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development and implementation of other strategies based on classical infection-control measures—for example, interruption of the transmission of drug-resistant pathogens, or vaccination.

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ApoE–viral interactions

To the editor—In your September issue, Corder *et al.* showed that as a group, HIV-infected subjects with an E4 allele for apoE have excess dementia and peripheral neuropathy[1]. They have subsequently pointed out[2] a parallel to our results on brain specimens from elderly normal people and Alzheimer disease (AD) patients; the latter show that the combination of an E4 allele for apoE and the presence of HSV1 in the brain confers an increased risk of developing of AD[3,4]—the first report of an environmental agent acting with an inherited factor in a neuropsychiatric disease.

We would like to emphasize another interesting aspect of these studies: Herpes labialis is known to be caused by HSV1. The virus resides latently in the PNS of almost all adults and reactivates periodically, causing 'cold sores' in some 20–40% of people. We found that apoE4 is a strong risk factor for herpes labialis, and from those data (on volunteers) and independent data on post-mortem AD brains, we deduced that the interaction of virus and genetic factor is particularly damaging in the nervous system[3,4]. It is interesting to note that Corder *et al.* also found viral (HIV-1)-induced PNS damage associated with apoE4.

We have speculated that HSV1 and apoEs might compete for entry into neuronal cells through heparan sulphate proteoglycan molecules (the initial site of attachment for entry for each), with apoE4 competing less efficiently than the other isoforms, consistent with studies showing the reduced entry of apoE4 compared with that of apoE3 into neuronal cells in culture. In principle, this mechanism may also apply to the apoE4/HIV-1 finding of Corder *et al.* as heparan sulphate proteoglycans are involved in HIV attachment and entry into cells[5].

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