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 reports[1] that it is unrestricted intake of oral or intravenous water that is inappropriate.

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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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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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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