trained personnel or sophisticated laboratory facilities. Such a test exists in the form of an immunoassay to measure the diphtheria antitoxin *in vitro*, rather than the established and more complex *in vivo* (guinea pig) or Vero cell culture assays. A rapid dot-ELISA anti-diphtheria toxin IgG assay would provide an adequately sensitivity and reproducible test allowing the primary care worker to establish the presence of antitoxin levels exceeding 0.01 IU per ml, the level agreed as providing basic or better protection against the disease[2].

This test could be supported by the more selective application of a PCR-based assay for the presence of *Corynebacteria*, available at central referral laboratories[3].

This protocol would ensure that all those at risk, regardless of age, social status or other factors, could be detected and treated with the appropriate low-potency diphtheria toxoid and that the immediate contacts of such patients could likewise be screened and protected. In conjunction with a widespread immunization effort, this worrying epidemic might yet be stopped.

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1. Maple, P.A., Efstratiou, A., George, R.C., Andrews, N.J. & Sesardic, D. Diphtheria immunity in UK blood donors. *Lancet* **345**, 963–965 (1995).
2. Manghi, M.A. *et al.* Development of an alternative method for testing the immunogenicity of diphtheria vaccines. *Vaccine* **13**, 597–601 (1995).
3. Pallen, M.J., Hay, A.J., Puckley, L.H. & Efstratiou, A. Polymerase chain reaction for screening clinical isolates of *Corynebacteria* for the production of diphtheria toxin. *J. clin. Path.* **47**, 353–356 (1994).

ApoE as a prognostic factor for post-traumatic coma

To the editor — Nicoll *et al.*[1] explored the association between the ε4 allele of apolipoprotein E (apo E) and fatal head injuries in the February issue of *Nature Medicine*. Deposition of amyloid β-protein (Aβ) in the brain occurs in approximately one-third of individuals who die shortly after a severe brain injury[2], and the frequency of apoE-ε4 allele was found to be significantly higher in those head-injured individuals with Aβ deposits[1]. Moreover, patients with apoE-ε4 allele who survive head trauma have a tenfold increased risk of Alzheimer's disease[3].

We have studied the apoE genotype in a small number of patients with prolonged post-traumatic unawareness and have found a higher frequency of the apoE-ε4 allele in those individuals who did not recover consciousness. Subjects of the study were 16 young patients (mean age 24 ± 8 years), ten males and six females in prolonged post-traumatic unawareness lasting more than 30 days. Outcome was evaluated according to the extent of recovery of consciousness, defined as the moment when the patient is able to establish a meaningful communicative contact with the environment by either motor, visual or verbal acts[4]. Ten patients recovered consciousness within one year (most of them before six months), whereas six remained in a state of prolonged unawareness, two of whom eventually died. For those patients who recovered, the frequency of apoE alleles (ε2 = 0.10, ε3 = 0.75, ε4 = 0.15) was comparable to control population. In the six patients who did not recover consciousness, there was a higher frequency of the apoE-ε4 allele (0.42) and an absence of the apoE-ε2 allele (0.0). (Three of the six 'no recovery' patients were ε3/4). The presence or absence of apoE-ε4 allele was a better predictor of outcome than age, length of coma, or the Glasgow Coma Scale (GSC) rating at admission (see table). These data confirm and extend *in vivo* the possible role of apoE genotypes in determining a genetic susceptibility to the effects of a head injury[1].

Finally, in a recent letter to the editor, Roses and Saunders[5] commenting on the absence of Aβ deposition in younger non-head injury controls in the Nicoll's paper raised the hypothesis that ε4 carriers have an altered metabolism leading to decreased recovery from head trauma. Our study provides experimental evidence in support of this hypothesis. All these data might be relevant for the prognosis of outcome in patients in a prolonged unawareness state and might lead to novel strategies of pharmacological intervention.

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1. Nicoll, J.A.R., Roberts, G.W. & Graham, D.I. Apolipoprotein E ε4 allele is associated with deposition of amyloid β-protein following head injury. *Nature Med.* **1**, 135–137 (1995).
2. Roberts, G.W. *et al.* β-Amyloid protein deposition in the brain after severe head injury: Implications for the pathogenesis of Alzheimer's disease. *J. Neurol. neurosurg. Psychiatr.* **57**, 419–425 (1994).
3. Mayeux, R. *et al.* Synergistic effects of traumatic head injury and apolipoprotein-ε4 in patients with Alzheimer's disease. *Neurology* **45**, 555–557 (1995).
4. Sazbon, L. & Groswasser, Z. Outcome in 134 patients with prolonged post-traumatic unawareness. *J. Neurosurg.* **72**, 75–80 (1990).
5. Roses, A.D. & Saunders, A. Head injury, amyloid and Alzheimer's disease. *Nature Med.* **1**, 603–604 (1995).

Prognostic parameters for 'no recovery' in patients in a prolonged unawareness state

Feature	Recovery	No Recovery	Significance
ApoE-ε4 frequency	0.15	0.42	<0.01
ApoE-ε3 frequency	0.75	0.58	<0.01
ApoE-ε2 frequency	0.10	0.0	<0.01
Age (years)	23 (± 7)	24 (± 9)	NS
Duration of coma (days)	35 (± 14)	37 (± 12)	NS
GCS rating	4.8 (± 2.4)	4.3 (± 1.4)	NS

Recovery, $n = 10$; no recovery, $n = 6$. GCS, Glasgow Coma Scale. NS, not significant. Patients are considered in coma until they spontaneously open the eyes; they are considered in an unawareness state until they establish a meaningful communicative contact with the environment by either motor, visual or verbal acts[4].