temporally associated with serial reduction of the lamotrigine dose. Valproate, acutely and chronically, alters the half-life of lamotrigine by as much as 100%. This case highlights this interaction and the potential for serious toxicity. Clearly the dosage of lamotrigine should have been modified when valproate was substituted for phenoxyin. However, the patient’s clinical status was satisfactory on this regimen for several months before decompensation. The measurement of lamotrigine blood levels was useful in highlighting a possible cause of encephalopathy and in guiding the subsequent improvement. We suggest that lamotrigine should be considered as a cause of unexplained encephalography in patients taking it, particularly in combination with sodium valproate.

We thank A Richens for his helpful criticism.

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Randomly amplified polymorphic DNA analysis in suspected laboratory Helicobacter pylori infection

SIR—Matysiak-Budnik and colleagues1 reported a case of accidental ingestion of Helicobacter pylori in the laboratory. The incident involved a laboratory strain, but they did not isolate the strain causing the symptoms.

We report a case of infection of a bacteriologist, also involved in H pylori research. She had no history of gastrointestinal disease, and was H pylori seronegative 4 months earlier. She had an attack of severe epigastric cramp, accompanied by nausea and fever at 38°C. 3 days later she underwent endoscopy, which revealed erosive gastritis; there was an inflammatory infiltrate with numerous polymorphonuclear cells. Culture was positive for an H pylori strain (S1) sensitive to macrolides, amoxycillin, and metronidazole (1 mg/L). The patient was treated with amoxycillin (2 g daily) and clarithromycin (500 mg daily) for 10 days, and lansoprazole (30 mg daily) for 1 month.

Symptoms disappeared 24 h after the start of treatment. A 13C-urea breath test done 1 week after the end of treatment was negative. Serum was collected at days 5, 15, 30, and 45. No antibody to H pylori was detected by ELISA (Cobas Core 2nd G, Roche, France) probably because of the early treatment.

Assuming that the incubation period after ingestion is between 7 and 10 days2 we did DNA fingerprinting by randomly amplified polymorphic DNA analysis (RAPD), as previously described,3 of its own strain and the four other strains with which the patient had worked for 2 months earlier (S2, S3, S4, S5). The five strains produced distinct patterns (figure). We cannot exclude an infection caused by a strain that could not be isolated (coccoid form). However, without molecular study of such strains, laboratory infection cannot be proven, especially since the prevalence of H pylori infection is 25–45% in the general population.4

We thank A Lecomte for doing the endoscopy.


Alzheimer’s disease in twins

SIR—Riihii and colleagues (March 2, p 573)5 contemplated the genetic contribution in Alzheimer’s disease (AD) in a Finnish twin cohort and reported a significantly higher incidence in monozygous (MZ) compared with dizygous (DZ) twin individuals with an adjusted monozygous/ dizygous incidence ratio of 1-8 (95% CI: 1-2-2-7). A higher frequency in monozygous twin individuals was also seen in Parkinson’s disease, multiple sclerosis, and in systemic rheumatic diseases. The pairwise concordance for AD was 18-6% in monozygous pairs and 4-7% in dizygous pairs. In line with prevailing opinion, they interpret their findings as a confirmation of the major genetic component for AD. However, the low concordance rate (18% instead of an expected 100%), is hard to reconcile with the genetic paradigm. Therefore, they admit the importance of identifying environmental triggers, eg, in utero experiences, including origins, placentation pattern, and fetal circulation circumstances.

Their conclusion concerning the genetic contribution would be attractive provided monozygous twinning and teratogenicity were independent phenomena. This, however, seems not to be valid. Experimentally-induced ageing of amphibian eggs before ovulation and/or fertilization leads to axial duplication and even to mono-ovular twins, but also to degenerative changes and deficiencies in organogenesis, particularly of neuration (disordered migration, resorption, failure of normal differentiation).6 In mammals, including human beings the same tendency towards monozygous twinning and developmental abnormalities has been reported following delayed ovulation.7 Interdependency of monozygous twinning and AD may therefore account for the too low concordance rate in monozygous twin individuals found by Riihii and colleagues.

Figure: H pylori DNA fingerprinting by RAPD

Lane 1, strain S1 (subject); lane 2, strain S2; lane 3, strain S3; lane 4, strain S4; lane 5, strain S5. Numbers on left are reference molecular size markers (basepairs). First primer was 5’GCCCCAGGGGCAGT3’, second primer was 5’AGTACGCCAC3’, and third primer was 5’TGGAGGTTATAGTCA3’.

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The association of non-familial and late-onset AD and, to some extent also, of monozygotic twinning with conditions related to non-optimal maturation and fertilisation of the oocyte, has been reported, i.e., first and/or high birth order, very young and/or advanced maternal age, winter birth excess, specific constitutions (e.g., reduced cognitive reserve capacity, proneness to aneuploid pregnancies). These environmental triggers may indicate that the quality of the oocyte at conception is related to monozygotic twinning and future AD. They have to be separated from the genetic contribution in AD, particularly in non-familial and late-onset AD, as in many other constitutional diseases of so-called multifactorial or polygenic origin.

The Danish Twin Registry, Odense University, DK-5000 Odense, Denmark.


Sir—We tried to corroborate in Danish registers1,2 the report by Raihii and colleagues (March 2, p 573)3 of a higher frequency of Alzheimer’s disease (AD) in individuals from monozygotic twin pairs, compared with individuals from dizygotic twin pairs. Furthermore, we compared the cognitive functions of elderly monozygotic and dizygotic twins using an interview-survey from 1995 among all Danish 75+ year old twins. In this age group AD comprises more than half the dementia cases.4

In our study all twins included were same-sexed and born before Feb 1, 1920. The Danish Hospital Discharge Register was established in 1977 and therefore only the 7144 twin individuals with known zygosity, who survived to 1977, were included. Of these 2690 survived to be eligible for the 1995 interview survey. We have previously reported that mortality trajectories throughout adulthood are similar in monozygotic and dizygotic individuals.5 In the Danish register, dementia cases were sought under the same international classification of diseases (ICD) codes as in the Finnish study. The ICD group 290 consisted virtually only of “dementia senilis” diagnoses and it is therefore presented as one group in our table. Encephalopathy (ICD 781.79) was found only in six cases.

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In the interview-survey the proportion of responders, responders by proxy and non-responders was similar for monozygotic and dizygotic individuals (73:7:20 vs 74:6:20). Furthermore, the proportion where dementia was given as reason for proxy-interview or non-response was similar in monozygotic and dizygotic twins (4-9% vs 4-6%, p>0.5). In the table the mini mental state cognitive screening examination (MMSE) scores of those individuals who had physical impairments (which might affect their score) are excluded, together with those individuals who were reluctant to participate in the test. Inclusion of these individuals in the MMSE distribution also failed to show any significant difference in cognitive functions between monozygotic and dizygotic individuals.

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Human cell-diploid rabies vaccine: efficacy of four doses

Sir—Rabies is a major health hazard and an economic burden for developing countries. Because of the cost of the human diploid-cell rabies vaccine (HDCV), Semple-type vaccines remain the usual treatment for patients bitten in these areas of the world. Unfortunately, neuroparalytic reactions are common with Semple-type vaccines, resulting in about 20% fatalities.

We compared serum rabies virus neutralising antibody (SRVNA) titres of 23 adults vaccinated following exposure to a rabid dog; none had received a rabies vaccine in the past 10 years. They were immunised with five, 1 mL intramuscular doses of HDCV (Merieux Inactivated Rabies Vaccine, Pasteur Merieux Serums and Vaccines, Lyon, France), according to the recommendations of the World Health Organization.1 Blood samples were taken at 16 and 45 days, after the fourth and fifth doses of the vaccine. SRVNA titres of double-blind coded sera were determined by the rapid fluorescent focus inhibition test.2 Titres were adjusted to international unit/mL (IU/mL) with US Standard Human Immune Globulin R3 as a reference serum. Mean SRVNA titres after the fourth vaccination

<table>
<thead>
<tr>
<th>SRVNA levels</th>
<th>Fourth doses</th>
<th>Fifth doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects (n)</td>
<td>23</td>
<td>23</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>33 (86)</td>
<td>16 (24)*</td>
</tr>
<tr>
<td>Median</td>
<td>60</td>
<td>75±5</td>
</tr>
<tr>
<td>Range</td>
<td>15-120</td>
<td>3-75-120</td>
</tr>
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<td>*p&lt;0.01.</td>
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Table: SRVNA (IU/mL) after fourth and fifth doses of HDCV