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ORIGINAL RESEARCH

Dementia as an Exclusion to Tissue Donation

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Abstract: The risk of transmission of potentially fatal infectious diseases from donor to recipient via tissue transplantation cannot practically be eliminated, but must be minimised. Careful screening of potential and actual donors is the major available tool to achieve this. Screening usually involves investigation of patient medical records for not only diagnoses, but also risk factors or markers for disease. Dementia is one such marker identified by tissue banks as it is one of the few indicators of Creutzfeldt-Jakob Disease (CJD). However, CJD accounts for only a very small percentage of dementia cases in Australia and dementia is extremely common in the potential donor population.

Aim: The aim of this investigation was to analyse the reasons for excluding potential donors from donation and to compare the number of individuals excluded due to dementia with the expected number of deaths due to CJD during the same period.

Methodology: The Queensland Eye Bank is automatically notified of deaths which occur within many Queensland hospitals. Each notification is investigated to determine suitability for tissue donation using a standard procedure and the reason for exclusion from donation and/or transplantation is recorded. The death notifications received by the Queensland Eye Bank in 2007 were analysed to determine how many potential and actual donors were excluded due to dementia.

Results: In 2007, of the 4053 death notifications received by QEB, 3575 were not considered suitable for donation. Of these, 168 (4.2%) were excluded on the basis of dementia.

Keywords: dementia, Creutzfeldt-Jakob, cornea, donation, transplant

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Introduction

The Queensland Eye Bank (QEB) may be notified of deceased individuals with the potential for tissue donation in a variety of ways. The vast majority of the 4053 notifications received by QEB in 2007 were provided by an automatic system which is linked to the death registration database employed by many Queensland public hospitals. For these notifications, all screening for medical suitability for tissue donation was therefore undertaken by QEB staff.

Several tools are used sequentially by QEB staff in this process (see Fig. 1). The assessment is ceased if a contraindication to tissue donation is discovered at any time.

QEB currently lists over 70 donor exclusion criteria. The rationale underpinning the majority of these exclusions relates to preventing the transmission of disease from donor to recipient. The method in Figure 1 has been developed in an attempt to achieve this outcome. However, there is inherent risk associated with the transplantation of human tissues. Risk assessment usually involves a calculation of the probability of disease transmission and the severity of the consequences of disease transmission. However, because eye tissue transplantation is generally a sight-restoring, rather than life-saving, procedure, the calculation may be biased toward the latter factor for those diseases with consequences out of proportion to this benefit.

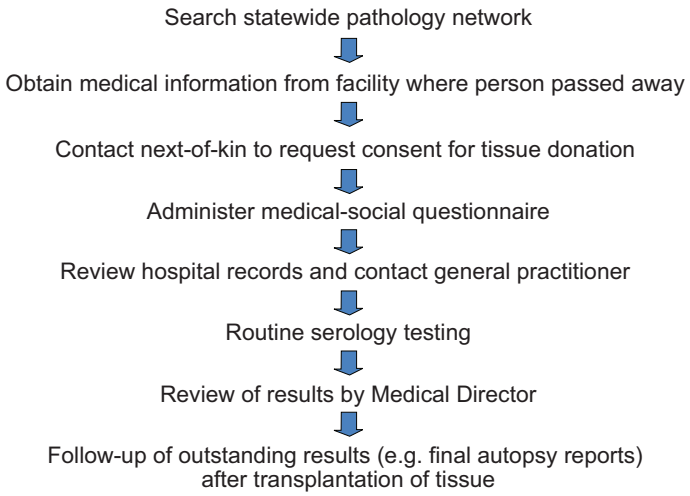

Figure 1. QEB process for screening for contraindications to donation and transplantation.

Creutzfeldt-Jakob disease (CJD)

An example of such a disease is CJD. According to Klug et al[1] the incidence of CJD worldwide is reported to be 1 case per million population per year. The situation in Queensland is consistent with these results; with the reported mean-age adjusted mortality rate in this state being 0.98 deaths per million per year between 1993 and 2008 and CJD was reported to have caused only 16 deaths in Australia in 2007. Using a standard risk assessment model, very little weight should therefore be given to the probability of the disease in any one donor, and therefore the likelihood of its transmission. However, there have been several documented cases of possible or definite transmission of CJD by corneal transplant,[2–7] and the consequences of such transmission may be disastrous, as the disease is incurable and would inevitably result in the death of the recipient.[8] Consequently, QEB takes an extremely conservative approach with respect to CJD.

This approach is impacted by several factors. First is the difficulty with which CJD is diagnosed. The disease has an exceptionally long incubation period,[8] and consequently QEB must assess potential donors for risk factors which may have occurred many years ago. CJD also lacks unique signs or symptoms for diagnosis. Table 1 lists those that do exist. However, it can be seen that dementia is the only consistent symptom, and this feature is by no means pathognomonic.

Dementia

Dementia is a common occurrence in Australia, currently affecting an estimated 200000 people. While dementia is not a normal part of ageing, the

Table 1. Diagnosis of Creutzfeldt-Jakob disease.[9]

Certainty of diagnosis	Diagnostic features
Definite	Abnormal prion protein detected in brain tissue; and Histological identification of spongiform changes: neuronal loss, astrocytosis.
Probable	Rapidly progressive dementia; Characteristic EEG changes; and Any two of: myoclonus, visual and/or cerebral symptoms, akinetic mutism.
Possible	Those fulfilling above criteria but without typical EEG abnormalities.

incidence of dementia does increase with age, and with the increasing elderly population in Australia it is estimated that the prevalence may more than double by 2031.[10]

The majority of diseases which cause dementia are not considered to have an infectious aetiology, and therefore may be considered safe in a transplantation context. The two most common examples are Alzheimer's and vascular dementia.

Alzheimer's accounts for 65% of dementias in any age group and may affect up to 40% of people over 80 years of age.[5] The Eye Bank and Bone Bank in Queensland currently routinely accept donors up to 90 years of age, so it is clear that the potential donor pool may be significantly decreased with the exclusion of persons with Alzheimer's from donation. Unfortunately, similar to CJD, Alzheimer's lacks unique diagnostic clinical features. Persons with Alzheimer's are therefore currently excluded from tissue donation.

It could be argued that the only certain way to prevent transmission of infectious causes of dementia is to exclude all persons with dementia. However, there are some instances where the aetiology of a dementia is clearly non-infectious and in these cases QEB has determined that the benefit of donation did outweigh the risk. Persons with vascular dementia often have a stepwise deterioration in cognitive function as they experience several small strokes over time, and usually have obvious vascular risk factors,[5] therefore diagnosis is often straight-forward. Provided the individual possesses no risk factors for CJD, the risk of their vascular dementia masking CJD is considered negligible and QEB has released eye tissue for transplantation from donors with this disease.

Aim

The aim of this analysis was to determine the impact in 2007 of excluding persons with dementia from tissue donation. The number of persons excluded at each stage of the screening process was also assessed.

Materials and Methods

An analysis was conducted of all persons with the potential for tissue donation whose death was notified to QEB in 2007 to determine the number excluded from donation and/or transplantation due to dementia. All non-donors, intended donors and donors were included and the stage at which each person was excluded was determined from records kept by QEB for deaths which were reported to QEB to have occurred during this time.

Results

The exclusion of persons with dementia of uncertain aetiology from donation was found to cause 158 persons to be excluded from donation prior to a next-of-kin approach (non-donors), 5 persons to be excluded on the basis of information discovered after obtaining consent but prior to the retrieval of tissue (intended donors), and tissue which had already been retrieved from 5 persons (donors) to be excluded from transplantation. Of the non-donors, 45 were excluded during the first screening stage (searching the statewide pathology network) and 113 after speaking with staff from the facility where the deceased passed away.

Of 4053 death notifications received by QEB in 2007, 168 persons, or 4.2%, were ultimately excluded on the basis of dementia.

Figure 2 is a comparison of the number of persons excluded from donation due to dementia at the various stages of screening with persons excluded for all causes (including dementia).

Discussion

Creutzfeldt-Jakob Disease was likely to be rare in the 2007 Queensland potential tissue donor pool. However, the consequences of transmission of CJD from donor to recipient were considered by QEB to be severe enough as to exclude from donation many persons with dementia, a non-specific symptom of CJD which has a non-infectious aetiology in the majority of cases. This conservative risk management method was thought to approach a zero risk of CJD transmission, but it is acknowledged that it caused the exclusion of individuals to a level which was significantly out of proportion to the probability of transmission.

The supply of corneal tissue in Queensland currently meets routine demand. However, it is the author's opinion that this situation is unlikely to be sustained indefinitely. There may be a variety of reasons for this, but the increasing prevalence of dementia alone may account for a significant decrease

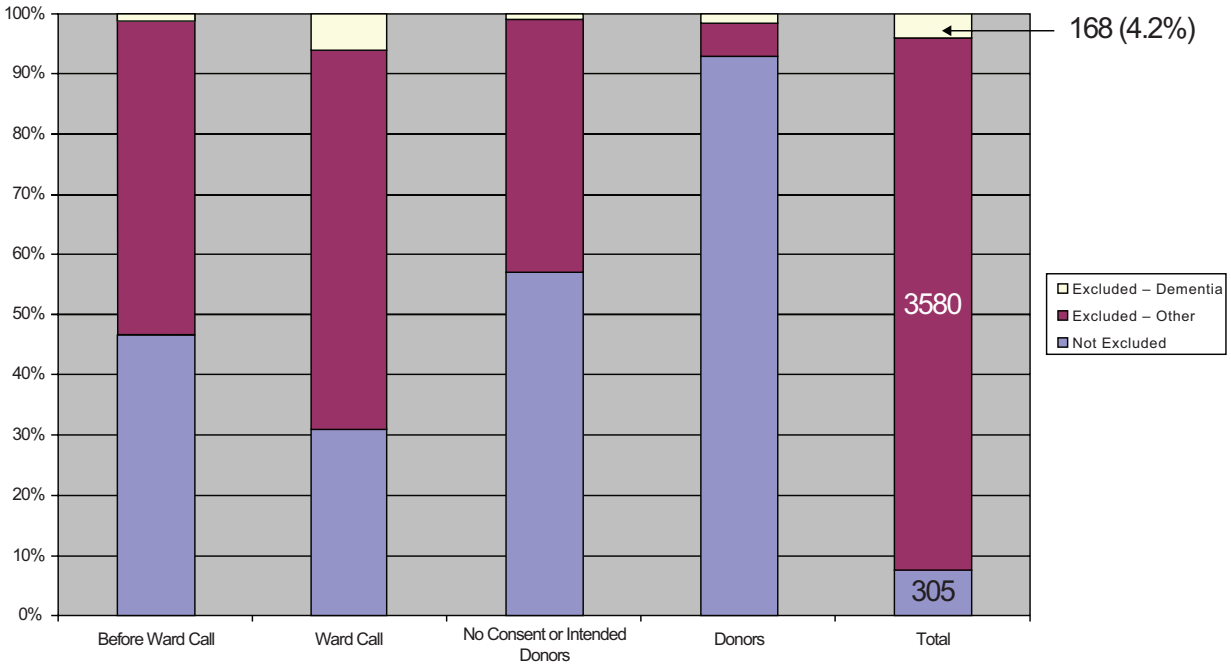

Figure 2. QEB notification outcomes 2007 by screening stage.

in the potential donor pool if current donor screening techniques continue.

Published data regarding CJD transmission in a tissue banking context generally supports consideration of the consequences of transmission in preference to the small probability that transmission could occur.[2,11–14] For example, Hogan et al[11] in reference to the the Eye Bank Association of America criteria indicated that only 0.0009% of all potential donors in the United States would be expected to have CJD, but suggested that "historical queries of potential corneal donors should be tightened too assure exclusion of donors with early neurological alterations". However, there is little emphasis on actions that may be taken to safely increase the potential donor pool.

It was noted in this study that most exclusions on the basis of dementia occurred early in the screening process, and were therefore based on limited information. There may be scope to investigate these cases more thoroughly to ensure that a true diagnosis of dementia existed and that if the patient was in fact diagnosed with dementia, that the cause of that dementia was not vascular. For example, if a potential donor was excluded during the first stage of the process due to a "dementia screen", perhaps ward staff or medical practitioners who managed the patient could still be contacted to gather further information, rather than ceasing the investigation at this stage. Care would need to be taken to ensure standards were maintained, i.e. that no potential donors with a true diagnosis of non-vascular dementia were progressed further.

There may be other techniques besides donor screening which may help to increase the potential tissue donor pool while still preventing the transmission of CJD from tissue donors to recipients. One notable example would be the development of an appropriate screening test for CJD. While a positive 14-3-3 protein test has been shown to support a diagnosis of CJD, this test is only useful in the presence of an adequate clinical context and a high differential potential for the disease.[15] While all potential donors with a positive 14-3-3 test should most definitely be excluded from tissue donation, this test would obviously not be suitable for screening potential tissue donors. A screening test which is sensitive and specific for CJD could be used in the same way as routine serology is employed currently to ensure that individuals otherwise assessed as low risk are free from the disease. Pauli[13] states that "the development of rapid, sensitive and specific diagnostic test systems is urgently required to test blood, organs and tissue of donors".

The transmission of Creutzfeldt-Jakob disease to the recipients of donated tissue is of great concern

to tissue banks worldwide. While a conservative risk management approach to the selection of donors should be maintained in order to minimise this risk, it has been shown that the current risk management procedure in place at the Queensland Eye Bank is potentially more conservative than necessary. Scope to alter this approach to increase the potential donor pool while maintaining safety standards may exist, and may in fact become necessary in future.

Definitions

Donor: person from whom tissue is retrieved.

Intended Donor: person for whom consent for tissue donation is obtained.

Non-donor: person not considered suitable for tissue donation.

Possible Donor: person with potential for tissue donation who is excluded prior to completion of the initial medical suitability assessment.

Potential Donor: person deemed medically and socially suitable for donation at time of next-of-kin approach.

Disclosure

The author reports no conflicts of interest.

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