Hypoglycaemia and hypothermia due to nimesulide overdose

Editor—Although toxicity due to chronic administration of nimesulide has been reported, 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 borderline glucose concentration (3.27 mmol/l) and mild acidosi (pH 7.35, bicarbonate 16.9 mmol/l). Gastric lavage with activated charcoal was performed. One third N saline in 16.9 mmol/l. Body temperature and blood pressure were the development of hypotension and became refractory to benzodiazepines. Intravenous access was difficult. The patient had a positive family history. In our children, pica had a history of childhood pica and 56% to which is cause and which event. Natural sponge 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 also frequently reported. 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 also frequently reported. 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 also frequently reported.
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 complication. In six cases the parents found the behaviour so unacceptable that they requested psychiatric 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.

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 Godfrey et al grouped women into categories of energy intake, and suggest that different results might have been obtained had “all the raw data points [been used] to determine potential relations between maternal nutrition and birth weight”. Yet as clearly indicated in both papers,1,2 this is precisely the analysis that was conducted. For information, figure 1 shows the relationship of maternal energy intake to birth weight in our study. In each panel, the cut points used in tables to illustrate the relationships between energy intake and birth weight were neither “unclear” nor “arbitrary” but were, as stated, tertiles. Symonds et al draw attention to the “striking difference” in energy intake between our study and that of Godfrey et al whilst also suggesting that we should combine our data in a meta-analysis. We argue that the differences are not particularly striking given the different methodologies used for dietary assessment. It would not be appropriate to combine in a meta-analysis data collected in contrasting ways from women at different stages of pregnancy. In any case, our study individually has sufficient statistical power to detect clinically important effects.

In animal experiments above observational epidemiology in humans, Symonds et al confuse two separate issues. First, there is the biologically interesting question of whether maternal diet can influence the outcome of pregnancy. This has already been demonstrated in animals. Second, there is the question of whether maternal diet does influence the outcome of human pregnancy. This question is of clinical and public health importance. It cannot be answered by animal experiments (unless one were to make the dubious 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 cannot be associated with birth weight. Under extreme circumstances, such as those in the animal experiments cited by Symonds, or in Third World countries, it may be. However, this is no basis for suggesting that has any importance to populations in industrialised countries.

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Nitrous oxide and vitamin B12

Editor,—The paper by Kanagasundaram et al1 on the use of nitrous oxide to alleviate pain and anxiety 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 methylenetetrahydrofolate 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.2

There is a long list of situations which put children at risk of cobalamin deficiency—for example, diets low in animal products, synthetic feeding of any description, small bowel malabsorption, any prolonged illness with disturbance of feeding behaviour, especially if combined with increased metabolic demands—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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Adrenaline syringes: community perspective

EDITOR.—We read with interest the paper by Unsworth regarding the over-prescribing of adrenaline syringes. We are sure 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 rare 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 guide camp 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 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. How do we instruct them 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 a paramedic ambulance, or even assume 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.

1 Unsworth DJ. Adrenaline syringes are vastly over prescribed. Arch Dis Child 2001;84:110–11.

Controversies in paediatrics?

EDITOR.—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 an informed debate about this topic, again including the topic cited. The absence of a contrasting viewpoint in the first contribution to the Controversy series is not to be taken four times a day. I have seen many complicated cases of children with medical problems. This principle is very relevant to developing areas of specialisation in which there is shortage of 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 independence from 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 in clinic to families with an allergic child. It is part of the integrated management plan, which appears to be effective though difficult to measure.

It is very hard to prove that epinephrine saves lives and I agree with the notion “number needed to treat” with epinephrine to prevent a death from anaphylaxis is very high. Unsworth’s title suggests that this “very high number” (my phrase) is too high. How has he measured that? What is too many? He quotes a prevalence of about 1% of American children having peanut allergy. That is approximately 3 million subjects. We do not restrict insulin syringes to just a few insulin dependent diabetics because diabetes is so common that we cannot adequately care for all of them. Every allergic child has the right to best available care, which is not restricted to the first 100 through the clinic door (if they can find an allergy clinic).

Laparotomy will not save every patient with a leaking aortic aneurysm. Epinephrine will not save every person who has anaphylaxis. Anaphylaxis is a critical situation in which prompt administration of epinephrine may (but occasionally may not) save a life. I think it unarguable that it is better to self treat and probably survive than not self treat and possibly die. Unsworth quotes one early paper about anaphylaxis from the US and more recent British data. These papers all all more than 30 years old. The adrenaline is no longer used due to unavailability or inappropriate training and patient confusion, rather than that it is ineffective. Most subjects did not have epinephrine available, several of the deaths where adrenaline “wore” were due to incorrect use of available epinephrine. In addition, epinephrine appears to be more dangerous in the hands of doctors who give it IV than in the hands of allergic subjects who self treat. This is encouraging screening and education should be used to prevent the disasters that have occurred.

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Controversial topics in paediatrics should be the first contribution to the Controversy series. Controversy because the article is not a balanced discussion. There are plenty of controversial topics in paediatrics, including the one cited. There are also plenty of paediatricians perfectly qualified to write an informed debate about this topic, again including the topic cited. The absence of a contrasting viewpoint in the first contribution to the Controversy series is not to be taken four times a day. I have seen many complicated cases of children with medical problems. This principle is very relevant to developing areas of specialisation in which there is shortage of 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 independence from parental supervision.

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kits 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 this is less than they are led to believe. 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, ensuring 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.

Letters

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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 current 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 pervades life 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 peanuts. Any person still of 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.1

As advocates of children, paediatricians are unlikely to hand out epinephrine syringes without due consideration of the impact 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. Sicherer 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 repeating prescriptions, members of a lay organisation for food allergy, and being reviewed by a trained nurse. Training packages for schools such as that devised by Vickers in Cambridge 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 450 anaphylaxis in one series.2 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 in allergic patients.3

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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Reply

Editor,—I was pleased to see that my article provoked lively discussion of this important issue. I am not surprised that likely to be even more concerned about poor compliance. I agree with Wolff and Runney that adrenaline should never be the sole prescription. In addition to antihistamines, prednisolone has a place. The idea of a written management plan also seems sensible.

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 result in hypoglycaemia and ill health in all cases, ranging from coma to retinopathy. The benefit risk ratio is clearly in favour of daily insulin use. By contrast, the “very high” number of adrenaline prescriptions required to (perhaps) prevent 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 describes “epinephrine to “most (but not all) subjects who have reacted to peanuts”. He is surely more likely to make some patients do not get the prescription. Those with a previous history of only mild reactions can go on to suffer severe life threatening reactions,4 so all allergic children 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 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 of school medical staff including doctors may administer adrenalineline incorrectly. That fact does not justify deligation of responsibility to the general public instate. 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 look forward to hearing from many thousands of children and adults experience unpleasant but even less benign reactions each year, very very few prove fatal.5 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 overprescribed. Arch Dis Child 2001;84:410–11.