gested by Salaman and Valdimarsson when they reported that nonspecific effects are more evident in tuberculin-positive than tuberculin-negative individuals, is generally overlooked and which contributes to the confusion in this area of research. It was formerly claimed by medical practitioners that there were no "diseases", only "patients". In other words, a given disease may have a different clinical course, before and/or during treatment, in different patients. This raises the question of recipient peculiarity or, in the case of DLE, "recipient specificity". The effects of DLE are also surely dependent on the specific characteristics of the recipient; for example, it can often be observed that, no matter how strongly positive a leukocyte donor is to a given set of antigens by skin testing, the DLE preparation obtained induces positive skin-test reactivity only to one of the antigens in some recipients and only to another in other recipients, and some show increased lymphocyte DNA synthesis in the presence of antigens *in vitro* whereas others do not[2-4]. Therefore, investigators who intend to study the effects of DLE should consider (at least until it is clearly demonstrated to the contrary) that they are probably dealing not only with an adjuvant-like material and a donor-specific substance (TFd) but also, in both cases, with recipient specificity, which can mask the effects of these substances—if indeed they exist.

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Permeability of blood–cerebrospinal fluid barrier during foetal and perinatal life

The high level of protein in early foetal cerebrospinal fluid (CSF) from human abortion material reported by Adinolfi *et al.*[1] is important confirmation of results obtained from earlier work on human[2] and animal foetal CSF[3,4]. Part of the high concentration of protein, however, may have been due to hypercapnia, since foetuses obtained from abortions are likely to be asphyxiated by the time CSF samples are taken. Hypercapnia increases the penetration of albumin[5] and other lipid insoluble molecules[6] from blood into CSF. This is suggested by the very high concentration of CSF protein in the 40-week foetus, compared with normal term newborn infant[7,8]. Adinolfi *et al.* suggest that their findings confirm the proposition suggested previously by several authors[9] that the blood–brain and blood–CSF barriers to protein are poorly developed in foetal and perinatal life. An alternative explanation for the high level of protein in foetal CSF, however, is that certain plasma proteins may be transported into foetal CSF at an early stage in brain development[4,10]. This was based on electron microscopical evidence that the tight junctions (which form the barrier to protein in adult brain[11]) of cerebral endothelial and choroid plexus epithelial cells are already well developed at a stage when the CSF protein level is very high. There is also evidence[4] from studies of isotopically-labelled protein that certain plasma proteins (for example, transferrin) may be transported into the CSF of early foetal brain, but not later in development. This finding has recently been supported by studies using human serum proteins detected by immunoassay[10] which showed that both transferrin (molecular weight 74,000) and α foetoprotein (molecular weight 64,000) penetrated from blood into CSF to a much greater extent than albumin (molecular weight 69,000) in 60-d-old foetal sheep—a stage when the CSF contained about 350 mg per 100 ml total protein (term is 147 d).

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Adinolfi et al. reply—We thank Saunders *et al.*[1] for calling our attention to their work[2], and as yet unpublished results[3]. Regarding the effect of hypercapnia, we do not discount it as a possible factor influencing the levels of plasma proteins in CSF. Saunders *et al.* must be aware of the difficulties of working with human foetal material; it is after all post-mortem material. We stated in our paper[4] that the results were based on a very selected group of foetuses. Many samples of foetal CSF were discarded because of contamination with blood and almost all foetuses obtained by termination with prostaglandin could not be used.

We acknowledge that the levels of some proteins were higher than expected in the 40-week-old foetus; whether this was due to hypercapnia or other factors we are unable to say. This does not, however, alter our conclusion that the permeability of the blood–CSF barrier is incomplete during foetal life.

Recent evidence, based on the estimations of the levels of specific plasma proteins such as albumin, α-foetoprotein, IgG and prealbumin in serum and CSF from the same foetus, suggests that the mechanisms of transfer vary among different proteins. Thus, for example, whereas the percentage of prealbumin in CSF, as compared with blood, varied between 40 and 70, the levels of other proteins varied from ~ 5 to 20%. These variations were found to be related to the ages of the foetuses.

In our paper[4] we merely presented our observations; at this stage of our work it seemed to be premature to advance any hypothesis on the mechanisms of transfer of plasma proteins from blood into CSF in human foetuses.

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