ent from the international non-proprietary name. On the other hand, the World Health Organisation cannot impose on these countries a name that they consider to be unacceptable. The most logical solution would be to set up bilateral discussions between the organisation's experts and the national nomenclature committees with a view to the adoption of a single non-proprietary name for those drugs for which discrepancies exist.

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- 1 George CF. Naming of drugs: pass the epinephrine, please. *BMJ* 1996;312:1315-6. (25 May.)
- 2 Navarro FA. La nomenclatura de los fármacos. II. Las denominaciones comunes internacionales en España. *Med Clin* 1995;105:382-8.
- 3 British Pharmacopoeia Commission. *British approved names*. London: HMSO, 1990.
- 4 World Health Organisation. *Dénominations communes internationales (DCI) pour les substances pharmaceutiques. International nonproprietary names (INN) for pharmaceutical substances*. Geneva: WHO, 1992. (Cumulative list No 8.)
- 5 Fleeger CA, ed. *USAN and the USP dictionary of drug names*. 31st ed. Rockville: USP, 1993.

BMJ should use "paracetamol" instead of "acetaminophen" in its index

EDITOR,—One drug is notably absent from C F George's editorial on the naming of drugs.¹ Paracetamol is widely used for pain and fever from cradle to grave. It is also the substance most commonly taken in deliberate self poisoning,² causing 150 deaths a year in Britain.³ It is a medicine that people travelling abroad take with them or buy when they get to their destination, so everyone should know what to call it. Yet it still has two names: paracetamol and acetaminophen. This creates two problems, one for the general public and one for doctors and medical editors.

Acetaminophen is the United States adopted name,⁴ and in the United States the substance is always and only called acetaminophen. Paracetamol is the recommended international non-proprietary name,⁵ the British approved name,⁴ and the name used for the substance throughout the world outside the United States. Two names for such a common over the counter drug must create confusion and risk for the public travelling to and from the United States. Ideally, the United States would abandon the name acetaminophen and adopt paracetamol. A pragmatic first step would be to label preparations as containing the substance "acetaminophen (paracetamol)" in the United States and "paracetamol (acetaminophen)" in Britain and other countries.

Doctors in Britain who do not know that paracetamol has another name could come unstuck clinically and in their reading. Here the *BMJ* has a role. Since 1992 (volume 305) the index for the *BMJ* has said "see acetaminophen" beside the entry for paracetamol. It then indexes all entries about paracetamol under the American name, even though the articles use the name paracetamol. I wonder why the *BMJ* does this, because it is not the usual or proper practice in Britain. The name paracetamol appears, without reference to acetaminophen, in the index and text of the March 1996 edition of the *British National Formulary*, the 1995 indexes of the *Drug and Therapeutics Bulletin* and the *Lancet*, and the 1995 edition of *A Textbook of Pharmacology*.⁵ It makes no sense for the *BMJ* alone to use acetaminophen as the reference name for this drug.

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- 1 George CF. Naming of drugs: pass the epinephrine, please. *BMJ* 1996;312:1315-6. (25 May.)
- 2 Hawton K, Fagg J. Trends in deliberate self poisoning and self injury in Oxford, 1976-90. *BMJ* 1992;304:1409-11.
- 3 Spooner JB, Harvey JG. Paracetamol overdosage—facts not misconceptions. *Pharm J* 1993;250:706-7.
- 4 Reynolds JEF, ed. *Martindale: the extra pharmacopoeia*, 31st ed. London: Pharmaceutical Press, 1996.
- 5 Ritter JM, Lewis LD, Mant TGK. *A textbook of clinical pharmacology*. 3rd ed. London: Edward Arnold, 1995.

*The *BMJ*'s index uses the medical subject headings published by the United States National Library of Medicine. These headings are used in *Index Medicus* and Medline and are an international standard; it is appropriate to use an international standard because the *BMJ* is read worldwide. As Nick Bradley points out, however, the headings do not always reflect current usage, and so at the beginning of this year we decided to make some changes; thus, for instance, the index now refers to cars instead of automobiles and, indeed, to paracetamol instead of acetaminophen.—EDITOR

Cerebral oedema after MDMA ("ecstasy") and unrestricted water intake

Values for plasma osmolality may have been wrong

EDITOR,—S M Matthai and colleagues report two cases of cerebral oedema associated with the syndrome of inappropriate secretion of antidiuretic hormone after ingestion of 3, 4-methylenedioxymethamphetamine (MDMA or "ecstasy").¹ Their letter is, however, somewhat misleading.

In case 1 the patient was reported to have a plasma sodium concentration of 119 mmol/l and a plasma osmolality of 156 mmol/kg. Some time later the urine sodium concentration was 6 mmol/l and urine osmolality 655 mmol/kg. In case 2 the patient was reported to have a plasma sodium concentration of 112 mmol/l and a plasma osmolality of 142 mmol/kg. Urinary sodium concentration was 99 mmol/l and urine osmolality 184 mmol/kg. They do not state whether the osmolalities were measured or calculated.

Plasma osmolality can be calculated from the equation: plasma osmolality = (2 × plasma sodium) + plasma urea concentration + plasma glucose concentration. Some people chose to include potassium concentration in the calculation. To have a plasma osmolality of 156 mmol/kg with a plasma sodium concentration of 119 mmol/l or an osmolality of 142 mmol/kg with a plasma sodium concentration of 112 mmol/l is extremely unlikely. In both instances there would need to be a drastic deficiency in anions and these values are probably not compatible with life. Both values may have been typographical errors and osmolalities in case 1 and 2 were 256 and 242 mmol/kg, respectively.

The features of the syndrome of inappropriate secretion of antidiuretic hormone are, however, a low plasma osmolality and low plasma sodium concentration with an inappropriately concentrated urine. There is usually a high urinary sodium concentration due to low urine volume in association with low circulating aldosterone concentrations. In case 1 urine osmolality was high and urinary sodium concentration low; this could be produced by severe dehydration (causing appropriately raised concentrations of antidiuretic hormone) in which rehydration fluids were deficient in sodium (such as from copious drinking of water). Severe hyponatraemia may also occur in acute alcohol intoxication. In case 2 the urine osmolality was not high (particularly if the plasma osmolality was incorrectly

quoted) and the values do not seem to be compatible with the syndrome of inappropriate secretion of antidiuretic hormone. Instead, they suggest more that simple (severe) water intoxication was the cause of cerebral oedema.

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- 1 Matthai SM, Sills JA, Davidson DC, Alexandrou D. Cerebral oedema after ingestion of MDMA ("ecstasy") and unrestricted intake of water. *BMJ* 1996;312:1359. (25 May.)

Hyponatraemia must be treated with low water input

EDITOR,—S M Matthai and colleagues have rightly brought our attention again to hyponatraemia as a complication of ingesting 3, 4-methylenedioxymethamphetamine (MDMA or "ecstasy"), adding two cases¹ to at least four previously described. The syndrome of inappropriate secretion of antidiuretic hormone has been proposed as the cause in five of these six cases.¹

I am unconvinced that the clinical and biochemical details presented in these cases point indisputably to the syndrome of inappropriate secretion of antidiuretic hormone. In this syndrome the inappropriateness is not that the urine is concentrated in the presence of dilute plasma, because this can occur in other diseases such as hyponatraemic dehydration complicating diarrhoeal illness, but rather that water is inappropriately conserved by the kidney in the presence of total body water overload. Overhydration explains the natriuresis and high urine sodium concentration that usually accompanies the true syndrome of inappropriate secretion of antidiuretic hormone, despite the hyponatraemia. Natriuresis was not present in case 1,¹ the urine sodium concentration of 6 mmol/l suggesting avid renal sodium conservation; it was also not documented in three of the four previous cases mentioned.¹ In case 2 the stated urine osmolality (184 mmol/kg) is accounted for entirely by the sodium concentration (99 mmol/l) and its attendant anion(s); the urinary urea concentration cannot have been high so this patient cannot have been avidly retaining water at that time. I assume that the stated plasma osmolalities of 156 and 147 mmol/kg should have read 256 and 242 mmol/kg. Urine osmolality was also far from maximal (365 mmol/kg) in one of the other cases alleged to be the syndrome of inappropriate secretion of antidiuretic hormone mentioned by Matthai and colleagues.¹

Severe dehydration, and presumably sodium depletion, caused by hyperthermia and sweating as part of the MDMA intoxication syndrome is well known and supported by experimental evidence in animals.^{2,3} Dehydration would explain why serum antidiuretic hormone concentrations might be appropriately high, even had they been measured. I think that the hyponatraemia was more likely to have been caused by a combination of sodium depletion from severe sweating or vomiting, or both, and excessive water intake without sodium repletion, as suggested by the title of the letter by Matthai and colleagues.¹

Though I disagree with the postulated pathophysiology, I agree that unrestricted water intake is to be discouraged; sports drinks containing salt might be more appropriate for supply at "rave" parties.

Cerebral oedema in cases 1 and 2¹ is not necessarily indicative of total body water overload (the person may still be dehydrated despite ingesting large amounts of water). It has been postulated to be caused by acute water ingestion (or administration), leading to a sudden lowering of plasma osmolality with intracellular water shift.^{4,5}

The management of severe hyponatraemia remains controversial,^{4,5} especially the use of hypertonic saline as advocated in one of the other previous reports.¹ Modern intensive care principles advocate very slow correction of hyponatraemia with a low water input (even if the patient is dehydrated), so I agree with this and other reports¹ that it is unrestricted intake of oral or intravenous water that is inappropriate.

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- 1 Matthai SM, Davidson DC, Sills JA, Alexandrou D. Cerebral oedema after ingestion of MDMA ("ecstasy") and unrestricted intake of water. *BMJ* 1996;312:1359. (25 May.)
- 2 Green AR, Cross AJ, Goodwin GM. Review of the pharmacology and clinical pharmacology 3,4-methylenedioxymethamphetamine (MDMA or "Ecstasy"). *Psychopharmacology (Berl)* 1995;119:247-60.
- 3 Dafters RI. Hyperthermia following MDMA administration in rats: effects of ambient temperature, water consumption, and chronic dosing. *Physiol Behav* 1995;58:877-82.
- 4 Wright M, De Silva P, Sinha S. Hyponatraemia in children. *BMJ* 1992;305:51-2.
- 5 Ellis SJ. Hyponatraemia in children. *BMJ* 1992;305:52.

Drug workers emphasise that water is not an antidote to drug

EDITOR,—S M Matthai and colleagues describe two cases of cerebral oedema after ingestion of 3,4-methylenedioxymethamphetamine (MDMA or "ecstasy").¹ They correctly criticise the practice of encouraging unrestricted intake of water, but we would like to make it clear that this is not currently recommended harm reduction advice for young people who use the drug. After reports of deaths after MDMA ingestion in patients who were found to have hyponatraemia and cerebral oedema,² drug workers involved with young people were advised to recommend drinking limited amounts of water to combat dehydration while dancing and to convey the message that water is not an antidote to the drug.³ It has also been suggested that MDMA may induce compulsive repetitive behaviour such as obsessive drinking in susceptible people.

The Health Education Authority's recent campaign (November 1995) advises that water is not an antidote to MDMA and is recommended as only one of several measures to avoid overheating. A postcard distributed in clubs and bars advises sipping about a pint of water an hour and eating or drinking something salty such as a salty snack or a sports drink to help replace sodium. This advice needs to be more widely known.

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- 1 Matthai SM, Davidson DC, Sills JA, Alexandrou D. Cerebral oedema after ingestion of MDMA ("ecstasy") and unrestricted intake of water. *BMJ* 1996;312:1359. (25 May.)
- 2 Kessel B. Hyponatraemia after ingestion of "ecstasy." *BMJ* 1994;308:414.
- 3 Ecstasy update. *Druglink* 1996;11:1.

Authors' reply

EDITOR,—We thank T M Cook, Barry Wilkins, and Emily Finch and colleagues for their comments. We acknowledge the typographical

error in the measured plasma osmolalities, which should indeed be 256 mmol/kg in case 1 and 242 mmol/kg in case 2. The point of our letter was to stimulate debate on the potential harm of unlimited intake of fluid in users of 3, 4-methylenedioxymethamphetamine (MDMA or "ecstasy") and the danger to unsupervised children. Note that high fluid intake is still often encouraged in clubs and "rave" scenes. It is not known how much water intake is safe in terms of combatting dehydration while avoiding fluid overload, hyponatraemia, and possible cerebral oedema.

As to the mechanism of hyponatraemia, suggestions so far have included severe dehydration with sodium loss in sweat and vomit followed by excessive intake of hypotonic fluid, simple (severe) water intoxication, and inappropriate secretion of antidiuretic hormone. Inappropriate secretion of antidiuretic hormone and excessive fluid intake are not mutually exclusive. In addition, the biochemical abnormalities are likely to vary depending on the time between intake of MDMA or fluid, or both, and presentation at hospital.

In case 1 the urine osmolality was inappropriately high for the corresponding plasma osmolality. This patient presented more than 12 hours after intake of MDMA and fluid. It would be expected that the effects of severe dehydration with appropriate increase in antidiuretic hormone secretion should not persist at this stage when renal function is normal. However, the effects, particularly hyponatraemia, were probably accentuated by the intake of large volumes of water.

The patient in case 2 presented even later. The urinary sodium loss was strikingly high in the presence of obvious hyponatraemia. This is not in keeping with simple water intoxication. We know that the effects of the syndrome of inappropriate secretion of antidiuretic hormone eventually resolve, and this is the likely explanation for the low urine osmolality when urine was obtained. Both patients had obvious diuresis during the recovery phase, indicating that they were indeed overloaded with fluid.

Holden and Jackson reported hyponatraemic coma in a 20 year old woman who took MDMA.¹ They measured plasma arginine vasopressin concentration and found it to be inappropriately high, and they surmise that vasopressin release was the primary pathogenetic mechanism rather than water intoxication. We contend that the clinical effects seen are the result of a combination of different pathophysiological mechanisms including the syndrome of inappropriate secretion of antidiuretic hormone. Clearly, there is inadequate information about the short and long term effects of MDMA in humans. A rational protocol for the investigation and monitoring of these patients is necessary.

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Area of skin disease can be used to indicate amount of treatment needed

EDITOR,—The area covered by one hand has been used not only to estimate the surface area of burns but also to assess the extent of skin disease. We were therefore interested in R J Perry

and colleagues' findings,¹ which closely agree with ours.² We compared the area of one side of a hand (with the fingers and thumb pulled together) with the calculated body surface area in 50 adults and found that the hand represented a mean of 0.76% of the body surface area in men and 0.70% in women. This information was used to devise the "rule of hand," a simple method for determining the amount of topical treatment to prescribe.² The rule states that four (adult) hands is equivalent to 1 g or two fingertip units.³ Thus, for example, a patient who has the equivalent of four "hand areas" of eczema will require 1 g of ointment or two fingertip units for each treatment.

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- 1 Perry RJ, More CA, Morgan BDG, Plummer DL. Determining the approximate area of a burn: an inconsistency investigated and re-evaluated. *BMJ* 1996;312:1338. (25 May.)
- 2 Long CC, Averill RW, Finlay AY. The rule of hand: 4 hand areas = 2 FTU = 1 gram. *Arch Dermatol* 1992;128:1130.
- 3 Long CC, Finlay AY. The fingertip unit: a new practical measure. *Clin Exp Dermatol* 1991;16:444-7.

Neurological effects of organophosphate pesticides

EDITOR,—Intoxication with organophosphates may produce acute and delayed neurotoxicity in humans as well as the chronic neurological effects recently described by Kyle Steenland.¹ However, Steenland did not discuss the intermediate neurotoxic syndrome, which usually develops 24 to 96 hours after ingestion and is characterised by cranial nerve palsies, neck and proximal limb weakness, and respiratory paralysis.² We recently reported that this syndrome could also be due to carbamate intoxication.³ It is unresponsive to atropine or pralidoxime, and its frequency, pathomechanism, and long term deleterious effects remain unknown.

We performed a Medline search of published work on insecticide intoxication from 1965 to 1995 and found that the intermediate neurotoxic syndrome and the like occurred in between 20% and 68% of affected patients; parathion was the causative agent in up to 75% of cases. Pseudocholinesterase activity was usually more depressed than acetylcholinesterase concentration. In fact, the lower the pseudocholinesterase concentration (usually less than 10% of normal values) the stronger the possibility of developing the intermediate neurotoxic syndrome.

Butyrylcholinesterase has a regulatory effect on acetylcholinesterase,⁴ and it also serves as a buffer against insecticides, interacting with the poisons and lowering their effective concentration at the neuromuscular junction.⁴ However, blood butyrylcholinesterase has a lower capacity than acetylcholinesterase to interact with and detoxify some of the toxic substances, which results in larger effective doses of organophosphates (such as parathion) and carbamates reaching the neuromuscular junction.⁴ Interestingly, the degree of intoxication with organophosphates (such as parathion), carbamate, and anticholinesterase drugs is linked to the presence of "atypical" butyrylcholinesterase.⁵ This link might explain the clinical and neurophysiological similarities among the conditions named above, including the so called intermediate neurotoxic syndrome.^{2,3} Allelic variants of the human butyrylcholinesterase gene and the fact that some people are poor metabolisers of pesticides may explain why only some intoxicated patients