Hypoglycaemia and hypothermia due to nimesulide overdose

Editor—Although toxicity due to chronic administration of nimesulide has been reported,1 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 dosage.

Physical examination was unremarkable. Laboratory findings, including hepatic and renal function, were normal, except for low to moderate hypoglycaemia and acidosis.

Six hours later, serum glucose concentration was 3.44 mmol/l, venous pH 7.28 and bicarbonate 18.5 mmol/l. His systolic blood pressure and body temperature fell to 60 mm Hg and 33.0 °C (axillary, respectively). The patient was rewarmed and the intravenous infusion rate increased to 2000 ml/m²/day. Six hours later, his serum glucose concentration was 4.44 mmol/l, venous pH 7.33, and bicarbonate 16.5 mmol/l. Body temperature and blood pressure rose and 20 hours after admission all vital signs became normal, mild acidosis resolving within 24 hours. He was discharged after 48 hours. Physical examination and laboratory findings were normal six days after discharge.

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 overdose, but hypoglycaemia due to the antipyretic action of nimesulide has not been reported. Nimesulide induces a decrease in body temperature by inhibiting COX-2, but its effect under normothermic conditions is not known. Although it has been reported that nimesulide might be given to children with hypoglycaemia,1 it may cause hypoglycaemia in high dosages.

We advise frequent monitoring of vital signs and being alert for hypoglycaemia and acidosis in managing acute nimesulide overdose.


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The editors will decide, as before, whether to also publish it in a future paper issue.


Port-A-Cath usage in children with refractory seizure disorders

Editor,—The use of a totally implantable venous access system (Port-A-Cath) in children has become widespread in the last 15 months when the catheter blocked. A second device has just been inserted. The third patient presented at 4 years with intractable to multiple anticonvulsants, and is often fortified with silica or calcium salts, however, synthetic sponge consists of cellulose alone. We cannot explain the predilection for sponge amongst our patients. Infants place everything in their mouth, and pica occurs in a variety of syndromes—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 commonest compulsive ingestion of non-nutritive substances—is more common in deprived and neglected children. Neuroligical complications are not uncommon in sickle cell disease (SCD) but none of our children had cognitive impairment.

Port-A-Cath devices are widely used in the management of clusters of generalised tonic clonic seizures in children who typically benefit have haemoglobin purity of more than 30% and are under 14 years of age. 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.1 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.


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 commonest compulsive ingestion of non-nutritive 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—more common in deprived and neglected children. Neuroligical complications are not uncommon in sickle cell disease (SCD) but none of our children had cognitive impairment.

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, 33% with pica had a history of childhood pica and 56% had a positive family history. In our children, four had a positive family history. The most common reasons for pica were the craving of an unidentified salt, scurvy, and 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. 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, this is precisely the analysis that was conducted. For information, figure 1 shows the relations of maternal energy intake to birth weight in our study. In each paper, 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 a population-based 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. Secondly, 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 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, it may be. However, this is no basis for suggesting is has any importance to populations in industrialised countries.

Letters


Maternal nutrition and pregnancy outcome


Nitrous oxide and vitamin B12

EDITOR,—The paper by Kanagasundaram et al 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 cob(II)alamin, 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. Status 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 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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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 over the five years and more will ensure 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 high impact of the 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 five sessions per 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 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 programme based on current calculations is 6.3 years. Reasons include sickness.
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 of 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. Even children with a history of asthmatic exacerbation have no instruction 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 antihistamines, 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 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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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 give an informed debate about them, 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 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 freely 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 of “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 Americans 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 be 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 refer to more than 60% having asthma, the second known association with severe reactions. According to current opinion, then, even after just one reaction to peanut most subjects are considered at risk of severe future reactions. Many minor reactors to peanut progress to more severe reactions and new epinephrine ‘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. I recommend your readers look at the report on the latest series of food related deaths.

In the absence of any perfect predictive test, allergists are confined to basing risk of future severe reactions on just a few variables. The first is a history of previous severe reactions. The majority of peanut allergies have had a severe reaction in the past and more than 60% have asthma, the second known association with severe reactions. According to current opinion, then, even after just one reaction to peanut most subjects are considered at risk of severe future reactions. Many minor reactors to peanut progress to more severe reactions and new epinephrine ‘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. I recommend your readers look at the report on the latest series of food related deaths.

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
kits allows normal life to go on, involving schools overnight stay 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 respond less anxiously 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, 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.

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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 many doctors are concerned about poor compliance. I agree with Wolff and Runnemy 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 create avoidance of insulin 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 one 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 peanut”. He does not explain why 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, so all informed families 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.

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

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