LETTERS TO THE EDITOR

Medical restrictions to driving: the awareness of patients and doctors

EDITOR—Kelly et al’s study of knowledge of medical restrictions on driving reveals worrying deficits in doctors’ knowledge.1 This accords with results of previous studies concerning knowledge of psychiatrists, but contrasts with a comparable study of knowledge2 after dissemination of the Driving Vehicle Licence Authority’s (DVLA) “at a glance guide to the current medical standards of fitness to drive”. We recently used an educational programme incorporating slide presentations and the display of relevant posters on the wards to try and increase awareness of driving restrictions. This produced only small improvements in the ability of doctors to record in the medical notes that they had considered a patient’s driving status and had advised them appropriately.3

We would agree with Dr Morgan that making driving regulations a specific topic for examination in Membership curricula may increase doctors’ awareness. However, undergraduate education should be the main priority. That way all doctors will learn to ask about driving as part of the routine social history and will have an awareness of the spectrum of medical conditions that affect fitness to drive.4

2 Medical Advisory Branch of the DVLA. At a glance guide to the current medical standards of fitness to drive. Swansea: DVLA, 1993.

Fish odour syndrome

EDITOR—We read with interest the excellent review article on fish odour syndrome (trimethylaminuria) by Rehm.1 However the author does not address the clinical relevance of trimethylaminuria (TMA-uria) well beyond the intermittent unpleasant body odour. TMA-uria is caused by the deficiency of the flavin-containing mono-oxygenase isoenzyme 3 (FMO3),2 which is also produced in the liver. E158K is the most common mutation (6% in German and Turkish controls and 57% in the study population). E308G (3%) is very common in the white population. TMA-uria has been shown to be associated with hypertension, or increased cardiovascular risk.2 Two adults with mild TMA-uria (one homozygous for E158K, E308G, one compound heterozygous for a severe mutation and the variant allele E158K, E308G) presented with hypertension.3 Population studies are required to analyse the spectrum of molecular variation at the FMO3 locus, and to evaluate the clinical relevance of mild, normally unrecognised FMO3 deficiency.


The author responds:

I agree with Kashyap and Kashyap that FMO3 is required for detoxification of many substances including the ones mentioned by them in addition to TMA, amphetamine, metamphetamine,1 clozapine,2 chlorpromazine, and methimazole. The FMO gene family has been localised to chromosome 1q and various mutations have been described to cause the metabolic defect. Individuals with these FMO3 gene mutations may have defective metabolic activity for many clinically used drugs. The human flavin-containing mono-oxygenase FMO3 enzyme (FMO3) gene family comprises at least five distinct members (FMO1 to FMO5) that code for enzymes responsible for the oxidation of a wide variety of soft nucleophilic substrates, including drugs and environmental pollutants.

Apart from the two adults with mild TMA-uria and hypertension described by Zschocke et al,1 I am not aware of any other related literature either to this particular
association or other cardiovascular risk factors. It could prove to be a chance association but I agree with Kashyap and Kashyap that population studies are required to evaluate the clinical significance of unrecognised F303 deficiency.

3 Zschosche J, Rohlmueller D, Quak E, et al. Mild trimethylaminuria caused by common variants in P450 3A5.

Drug induced syndrome of inappropriate antidiuretic hormone secretion

EDITOR—We read with interest the excellent adverse drug reaction report by Belton and Thomas.2 They state “Treatment of severe or persistent hyponatraemia is controversial” and highlight the danger of central pontine myelinolysis due to sodium infusion, particularly in patients with chronic hyponatraemia. In the learning points they mention “Sodium infusion is controversial and should only be considered in severe cases”.

We do not agree. Earlier it has been suggested that much of the brain damage associated with chronic hyponatraemia may be a consequence of improper treatment rather than hyponatraemic encephalopathy.1 In general, studies of patients suffering from chronic hyponatraemia lack information regarding whether the patients were symptomatic.1

Recent studies have demonstrated that the major criterion for use of intravenous sodium chloride treatment in patients with acute symptomatic hyponatraemia is the presence of central nervous system symptoms, regardless of the concentration of plasma sodium. It has been suggested that treatment with sodium chloride might be appropriately in patients with chronic symptomatic hyponatraemia.2 When pondering treatment options in patients with hyponatraemia, the pivotal issue is to determine if the patient displays encephalopathic symptoms of hyponatraemia. Ayus and Arieff have reported 53 postmenopausal women with chronic hyponatraemia who were all encephalopathic.17 Seventeen of these patients were seen before evidence of hypoxia or respiratory failure supervened. The remainder had already become hypoxic and required intubation and ventilatory assistance. The 17 patients without respiratory failure and 22 of the 36 patients with hypoxia were treated with saline or hypertonic saline to increase their plasma sodium concentration by more than 0.8 mmol/l per hour but not greater than an end point of 133 mmol/l. The average absolute change in plasma sodium concentration was 22 and 30 mmol/l in patients with and without hypoxia respectively. Patients with seizures were given sufficient hypertonic sodium chloride to increase serum sodium concentration by 8 mmol/l during the first hour. The remaining 14 hypoxic patients who were treated conservatively with water deprivation showed an average increase of plasma concentration of 3 mmol/l during the entire course of their treatment. All patients without hypoxia recovered completely. None of the patients available for magnetic resonance imaging one year later showed cerebral abnormalities. Six of the 11 patients treated with saline who had imaging studies performed before treatment showed evidence of cerebral oedema.

Of the saline treated patients who were hypoxic, two recovered completely, six recovered partially, and the remainder either developed irreversible disabling brain damage or died. In contrast, each hypoxic patient treated with simple water deprivation either died or experienced permanently disabling brain damage. None of 18 patients treated with saline examined with imaging techniques after treatment showed demyelination. This finding suggests that hypotonic saline, if used appropriately, does not impose that risk.

The presence of cerebral oedema on cerebral imaging before treatment in six of 11 patients treated with saline implies that cerebral adaptation to hypotonicity does not always occur. Furthermore this justifies the use of hypotonic saline solution. The outcome was universally tragic in patients treated with simple water deprivation and indicates that this treatment should be abandoned because of patients with symptomatic hyponatraemia. Thus, central nervous system syndromes would appear to be an indicator of the need for initiation of treatment with hypertonic sodium chloride in chronic hyponatraemia.4

Elderly patients with chronic hyponatraemia have a very high mortality rate: among 295 such patients, the mortality rate was 25%. Of these, neither the percentage of those with encephalopathy or who died of hyponatraemia can be ascertained, but at least part of this total appears to be associated with reluctance to treat chronic hyponatraemic patients with intravenous sodium chloride.5

A S KASHYAP
Department of Medicine, Armed Forces Medical College, Pune 411040, India

SUREKHA KASHYAP
Department of Hospital Administration, Armed Forces Medical College, Pune 411040, India


The authors respond:
We are grateful to Kashyap and Kashyap for their remarks on our paper and for allowing us to comment on the report of Ayus and Arieff, which was published after our adverse drug reaction report was accepted for publication.1 This study compared outcomes in postmenopausal hyponatremic women treated in three different ways. Hyponatraemia was of mixed aetiology and only five of the 53 patients had inappropriate antidiuretic hormone secretion. Other causes were polydipsia (21), thiazide diuretics (17), and being postoperative (15). Group 1 (17 patients) were treated with intravenous sodium chloride before the onset of respiratory insufficiency. Group 2 (n = 22) received intravenous sodium chloride after the onset of respiratory insufficiency and group 3 (14 patients) were treated with fluid restriction only. All patients had neurological features. Outcome in group 1 was good for the nine patients successfully followed up but eight patients were lost to follow up. For group 2, two patients recovered completely, six recovered partially and were able to live independently, but 14 either died or developed neurological impairment severe enough to require institutionalisation. For group 3 all 14 patients either died or experienced permanent neurological damage and 10 died within 24 hours.

As Drs A and S Kashyap suggest, cerebral oedema was commonly present on cranial imaging before saline infusion was given, and no evidence of central pontine myelinolysis was found in the 18 patients who were evaluated at least four months after recovery.

At face value these results do suggest a very poor outcome for patients treated with fluid restriction alone. However, outcome was also poor in group 2 with only two of 22 patients recovering completely in spite of saline infusion. Furthermore, it is important to appreciate that this was not a randomised comparison but was preselected as patients who had not responded to conservative treatment and were referred to a specialist team by the general physician. We do not know how many patients who would meet entry criteria for group 3 actually recovered with simple fluid replacement and as a result were not referred for more intensive treatment. It is also important to note that there was no relationship between the rate of correction of plasma sodium and the outcome. Furthermore, as Ayus and Arieff point out, over-rapid correction of plasma sodium also contributes to brain injury.

We accept that the data of Ayus and Arieff indicate that in severe hyponatraemia associated with neurological symptoms the benefits of sodium infusion at an appropriate rate are likely to outweigh the potential risks. However, as we suggested in our original paper, sodium infusion should only be advocated for patients with severe symptoms associated with hyponatraemia. All patients with neurological features would fall into this category. Drs A and S Kashyap’s implication that sodium infusion should be considered in non-severe cases in something that we would agree with. Under these circumstances the risks of sodium infusion are likely to outweigh benefits in this group of patients who often do well with conservative treatment.2


10.1136/pmj.76.895.318b
Postgrad Med J: first published as 10.1136/pmj.76.895.318b on 1 May 2000. Downloaded from http://pmj.bmj.com/ on April 12, 2022 by guest. Protected by copyright.
3rd European Conference on Psychosomatic Research
17–21 June 2000: Oslo, Norway
Details: Congress-Conference AS - CONGREX, Thomas Heftyes gt. 2, PO Box 2694 Solli, N-0204 Oslo, Norway (tel: + 47 (0) 2256 1930, fax: + 47 (0) 2256 0541, e-mail: ecpr2000@congrex.no).

Falk Symposia
9/10 June 2000: Cholestasis and gallstones (Cluj Napoca, Romania)
1/2 October 2000: Non-neoplastic diseases of the anorectum—an interdisciplinary approach (Freiburg, Germany)
3/4 October 2000: Immunosuppression in inflammatory bowel diseases—standards, news, and future trends (Freiburg, Germany)

Columbia University College of Physicians and Surgeons, New York
28–31 July 2000: 10th Annual Course. A comprehensive review of movement disorders for the clinical practitioner
30 July–5 August 2000: 5th Annual Course. Update and intensive review in internal medicine
Details: Center for Continuing Education, Columbia University College of Physicians and Surgeons, 630 West 168th Street, Unit 39, New York, NY10032, USA (tel +1 212 781 5990, fax: +1 212 781 6047, e-mail: cme@columbia.edu).

Ninth International Symposium on Celiac Disease
10–13 August 2000: Hunt Valley, MD, USA
Details: Althea Pusateri, Program Coordinator, University of Maryland School of Medicine, 655 W Baltimore Street, Baltimore, MD 21201, USA (tel: +1 410 706 3957, fax: +1 410 706 3103, http://www.celiaccenter.org).

30th Annual Congress on Neonatology for the Non-specialist: Teaching, Training, and Continuing Education
14/15 September 2000: Charing Cross Hospital Medical School, London, UK (congress conducted in both French and English)
Details: Secretariat APEE 2000, PO Box 3219 Barnes, London SW13 9XR, UK (tel: +44 (0)20 8741 1311, fax: +44 (0)20 8741 0611, e-mail: CourseRegs@aol.com).