our results are representative. The MONICA project is well known and well regarded among the people in this part of Sweden, where it has been running since 1985, and the great willingness to give consent to genetic research emphasises the importance of close researcher-participant interaction.

We conclude that (a) it is feasible to obtain individual consent for genetic research many years after blood was donated; (b) people's readiness to contribute to genetic research is high, at least in the framework of a carefully conducted study that is well known to the population; and (c) consent is given nearly as often for industrial genetic research as for academic genetic research, provided that the blood samples are anonymised and an ethics committee has approved the research.

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Drug points

Gabapentin induced cholestasis

Charles E Richardson, Department of Gastroenterology, Dylan W Williams, Jeremy G C Kingham, Department of Pathology, Singleton Hospital, Swansea SA2 8QA

Correspondence to: JGC Kingham (jkingham@swansea-tr.wales.nhs.uk)

The treatment of painful diabetic peripheral neuropathy is troublesome and limited by the range of effective treatments available. Optimal control of diabetes is important, and simple analgesics such as aspirin and paracetamol may be beneficial. Further relief of symptoms may be achieved with tricyclic antidepressants and anticonvulsants.^{1,2} Unfortunately, despite these treatments many patients still have symptoms and the search for more effective therapy continues. Preliminary studies have shown that the anticonvulsant gabapentin is beneficial in the management of this condition, but this remains an unlicensed indication. We report a case of serious hepatotoxicity associated with gabapentin.^{3,4}

During a routine visit to a diabetes clinic, a 50 year old man complained of symptoms attributable to his peripheral diabetic neuropathy. He was subsequently treated with an escalating dose of gabapentin (day 1, 300 mg once daily; day 2, 300 mg twice daily; day 3 and thereafter, 300 mg three times a day). Three years previously he had been diagnosed as having maturity onset diabetes, at which time evidence of retinopathy and neuropathy was noted. He was initially treated with gliclazide, which was discontinued one year later and Human Mixtard 30 started. His other drugs consisted of metformin 1 g twice daily, amitriptyline 50 mg nightly, dihydrocodeine 30 mg as required, and ramipril 5 mg once daily—he had been taking all these for more than 12 months.

After taking the gabapentin for two weeks he developed the clinical characteristics of cholestasis—namely, jaundice, dark urine, pale stool in association with fatigue, and epigastric tenderness. Physical examination confirmed jaundice and the previously noted retinopathy and neuropathy. Liver function tests at this stage showed aspartate transaminase 104 U/l (reference range 10-40 U/l), bilirubin 199 µmol/l (5-20 µmol/l), alkaline phosphatase 210 U/l (25-115 U/l), and γ-glutamyltransferase 839 U/l (<85 U/l). Other serological investigations excluded viral hepatitis (negative IgM anti-hepatitis A, hepatitis B surface antigen, antibody to hepatitis B core and antibody to hepatitis C) and autoimmune hepatitis (negative antinuclear antibody and anti-smooth muscle antibody). A full blood count, renal profile, and liver ultrasound scan were also normal.

Gabapentin induced cholestasis was thought likely and the drug was stopped. After this, clinical symptoms

Liver function tests after withdrawal of gabapentin

and liver function tests improved gradually (figure). A liver biopsy showed normal liver architecture with evidence of portal tract expansion by a chronic inflammatory cell infiltrate that incorporated eosinophils and neutrophils. Patchy steatosis, cholestasis, and some foci of chronic inflammation were evident within the lobules. We thought that these features were consistent with a drug induced aetiology. The temporal relation between ingestion of gabapentin and the development of a reversible cholestasis on its withdrawal strongly support causality.

We submitted a yellow card to the Committee on Safety of Medicines and discussed the case with the drug manufacturers. There have been four reports of jaundice (one cholestatic) associated with the use of gabapentin and, as far as we know, none of these have been published. To the best of our knowledge this is the first reported case of gabapentin induced cholestatic jaundice. Gabapentin should be added to the list of drugs capable of producing this adverse reaction.

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