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## PREDICTING THE FAILURE OF AMYLOID- $\beta$ VACCINE

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Sir—After the news of the trial suspension, the rush to test a vaccine for Alzheimer's disease<sup>1–4</sup> has proven ill-fated. Indeed, although it is no surprise that the inappropriate deposition of protein in the normal mouse brain because of massive overexpression of amyloid- $\beta$  protein precursor modifies function, nor that its removal can then restore function,<sup>2,3</sup> there is not, nor ever was, any evidence that interventions designed to remove or alter the deposition of amyloid- $\beta$  would benefit patients with Alzheimer's disease.<sup>5</sup> Treatment strategies based on removal of a naturally occurring endogenous substance harkens back to the time of leeches and exorcism for the removal of bad humour and spirits to restore function. Thankfully, such concepts died with the understanding of homeostatic balance that defines modern biology. Or did they?

Therapeutic strategies arguing for the removal of amyloid- $\beta$  beg the question of why deposits of this substance develop with age in the first place. Amyloid develops in many long-lived mammalian species and, in human beings, most people older than 40 years have amyloid in their brain. Removal of this amyloid- $\beta$  from the aged or diseased brain, we argue, is more likely to destabilise age-related or disease-related compensations and be harmful.<sup>5</sup> Unfortunately for patients who have Alzheimer's disease, this scenario seems true.

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2 Lemere CA, Maron R, Spooner E, et al. Mucosal administration of A- $\beta$  peptide decreases cerebral amyloid burden in PDAPP transgenic mice. *Soc Neurosci Abstr* 1999; **25**: 1291.

3 Janus C, Pearson J, McLaurin J, et al. A- $\beta$  peptide immunization reduces behavioral impairment and plaques in a model of Alzheimer's disease. *Nature* 2000; **408**: 979–82.

4 Morgan D, Diamond DM, Gottschall PE, et al. A- $\beta$  peptide vaccination prevents memory loss in an animal model of Alzheimer's disease. *Nature* 2000; **408**: 982–85.

5 Perry G, Nunomura A, Raina AK, Smith MA. Amyloid- $\beta$  junkies. *Lancet* 2000; **355**: 757.