Genetic Testing - prion protein gene (*PRNP*) test - for families to rule out or establish a genetic cause for Creutzfeldt-Jakob disease (CJD) or other prion diseases.

If a family want to rule out a genetic cause for their loved one's diagnosis of CJD the most appropriate way is to request that a blood sample be taken in life from the patient with the DNA extracted and stored providing the opportunity for future testing.

If the DNA test for a genetic mutation on the patient is negative then relatives have the same risk as the general population of developing CJD, one to two in a million per head of population per year.

CJD can only be definitely confirmed by a brain only autopsy but the autopsy does not provide information on whether the patient suffered with sporadic CJD or an inherited form of prion disease. Further investigations, involving a DNA test, must be consented to in order to rule out or establish a genetic cause.

Furthermore, establishing that the patient carries a genetic mutation to CJD does not necessarily prove that the patient is suffering with, or died of CJD. Although highly likely if symptoms and tests all indicate a diagnosis of CJD an autopsy should still be considered to confirm the diagnosis.

85% to 90% of CJD cases are sporadic, with no known cause, but if in the rare case a genetic test gives a positive result for a genetic mutation to CJD or other prion diseases then each child of the patient has a 50% chance of inheriting that mutation. This also has implications for siblings of the patient and possibly their children. If there is a positive result to the DNA test that establishes that the patient suffered from familial CJD or another genetic form of prion disease, then first degree relatives of the patient (children, brothers and sisters) can choose whether or not to consent to predictive testing to see if they have inherited the genetic mutation.

Predictive Testing can determine in a healthy first degree family member of a patient, where a genetic cause for CJD has been established, whether he or she has inherited the impaired gene and is at risk of developing prion disease in the future. Testing can be organised through a local genetic service. This involves two blood samples being taken from the individual family member who will be required to consent to testing of their own DNA extracted from the blood samples. Genetic counselling is always involved in this process before testing can be arranged.
A person who carries a genetic mutation to CJD or other prion disease is most likely to develop genetic prion disease during their lifetime but in some cases a person with a mutation can live to be elderly and remain healthy or die of another cause first.

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If there is a strong family history of prion disease then the DNA testing can be organised by the treating doctor while the patient is still alive from a blood sample but if there is no known family history then it is preferable to wait until CJD has been confirmed by autopsy. In a case where an autopsy is not consented to by the family, it is preferable to wait until the diagnosis is considered to be highly probable.

There are two ways to organise for *PRNP* testing. DNA can be extracted from blood (taken in life) or autopsy brain tissue (unfixed).

Option one: The CJD Support Group Network (CJDSGN) recommends having a blood sample taken from the patient in life so that the DNA can be extracted and stored by either of the testing laboratories. Storing DNA extracted from a blood sample is easy, there is no cost involved for the family and the sample can be stored for a long period of time until the family decide if/when they want to consent to testing.

The doctor treating the patient should be able to organise for a blood sample to be taken. The sample is a 5-7mils EDTA Blood marked 'DNA extraction and storage'. The CJD Support Group Network can provide the family with a 'request for DNA extraction and storage' form.

This is a good option as often families are not all in agreement about having an autopsy or something can go wrong. DNA extracted and stored from a blood sample taken in life also alleviates the cost and delays involved in obtaining DNA from autopsy brain tissue. If there is no tissue available from an autopsy and no DNA stored from a blood sample then there is no way in the future for the family members to be able to establish for certain if the patient suffered from genetic prion disease or sporadic CJD. Ruling out a genetic cause for the patient's illness answers that question for all other family members.

When DNA from a blood sample is stored then family members can, at any time in the future, choose to contact a genetic service in their local area to discuss, and if appropriate, consent to testing. Contacting the service does not mean you have to consent to testing on the DNA of your loved one but does give family members the benefit of expert advice during the decision process. Deciding to have genetic testing done is not always easy with family members often not in agreement so discussion with a genetic counsellor may help.

Option two: The Australian National CJD Registry (ANCJDR) is the only laboratory in Australia that can provide extraction of DNA from autopsy brain tissue. A service fee will be incurred and delays may be experienced.
Once an autopsy confirms CJD and extracted DNA is available from tissue families can request and consent to a *PRNP* test on the extracted DNA through a genetic service in their state or through a specialist clinician who can order the test and provide the results to the next of kin.

***PRNP* Testing**

Testing is currently only carried out at Department of Diagnostic Genomics in Perth WA. The next of kin will be required to sign a consent form, and once testing is done, the results will be sent to the requesting genetic service or specialist. Our experience is that using a genetic service is the preferable option as the expert experience of a geneticist is available if, in the rare case, the result is positive.

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Choosing to proceed with genetic testing to rule out or establish a genetic cause for your loved ones illness is a personal choice but as the chances of genetic CJD are very low, approximately 10%, some families prefer to rule out the possibility but with this does come the very slight chance of a positive result.

By choosing to attend a genetic service, in the rare case where a DNA genetic test on the patient does establish a genetic cause for their illness, genetic counselling support is available for the family and an established relationship for those individual family members who do elect to consent to predictive testing.

Genetic services are free in all states but you do need to make an appointment and in some states you may need a referral from your local doctor. Some services do have waiting lists so it is advisable to book ahead when you can.

If you elect to consent to DNA testing in the future to establish if your loved one died of genetic or sporadic CJD then it is important to consent to the sharing of information with the ANCJDR as this information is invaluable for surveillance and research in Australia. By providing this information you are assisting future families. Information supplied to the ANCJDR is confidential and will not be shared with a third party.

For further information contact the CJDSGN

National Toll Free Number 1800 052466

Email: contactus@cjdsupport.org.au

Inherited or genetic forms of CJD and other prion diseases accounts for 10 – 15% of all cases of prion disease.

These include the following:

Familial CJD (fCJD)
Gerstmann Sträussler Scheinker Disease (GSS)
Fatal Familial Insomnia (FFI)

For more information refer to our brochure 'What is CJD'