Huntington Disease Presymptomatic Gene Detection

The University of Pittsburgh provides direct gene testing for presymptomatic detection of the gene for people at risk for Huntington Disease (HD). I understand that this is a clinical test and is not a research study. HD is a genetic condition which results in progressive dementia and neurologic deficit. It is a fatal disease with symptoms usually appearing in the third or fourth decade of life. Some individuals at risk wish to know if they have the gene before symptoms appear. This program is designed to offer presymptomatic testing to appropriate individuals in conjunction with psychosocial and medical follow-up care.

In the past, gene testing for HD was limited to following genetic markers through a family that were closely linked to the gene in the attempt to identify those at an increased or decreased risk for carrying the HD gene. This testing was not diagnostic and was not 100% predictive. It relied heavily on the diagnosis being correct in "affected" individuals and was able to only predict, with a certain percentage of accuracy, how likely the at-risk family member was to be carrying the gene. Blood from many generations and many family members was necessary and the testing was very costly. This testing is referred to as linkage analysis.

In 1993 direct gene analysis became available. That is to say, we are now able to evaluate the gene responsible for HD in any individual and look for the gene change known to cause the disease. The test looks for a repeating segment of genetic material called a trinucleotide repeat (CAG). Individuals with 26 or fewer CAG repeats are negative for the HD gene. Those who have 40 or more repeats are positive for the HD gene and would be expected to develop the condition. Those with 27-39 repeats are inconclusive meaning it is not clear whether or not they will develop HD. When an inconclusive result is found, the diagnosis can only be made on a clinical basis, and presymptomatic testing for at risk family members may not be available (except by the former genetic linkage testing).

Even direct gene analysis has some limitations. There is not yet enough experience with the testing to know if absolutely everyone with Huntington Disease has the same change in their gene. This means that a normal test result most likely rules out the diagnosis but at this time we cannot be 100% sure. Presymptomatic testing is not usually available to individuals unless a sample of blood or stored DNA is also provided from a family member who has been diagnosed with HD by a neurologist. Confirming the diagnosis in a relative makes the direct gene test much more accurate. For individuals who are unable to obtain blood or DNA from an affected family member,

confirmation of the diagnosis of HD in that individual by a neurologist or geneticist will suffice.

The following outlines the clinical program for at risk individuals. Individuals interested in presymptomatic testing must follow a set program. Three or more visits at the University of Pittsburgh or at a designated center are necessary.

The total charges for testing are approximately $500. Costs are subject to change. The following are approximate charges: neurological examination $200; pathology (lab) $315. Discrimination by insurance carriers may be possible and you should be aware that loss of insurance is possible due to testing or other documentation of the diagnosis. If you do not wish to bill your insurance company for these fees, advance payment is appreciated on the day of service.

Visit #1:

Complete intake forms, give family and medical histories; receive genetic counseling; receive complete neurologic examination; plan psychological consultation and discuss impact of testing.

Psychological evaluation.

Blood collection and consent forms signed.

Visit #2:

Disclosure of results.

Follow-up counseling will be done over the phone or in person, subject to the discretion of the medical team and/or the patient's own desires.

For individuals traveling a great distance, it may be possible to combine various components of the protocol in the same visit. The laboratory will accept specimens from families who do not wish to come here for evaluation and counseling provided these families are able to identify a center in their region offering appropriate services. The center should be able to provide genetic counseling services, neurologic and medical care services specific to HD and supportive counseling services. We are able to assist with these arrangements.

Laboratory results will not be given to family members over the telephone. Persons coming to the University of Pittsburgh for testing are encouraged to identify a contact person for follow-up supportive care (i.e., psychiatrist, counselor, doctor, clergy) unless these services are obtained at the University of Pittsburgh. We may refuse to test individuals under 18 years of age or cases involving ongoing pregnancies. Testing shall be postponed indefinitely for those who we believe lack appropriate support systems. In

most cases, medical insurance will not pay for this testing. Many people also find that asking medical insurance for help is inadvisable as some companies have been known to discontinue coverage. **Whether you wish the charges for this testing to be submitted to an insurance carrier on your behalf is your voluntary decision. If you decide to authorize us to submit our testing charges to your insurance carrier, we cannot promise confidentiality of test results since receipt of the test results may be required by the insurance carrier before it will pay for the testing charges**. Individuals may withdraw from the program at any time. DNA samples will be held indefinitely.

Consent forms for at risk individuals who wish to know if they have the gene and for individuals affected with HD and are providing a sample of blood or stored DNA for testing are enclosed with this information packet. Please read these through carefully. If you are interested in setting up an appointment for visit #1 here at the University of Pittsburgh or at a center in your state after reading and discussing this information with appropriate family members, please contact us at the number below. We can help those interested in testing at an out of state center arrange for an appropriate testing site. Feel free to call with questions or concerns.

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