Dentatorubral-Pallidoluysian Atrophy (DRPLA)

Division of Human Genetics
University of Cape Town

What Is DRPLA?
DRPLA is a progressive disorder involving the failure of muscular co-ordination, involuntary movements in the body and progressive intellectual deterioration or personality changes.

Considerable variation is seen in the clinical manifestation and age of onset within the family. The age of onset varies from less than ten years to over 70 years. Individuals with juvenile onset usually show a more rapid disease progression compared to those with late onset.

What Causes It?
The cells of the body contain information, in the form of genes, for the body to make all the necessary components and chemicals to ensure normal function. The information for our cells to make a protein that is thought to be important for brain function, called atrophin 1, is contained in a gene on chromosome 12. There are two copies of this chromosome in every cell and therefore two copies of the gene that codes for atrophin 1 (this gene is called DRPLA). When the gene is changed it cannot function properly and the information contained in the gene and its products are faulty.

What Is The Genetic Fault That Causes DRPLA?
The condition of DRPLA is associated with an unstable trinucleotide repeat (CAG) within the gene. An unaffected individual can have up to 34 repeats, while individuals who are affected have been shown to have 49 or more of these repeats.

How Are These Faulty Genes Inherited In A Family?
The DRPLA is inherited in an autosomal dominant manner (see fact sheet 9) where only one faulty copy of the gene is necessary for DRPLA to develop. A parent with this faulty copy has a 50 % chance of passing the DRPLA gene on to his/her children, and a 50% chance of passing on the normal copy.

Genetic Testing And DRPLA
The Division of Human Genetics at UCT provides genetic testing for people affected with DRPLA (diagnostic testing) and for their unaffected at-risk family members if they are over the age of 18 years old (predictive testing). This test can determine if the individual has inherited the faulty gene (the expanded CAG repeat region) and usually takes about 4 weeks before results can be given.

DRPLA Predictive Testing Protocol
The predictive test for DRPLA allows testing of family members that may be at risk, before any clinical signs present. A programme or protocol has been recommended by doctors and geneticists based on their experiences in dealing with individuals and families at risk for the disease. If, after careful consideration, you decide to take the test, you will be requested to come to the Groote Schuur Hospital Neurogenetic Clinic or the Department of Human Genetics on at least four occasions to see the doctors involved in running the programme.

The full protocol for predictive testing is available at the following website:
http://www.humangenetics.uct.ac.zas.

Genetic counselling
As this is a genetic condition, genetic counselling is strongly recommended. Genetic counselling provides information on the condition, its inheritance pattern, risks to other family members and the prognosis. The Division of Human Genetics at the University of Cape Town (UCT) can be contacted in this regard.

What Are the Important Issues To Consider Prior To Predictive Genetic Testing?
The test allows the individual at-risk for developing DRPLA, to determine if they have inherited the faulty gene, before the clinical symptoms present.

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There are many important issues to consider before having predictive genetic testing, which a genetic counsellor will discuss with you prior to the testing, including:

– The advantages and disadvantages

– The test may raise issues for relatives who may have DRPLA and could also have important implications for other family members, who may find that they are at an increased risk

– The implications of a positive or negative result for the person undergoing testing

Is There Any Treatment Or Cure For DRPLA?

No cure exists for the DRPLA at present. Certain symptoms of this disorder, however, can be treated with medication.

Further Information On DRPLA Can Be Found At:

http://www.humangenetics.uct.ac.za

http://www.geneclinics.org/profiles

Contact Details:

Neurogenetic Clinic at Groote Schuur Hospital (First Thursday of every month)

Genetic Nurse:

Tel: (021) 404 6235/(021) 406 6304