Corneal transplantation and infectious hepatitis

Corneal tissue is not usually taken from persons with signs of viral hepatitis at the time of death. The viruses responsible are highly infectious and the practice would be considered hazardous both to the recipient of the cornea and to eye bank personnel. The hepatitis A and E viruses are transmitted principally by the faecal-oral route, have a relatively brief viraemic phase, and do not persist after recovery from illness. Hepatitis D virus (HDV) can persist, but is able only to multiply in cells that are co-infected with hepatitis B virus (HBV). The two agents of particular concern in transplantation are HBV and hepatitis C virus (HCV) because of their ability to persist in some individuals for years after resolution of symptoms. The blood of most HBV carriers has a high titre of infectious particles.[1] Acute infection with either virus can result in cirrhosis, and chronic infection is associated with liver cancer. As testing donors for HBV and HCV is a significant component of an eye bank's budget, what evidence is there that it is necessary?

The medical standards published by the Eye Bank Association of America (EBAA) have been the benchmark for eye bank practice.[2] The contraindications listed for eye donation include evidence for infectious diseases or their agents known to have been transmitted to recipients by corneal transplantation, such as Creutzfeldt-Jakob disease[3] and rabies,[4–6] or suspected of having this potential, such as syphilis, rubella, and the human T cell leukaemia viruses. HBV is in the first category and HCV and human immunodeficiency virus type 1 (HIV-1) are in the second. Although three corneas from two HIV-1 seropositive donors[7] and two from a seronegative 'window period' donor[8] are known to have been transplanted, the recipients did not seroconvert and remained healthy. They may have been fortunate as Qavi *et al*[9] were able to culture HIV-1 from corneal specimens of two of 35 asymptomatic HIV-1 carriers and two of 10 AIDS patients. Suspicions as to the possible transmission of HBV by corneal transplantation were raised following the detection of surface antigen (HBsAg), an indicator of active infection, in corneal tissue of carriers.[10 11] In one report, three patients received corneas from HBsAg seropositive donors but remained free from disease.[11] One patient was given specific immunoglobulin, another received immunoglobulin and HBV vaccine, and the third had existing anti-HBV antibody. However, two cases of hepatitis B almost certainly transmitted by corneal grafts were presented at the American Academy of Ophthalmology Annual Meeting in 1988 by Hoft *et al*. This prompted the EBAA requirement for HBsAg serology on all corneal donors.

In Western countries, positive HBV serology is a relatively infrequent reason for withholding eye bank material. This is due to the low prevalence of HBV carriage (<1%) and the donor exclusion criteria in place to counter HIV-1. In regions of high carriage, however, the loss of otherwise useful tissue can be significant. For example, the prevalence of HBsAg seropositivity in Cairo has been given as 6·2%,[12] no doubt motivating the study from Khalil *et al* appearing in this issue (p 6). Their results suggest that up to 30% of carriers have HBsAg and HBV DNA in the cornea. The detection of viral genome correlates with the presence of virions and is, therefore, a good marker of infectivity of the tissue.[13] Given the problems of antigen detection in cadaveric sera,[14] the time for routine HBV DNA assay of serum or ocular tissue from eye donors may have arrived. This approach might also be an improvement over the antigen tests in that a significant number of patients with evidence of subclinical acute HBV infection apparently never have detectable HBsAg.[15] In several cases, Khalil *et al* detect HBV DNA in the cornea but not HBsAg in the blood. Overall, the study supports Hoft's circumstantial evidence for transmission and suggests that the post-surgical antiviral measures used by Raber and Friedman[11] are warranted. In contrast, using the polymerase chain reaction, Laycock *et al*[16] failed to detect HCV genome in corneal tissue of 23 donors seropositive for HCV antibody +/− RNA. While the significance of a positive HCV serum antibody test for eye donation remains to be determined, the detection of HBV antigen or DNA is clearly important.

The transmission of any of these diseases to an otherwise healthy recipient is unacceptable in the context of an elective procedure. Most eye banks accept a positive HBsAg blood test as being a contraindication for use of the material and do not request further evidence of infectivity. Where there is a high prevalence of HBV infection and a scarcity of graft material, an eye bank might be tempted to offer tissue from HBsAg positive donors to HBV antibody positive recipients. Given that our understanding of the pathogenesis of HBV (and particularly HDV) infection is far from complete, this would have to be regarded as a risk justifiable only in an absolute emergency. Eye banks should err on the side of caution when assessing the suitability of donors. If there is a suspicion that an infectious agent has been transmitted through a corneal graft, an eye bank that has based its operation on the EBAA standards is well placed to defend itself.

P R BADENOCH

Department of Ophthalmology,
Flinders Medical Centre,
Bedford Park, South Australia 5042

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