



***In conjunction with the Advisory Committee on Dangerous Pathogens
TSE Working Group***

CJD Guidance for Ophthalmologists

Creutzfeldt-Jakob Disease (CJD) is an invariably fatal human disease caused by a pathological accumulation in the brain of an aberrant form of prion protein (PrP^{Sc}). Sporadic CJD (sCJD) is the most commonly encountered form of the disease with an incidence of 1 case per million, thus giving approximately 60 new cases per year in the UK. Patients with sCJD are mainly over 60 years of age and as such come into contact with ophthalmologists through a range of unrelated ophthalmic conditions or because of visual symptoms caused by their condition.

In 1996, a new form of CJD, now known as variant CJD, was identified in the UK. Epidemiological evidence linked the emergence of this disease with the large outbreak of bovine spongiform encephalopathy (BSE) in UK cattle; subsequent experimental studies found that the transmissible agents in BSE and vCJD have very similar biological properties, distinct from those of sporadic CJD. Case control studies have found that the most likely route of human exposure to the BSE agent was the consumption of BSE-contaminated beef products.

Although the majority of the human population of the UK may have been exposed to PrP^{Sc} by ingestion of contaminated beef products at some time until 1996, when controls were established, the precise prevalence of preclinical infection of vCJD in the UK is unknown. The most reliable evidence suggests a prevalence of up to approximately 1 in 4000 population (237 per million). Although the infective risk of these preclinical cases is uncertain there is the obvious potential for iatrogenic transmission in a significant number of cases.

Iatrogenic vCJD has been associated with blood transfusion. Treatment with human pituitary hormones, dura mater transplantation, contaminated neurosurgical instruments/EEG needles, and a single case of corneal transplantation from the US in 1974 have been associated with iatrogenic sCJD. There are no other known cases of ophthalmic surgery or diagnostic procedure having resulted in CJD transmission between patients.

Examination of ocular tissues from sCJD and vCJD cases have found high levels of PrP^{Sc} in the retina, comparable to levels with cerebral cortex, and lower levels in the optic nerve. However, no detectable levels of PrP^{Sc} have been found in cornea,

sclera, iris, lens, ciliary body vitreous or choroid. As prion proteins adhere strongly to materials including smooth metal surfaces and are not removed entirely by routine cleaning and autoclaving then there is the potential for iatrogenic transmission of PrP^{Sc} particularly during surgery involving the retina and optic nerve. Although the fact that PrP^{Sc} has not been found in other ocular tissues is reassuring, the **most likely case of transmission of CJD** through corneal transplantation suggests that practical precautions during diagnostic and surgical procedures are advisable to reduce the risk of iatrogenic transmission.

Previously, several sources of guidance have been produced to reduce the risk of iatrogenic CJD transmission in ophthalmic care by the Medical Devices Agency, the College of Optometrists, the Association of British Dispensing Opticians, the Royal College of Ophthalmologists and the National Institute for Health and Clinical Excellence (NICE).

The Advisory Committee for Dangerous Pathogens (ACDP) set up a working sub-group to specifically advise on CJD management in Ophthalmology. The membership of this working group consisted of ophthalmologists, optometrists, microbiologists, virologists and many other expert members reviewing and assessing the available evidence and existing guidance of CJD iatrogenic risk in ophthalmology. The purpose of this latest document is to consolidate and update the available guidance and offer pragmatic solutions to aid implementation of such guidance in a single source document. The guidance can be found at: (http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@ab/documents/digitalasset/dh_104848.pdf)

A key aspect of the guidance was to assess the relative tissue infectivity risk status for anterior and posterior segment tissues. Previous guidance from ACDP had stratified tissue infectivity risk in to high (posterior eye), medium (cornea and anterior eye) and low (other ocular tissues). There is little controversy that posterior segment tissue should be considered as high risk tissue for CJD infectivity and robust adherence to advice on high risk tissue should be promoted. However, the working group agreed unanimously that anterior segment tissue should be effectively down graded to low infectivity risk. In essence, we now have only 2 infectivity risk states (high – for posterior segment tissue and low – for everything else). A similar down grading was recently introduced by the Australian Department of Health in December 2007. This grading now accords with the WHO *Guidelines on tissue infectivity distribution in transmissible spongiform encephalopathies (2010)*, which places retina and optic nerve in the high-infectivity category and groups cornea with the lower-infectivity tissues.

The latest guidance helps clarify some key issues as to which surgery constitutes anterior low risk surgery and which should be considered high risk posterior segment surgery for purposes of iatrogenic CJD transmission. In addition, there are sections covering pre-operative assessment, surgical management of known cases of CJD or patients with increased risk of CJD, ocular tissue transplantation and management of CJD incidents within an ophthalmic unit (approximately 10 ophthalmic units per year in UK).

A potential contentious area within the guidance is with respect to cleaning/disinfection of ophthalmic lenses and devices. The generic advice includes disinfection steps to reduce significantly the problem of cross infection by conventional organisms such as viruses and bacteria, and thorough washing steps to reduce the level of residual protein and possible prion infectivity. The proposed regime is much more involved than that presently practiced in the majority of UK ophthalmic units but is considered as an effective method for reducing iatrogenic transmission of these organisms and prion protein. Due to the complexity of the regime in busy outpatient clinics several pragmatic solutions are identified to aid its implementation.

We hope that this latest guidance is accepted by colleagues as a document to clarify many confusing aspects of risk reduction of iatrogenic CJD transmission and aid local implementation.

We would encourage ophthalmic units to work closely with local infection control and decontamination units to assess their practices to reduce the risk of iatrogenic transmission of CJD without compromising ophthalmic care to their patients.

The guidance given in Annex L is a distillation of the views of a multidisciplinary expert advisory group. This guidance is however advisory. Should individual units take the view that the measures in Annex 3 are impractical for whatever reason, then they are strongly advised to seek the advice of their Infection Control Advisors and draw up a written local policy that is both practical and likely to be effective. The use of either Appendix 3 or the local policy should be audited on a regular basis to ensure compliance and hence safety, without compromising care of ophthalmic patients.

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