tive function over 12 months, whereas patients who did not produce such antibodies continued to show cognitive decline[8]. It is tempting to speculate that in the patients who produced plaque-binding antibodies, Aβ was removed from the brain, and this stablized cognitive function.

We were careful to point out that some or all of the features we described might have been a chance finding unrelated to immunization[1]. However, the brains of additional patients immunized in the Elan trial are now being examined (ref. 9 and E. Masliah, personal communication), and show essentially the same findings[1]. These data provide strong evidence that removal of Aβ plaques is a direct consequence of immunization, although we agree that the detailed mechanisms of Aβ removal remain to be established.

We described two different types of brain inflammation microglial activation and T-lymphocyte infiltration[1]. Either of these inflammatory processes alone might have resulted in the acute neurological events termed 'encephalitis', so it is important to know which was responsible. Either cell type can have harmful effects, but whereas microglia are probably involved directly in the (presumably beneficial) Ab removal, the T lymphocytes are unlikely to be directly involved. This is important because efforts in devising the next generation of Aβ immunotherapy are being targeted at avoiding the T-lymphocyte reaction, but it may be the microglial activation that causes the harmful side effect. Furthermore, is harmful encephalitis necessary for removal of Aβ, or did the ~95% of patients in the trial who did not have encephalitis also experience potentially beneficial removal of Aβ plaques? Clearly, we still have much to learn from this trial.

COMPETING INTERESTS STATEMENT
The authors declare that they have no competing financial interests.

James A R Nicoll[1,2], David Wilkinson[3], Clive Holmes[3], Phil Steart[2], Hannah Markham[1,2] & Roy O Weller[1,2]
[1]Division of Clinical Neurosciences, University of Southampton, Southampton General Hospital, Southampton, SO16 6YD, UK. [2]Neuropathology, Department of Pathology, Southampton General Hospital, Southampton, SO16 6YD, UK. 3Division of Clinical Neurosciences, University of Southampton, Memory Assessment and Research Centre, Moorgreen Hospital, Southampton, SO30 3JB, UK.
e-mail: j.nicoll@soton.ac.uk

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International cooperation on xenotransplantation

To the editor:

We are writing on behalf of the Ethics Committee of the International Xenotransplantation Association (IXA). Our committee recently expressed concern about the need for international guidelines for overseeing clinical xenotransplantation. We have published letters in scientific journals and corresponded with representatives of the World Health Organization (WHO) regarding these concerns. Although clinical xenotransplantation provides a potentially promising solution to the shortage of human organs and tissues, the potential to introduce new infections from xenogeneic source animals into the human populace is a concern that mandates extreme caution. In view of this risk, considerable effort has gone into the development of guidelines and oversight procedures for husbandry of source animals and recipient monitoring in several countries. However, clinical xenotransplantation is also carried out in countries lacking such guidelines and oversight. Some of these transplants are commercial enterprises providing cosmetic and medical treatments, whereas others are clinical trials. Given that individuals may freely travel from one country to another to undergo such procedures, international cooperation is needed to develop universal oversight procedures and standards, including ethical and monitoring guidelines.

Last October, international health officials representing more than 20 member states, members of the transplantation community and WHO representatives met in Madrid to discuss policies on transplantation. This meeting resulted in a report by the WHO secretariat, which has recently been published online (http://www.who.int/gb/EB_WHA/PDF/EB113/eeb11314.pdf). This document includes a draft resolution to be considered by the WHO's executive board in January 2004. The draft resolution recognizes both the potential benefit and the potential infectious risks associated with xenotransplantation. Most importantly, it urges the adoption of appropriate regulation and surveillance of xenotransplantation by national health authorities of member states, as well as the development of protective measures to prevent transmission of infections that may arise after xenotransplantation. Member states are further urged to support international collaboration on the prevention and surveillance of infections resulting from xenotransplantation. Our committee believes that adopting all of these measures would be of enormous value in minimizing the potential risks of xenotransplantation. The draft resolution further requests that the WHO's director-general support such international cooperation, create a global evidence base for evaluation of xenotransplantation practices, and provide technical assistance and expertise to support xenotransplantation efforts and oversight in member states.

The IXA's ethics committee is highly encouraged by the drafting of this resolution and strongly urges its adoption by the WHO's executive board. If this resolution is ultimately adopted by the fifty-seventh WHO assembly, it will be a major step toward minimizing infectious risks associated with xenotransplantation. Without organized international cooperation, the best efforts at minimizing these risks in countries with appropriate regulatory oversight may be thwarted by the free travel of individuals undergoing unmonitored xenotransplantation in countries lacking such regulation.

Megan Sykes[1], Mauro Sandrin[2] & Emanuele Cozzi[3]
[1]Massachusetts General Hospital/Harvard Medical School, Boston, Massachusetts 02129, USA. [2]Austin Repatriation Medical Center, Austin Research Institute, Heidelberg, VIC 3084, Australia. [3]Department of Surgery & Medical Sciences, Clinica Chirurgica IV, University of Padua, Padova 35128, Italy.
e-mail: Megan.Sykes@TBRC.MGH.harvard.edu