothermia has been reported due to non-steroidal anti-inflammatory drugs: the effect of nimesulide compared with naproxen on the human gastrointestinal tract. 

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Editor—The use of a totally implantable venous access system (Port-A-Cath) in children has become widespread in the last 15 years. We report a series of three children for whom the Port-A-Cath improved management of their refractory seizures.

Two patients both females with a diagnosis of severe myoclonic epilepsy of infancy and recurrent status epilepticus presented in the first year of life. Both had seizures, which were intractable to multiple anticonvulsants and became refractory to benzodiazepines. Intravenous immunoglobulin therapy was started with some success. Again venous access was difficult and a Port-A-Cath was implanted at the age of 16 months in one patient and at 18 months in the other.

The third patient presented at 4 years with Lennox-Gastaut syndrome. Hospitalisation every 2–3 weeks became necessary for convulsant therapies, intravenous immunoglobulin therapy once every 2 weeks was started with some success. Again venous access was difficult and a Port-A-Cath was implanted at 4½ years.

The first patient developed a candida albicans infection 9 months after insertion. Amphotericin B was given for 14 days and the Port-A-Cath removed. A second device was inserted after the infection was treated and remained in place 6 years later with no further complications. The second patient had her Port-A-Cath removed after 6 years and 5 months when the catheter blocked. A second device has just been inserted. The third patient had no complications nine months after insertion.

Port-A-Cath devices are widely used in the management of children requiring venous access for longer than 3 months, when peripheral access is difficult and for administration of medications or blood products.1,4 Children who typically benefit have haemophilia, cystic fibrosis, or malignancies. To our knowledge, the present patient is, to our knowledge, the first patient with a previous reference to Port-A-Cath usage in neurological disease. In this study of 81 children, one child had the device inserted for home administration of medication. This was removed after a portal infection 3 months after insertion.

The benefits to a Port-A-Cath include rapid reliable venous access, low maintenance, fewer restrictions on lifestyle, low incidence of infection and malfunction, when compared with externalised systems. These benefits are attractive for children with a refractory seizure disorder and their families. Rapid venous access is invaluable to the physician when managing status epilepticus.

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Pica in sickle cell disease: “She ate the headboard”

Editor—Within our sickle cell population, there are a small number of school aged children who eat sponge. Knowing that pica—the compulsive ingestion of non-nutritive substances—is more common in tropical countries where cultural and dietary factors play a role, it may not be a surprising finding. However geophagia (soil), pagophagia (ice), and trichophagia (hair) are the most common substances eaten. We cannot explain the predilection for sponge amongst our patients.

Infants place everything in their mouth, and pica occurs in a variety of syndromes associated with brain damage and developmental delay. It is also more common in deprived and neglected children. Neurological complications are not uncommon in sickle cell disease (SCD) but none of our children had cognitive impairment or developmental delay.

There is a recognised association between iron deficiency and pica, leading to debate as to which is cause and which effect. Natural sponge contains various proteins and minerals, and is often fortified with silica or calcium salts, however, synthetic sponge consists of cellulose alone. We wondered whether a craving of an unidentified salt fuels the eating of sponge, or whether the texture of sponge is simply orally stimulating.

In one study of pregnant women, 35% with pica had a history of childhood pica and 56% had a positive family history. In our children, four have a positive family history. Therefore, pica can be a response to a nutritional deficit,
it can be familial suggesting a learnt behaviour, or developmental and emotional issues may be involved. In America it is classified as an eating disorder, in the UK it is considered a behavioural disorder; it can also be an obsessive-compulsive disorder, or a manifestation of depression.

Our children could shed no light on their compulsion. In six cases the parents found the behaviour so unacceptable that they requested psychological intervention and in four, the behaviour has now stopped. Thus whilst we find this behaviour fascinating, we are no clearer in understanding the aetiology of pica for sponge in this small population of children with SCD.

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Maternal nutrition and pregnancy outcome

EDITOR,—Symonds et al raise interesting issues about the potential use of animal models in examining the impact of nutrition during pregnancy on future risk of adult disease.1 However, their discussion of recent epidemiological research in humans includes several important factual inaccuracies. The authors imply that our analyses and those of several important statistical power to detect clinically important effects.

Figure 1 Birth weights were individually adjusted to the mean sex and gestational age of the cohort and for maternal smoking and height answered by animal experiments (unless one were to make the diabolic argument that the errors associated with extrapolating data from animal models to humans are less than those from using self-reported data on human dietary intake). We do not argue that maternal energy intake can never be associated with birth weight. Under extreme circumstances, such as those in the animal experiments cited by Symonds, or in Third World countries, this may be. However, this is no basis for suggesting that has any importance to populations in industrialised countries.

Maternal nutrition and pregnancy outcome

EDITOR,—The paper by Kanagasundaram et al on the use of nitrous oxide as an anesthetic during painful procedures fails to mention the effect of this gas on cobalamin metabolism. Nitrous oxide inactivates cobalamin, the active derivative of vitamin B12, and essential cofactor for the transfer of the methyl group from methyltetrahydrofolate to homocysteine to form methionine. For subjects with good body stores of cobalamin this effect is unimportant, but no-one using this agent should remain unaware of the potentially devastating complications in the nervous system of using nitrous oxide in subjects who are of borderline or deficient vitamin B12 status. Onset of subacute combined degeneration affecting the brain and spinal cord is a well documented event when individuals with low body stores of cobalamin are exposed to nitrous oxide.

There is a long list of situations which put children at special risk of cobalamin deficiency—for example, systemic malignancy or chemotherapy. Children with chronic conditions often need painful procedures, and depleted cobalamin stores may not be apparent unless measurements of serum B12 are made routinely. What is more, repeated use of nitrous oxide depletes the body stores of cobalamin even in well people.

Given the scale of use which would result from routine use of nitrous oxide in children undergoing painful procedures, there should be real concern about the potential for an accident in a child with occult cobalamin deficiency. The message must be: never forget vitamin B12 when thinking of using nitrous oxide.

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The outcome of specialist registrars in the southwest region

EDITOR,—The UK national directive is to increase consultant paediatric numbers substantially over the next 5–10 years which requires the delivery of suitably trained doctors. Higher specialist training in paediatrics is five years in length and there is the possibility that the current number of trainees will produce more consultants than there are posts, so trainee numbers will still have to be reduced. The southwest regional training committee has expressed concern that trainees are not completing training within five years for a variety of reasons. We therefore reviewed the training times and outcome of the 90 specialist registrars (SpRs) who have trained in our region since the introduction of the Calman training scheme.

The impact of the high proportion of women entering paediatrics needs to be addressed. Our review confirms that 29% of trainees are training flexibly, which will increase their training time for anything up to 10 years. All these are in the flexible training scheme that requires at least one full week. In regions where trainees have access to the retainer scheme and train for only two sessions per week, training times will be even further extended. Also our training committee is concerned that five SpRs have resigned before completing training. Four of these are women who resigned because, despite working part time, they felt that the career process was incompatible with family life.

Of the trainees who trained flexibly and who have obtained consultant posts, four have chosen to work as part time consultants. The other two would have done so had the opportunity been available. Female trainees will be longer to train, both because of flexible training and also time out for maternity leave. Moreover, every trainee will not necessarily translate into one whole time equivalent consultant.

In our region 47% of trainees are having their Certificate of Completion of Specialist Training (CCST) date reviewed; the average time for them to complete a five year CCST is 6.3 years. Reasons include sickness.

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Adrenaline syringes: community perspective

Editor,—We read with interest the paper by Unsworth regarding the over-prescribing of adrenaline syringes. We are sure that we are not the only community paediatric team who have similar concerns, although perhaps from a different perspective. Dr Unsworth writes of the safety issues. We have more experience of the practical problems.

Thanks to the availability of prompt training for school staff by community personnel, it is now not uncommon for a child to actually be excluded from school because they have an adrenaline injection device. However, they may very well be excluded from other activities such as guided tours or trips abroad.

There is also the increasing problem of young people with adrenaline injection devices moving on to college or work places. Who should train staff there?

Other problems with adrenaline injection devices in our local community include two being lost on the bus, and one being accidentally fired into the interphalangeal joint of a child’s thumb with the needle becoming bent like a fish hook.

There is also the issue of keeping them in date. Parents often forget to renew them, particularly those kept in school. Whilst it does not need to be kept in a refrigerator, adrenaline does deteriorate in warm conditions, and injection devices should be checked to make sure that the adrenaline inside remains clear and colourless.

Often, an adrenaline injection device has been prescribed with no demonstration to the child or family on how to give it, nor when to give it. Surely antihistamine should also be prescribed in every case? In most children, it is the only medication, which is going to be needed. Keeping up to date with instructions on when to call an ambulance. They could easily make the mistake of trying to take a deteriorating child to hospital in their own car, instead of calling the prehospital ambulance service, or even assuming that they do not need to go to hospital at all if they have given adrenaline. As Dr Unsworth points out, the adrenaline injection does not always save the child’s life.

We would suggest that when an adrenaline injection device is prescribed it must be demonstrated to both the parent and child (if the child is old enough). A dummy pen is helpful for this. Demonstration should be repeated with each repeat prescription of the device. The child and their family should always have a written management protocol, including instructions on expected symptoms, when to give antihistamine, when to call an ambulance, and when to give adrenaline. Such a protocol can then be passed rapidly to the community paediatric team to support the prompt training of school staff.

It is worth remembering that clinical responsibility for the safe administration of a drug rests with the prescriber.

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Adrenaline syringes are vastly over prescribed. Arch Dis Child 2001;86:410–11.

Controversies in paediatrics?

Error,—I was very disappointed to see that the first contribution to the Controversy series was not written by a paediatrician. There are plenty of controversial topics in paediatrics, including the one cited. There are also plenty of paediatricians perfectly qualified to write on this subject. Why do we need to go outside the specialty, and again including the topic cited. The absence of a contrasting viewpoint in the same issue suggested to me the feature should be called “Opinion” rather than “Controversy” because the article is not a balanced review of the current state of allergy practice. The BPA and latterly RCPCH have championed for decades the holistic approach to the care of children. Paediatricians are best placed to assess the integrated needs of a child with medical problems. This principle is very relevant to developing areas of specialisation in which there is short supply of expert advice, such as in allergy. Paediatric allergists assess the impact of the diagnosis on many non-medical facets of a child’s life, including family lifestyle, integration into schools and peer groups, and the facilitation of appropriate and independent parental supervision. It is tiring to have to rehearse the arguments for the adequate protection of subjects at risk of anaphylaxis. Epinephrine (as all doctors should now be calling adrenaline) is not prescribed for all peanut allergy subjects who have reacted to peanut, a food known to be associated with a risk of a severe allergic reaction.

Doctors must remember epinephrine is prescribed to be available for response to infrequent exposure at an uncertain future date, not to be taken four times a day. I have referred to this in the past as analogous to wearing a seatbelt on every car trip, every day, even though a serious car accident is unlikely on any individual day.

Unsworth is not up to date in his comments about the diagnosis of IgE mediated allergy. There are strong data from huge series of challenges, about the negative predictive values of the tests used in allergy clinics. Unsworth does not even mention formal challenges, the cornerstone of modern food allergy practice. The allergist would prescribe an epinephrine kit on the basis of a positive SPT in the absence of a significant history or formal challenge.

Children and adults at risk of food related anaphylaxis have enough of life’s pleasures denied to them. The provision of epinephrine

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kinds allows normal life to go on, involving school, overnight stays at friends, camping, and other normal activities of childhood. Anecdotally, parents seem to me less stressed when they leave clinic with information (however awful the scenarios described) and reassurance that things are better than when they arrive. I have never met a parent who reported being more scared of the epinephrine kits than of the prospect of allergen exposure (with or without epinephrine available).

Families must be taught when to use epinephrine and how to use autoinjectors. Until doctors can tell families that anaphylaxis will never happen we should continue to empower families, earning they are ready to respond as best they can to the disaster that allergen exposure represents. When anyone develops a real treatment for food related anaphylaxis I can stop prescribing epinephrine kits to people who currently need them.

Reply

EDITOR,—I was pleased to see that my article provoked lively discussion of this important issue. I am not surprised that there are concerns about poor compliance. I agree with Wolff and Runnney that adrenaline should never be the sole prescription. In addition to antihistamines, prednisolone has a place. The idea of a written management plan is a good idea.

Hourihane contrasted prescription of adrenaline with provision of insulin syringes in diabetes mellitus. We do not restrict provision of insulin syringes in that context because to do so would inevitably lead to hypoglycaemia and ill health in all cases, ranging from coma to retinopathy. The risk benefit ratio is clearly in favour of daily insulin use. By contrast, the “very high” number of adrenaline prescriptions in food allergy (perhaps) prevents death in food allergic individuals, does by contrast raise concerns about the risk benefit ratio. In our clinics, where we see large numbers of both adults and children, reviewing the last few years we have seen one fatal and two near fatal episodes related to adrenaline usage (submitted for publication). Admittedly, all three were in adults. Hourihane prescribes “epinephrine” to “most (but not all) subjects who have reacted to peanuts”. He allows some patients not to have adrenaline but I am sure many patients do not get the prescription. Those with a previous history of only mild reactions can go on to suffer severe life threatening reactions,5 so all at risk patients will surely demand adrenaline. He would not prescribe adrenaline in the absence of a significant clinical history of true nut allergy, (and I applaud that) but others regrettably do, and I know from personal experience that once the mistake is made, it is hard to reverse. I like the seat belt analogy, but seat belts have few side effects. Regarding positive and negative predictive values of IgE based allergy blood tests, my point is that often these tests are misleading: Patients with eczema, (a common finding in those presenting with possible nut or food allergy) typically have high background IgE levels and false positives are common. Dr Abay reminds us that under the medical staff including doctors may administer adrenaline incorrectly. That fact does not justify deligation of responsibility to the general public instead. They are surely more likely to make errors, despite training and/or management plans. Expecting the public to confidently decide whether to use the adrenaline or not, is expecting a lot. Fatal episodes do indeed tend to occur within minutes of allergen exposure and can evolve to anaphylaxis rapidly, even in cases where previous reactions have been benign. Families may well misjudge and/or err on the side of caution, giving adrenaline early for what was likely to turn out to be another benign reaction. Hence my keenness for restriction of community use and increased reliance on trained medical staff.

I would also like to remind readers that many thousands of children and adults experience unpleasant but essentially benign reactions each year, very very few prove fatal.6 In the community context, focusing on the higher risk groups including asthmatics would be my preference.

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1 Unsworth DJ. Adrenaline syringes are vastly over prescribed. Arch Dis Child 2001;84:410–11


Appropriate prescription of epinephrine remains the best available treatment

EDITOR,—Epinephrine kits enable a food allergic child at risk of anaphylaxis to lead a normal life and participate in childhood activities that could easily be denied by a parent terrified of another allergen exposure.

Avoidance of allergens rather than rescue epinephrine therapy is the basis of curricular management of food allergy. However, unexpected exposures are inevitable. Fifty eight per cent of children followed for five years experienced adverse reactions from accidental peanut exposure.1 Peanut is the most common food allergen causing anaphylaxis and perversely is often under used, in food processing. Anaphylaxis related to foods most commonly occurs in patients who have had previous severe reactions. However, minor initial reaction does not exclude a subsequent severe reaction to peanut. Any person with anaphylaxis deserves the best available protection. It is reasonable to always have two Epipens available both at home and at school. A second Epipen provides back up if a faulty technique is used or one syringe is damaged. Anaphylaxis may be biphasic, recurring in 3% of children admitted with anaphylaxis.7

As advocates of children, paediatricians are unlikely to hand out epinephrine syringes without due regard to the impact on the child and his or her family. A comprehensive plan with written information is essential for any child seen with a food allergy whether or not epinephrine is prescribed. Sicheret et al showed 20% of children did not carry epinephrine outside the home and only 55% had unexpired epinephrine on them. However, successful demonstration was associated with repeat prescriptions, membership of a lay organisation for food allergy, and being reviewed by a doctor.8 Training packages for schools such as that devised by Vickers in Cambridge9 are valuable.

Unsworth states that “Community use should be much more restricted with increased involvement and reliance on trained medical staff”. Food allergy is the most common cause of anaphylaxis in children outside hospital. Early recognition and use of epinephrine is vital for successful outcome. The median time to respiratory or cardiac arrest was thirty minutes in a study of unrefined anaphylaxis in one series.10 Surely this implies that the community is the setting where epinephrine should be given by appropriately trained parents and carers to a food allergic child with signs of anaphylaxis. Parents should be empowered as limited resources prevent medical staff being present immediately. Indeed, epinephrine IV by trained medical staff also appears to be more hazardous than the use of epinephrine by allergists.5

In the absence of any other treatments for food related anaphylaxis, the considered use of epinephrine kits as part of an integrated management plan is the best choice.

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The outcome of specialist registrars in the southwest region

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