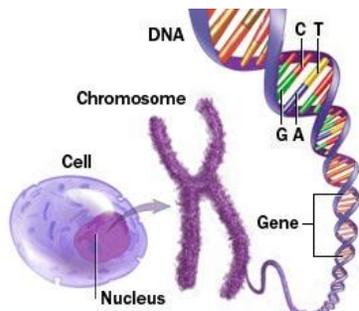


HD Genetics:

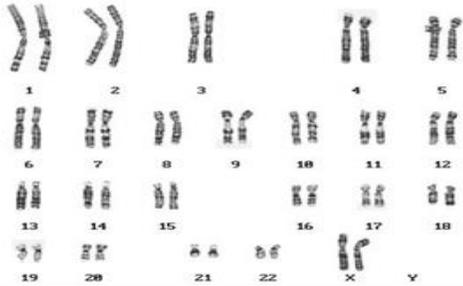
Mara Sifry, LCGC

Genetics 101

Our bodies are made of cells and in each cell we carry our genetic material in the nucleus. This genetic material is the “recipe” or “blueprint” about how to make each of us. Our DNA contains all of our genes and these genes make proteins that create and determine everything about our bodies, from the chemicals that help us digest our food, to our hair color, skin color, and whether or not we will get HD in our lifetime. The DNA is packaged into structures called chromosomes that we can see under the microscope.



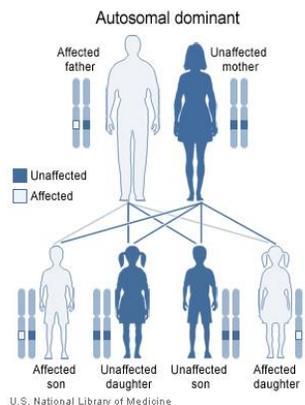
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We all have 46 chromosomes which come in pairs; one of each pair comes from each parent. This means that 23 chromosomes are from the mother, and 23 chromosomes are from the father.

We know that the gene which causes HD is on chromosome 4 and the gene for HD makes a protein called “huntingtin.” Huntington’s disease is **dominantly inherited** which means that it takes only one abnormal copy of the HD gene to cause the disease.

A person with HD has a 50% risk of passing on this condition to each of their children. This doesn’t mean that if a person with HD has 4 children, then 2 will inherit the condition and 2 won’t. The 50% risk is for each child. So in this example all 4 children could inherit the gene, or 3, or 2, or 1, or none. It’s like flipping a coin each time a person with HD has a child. Males and females have the same 50% risk of inheriting the condition from a parent who has HD.

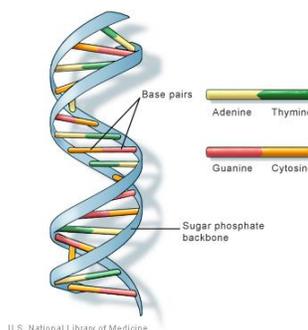


U.S. National Library of Medicine

What is the genetic change in HD?

The HD gene is on chromosome 4.

Remember that genes are made up of DNA. DNA is a twisted double helix. You can imagine this molecule as a twisted ladder. The DNA is made up of a sugar phosphate backbone (the sides of the ladder) and then bases that hold the 2 sides together (the rungs of the ladder). These bases have names (**A**denine, **T**hymine, **G**uanine, **C**ytosine). The HD gene contains a series of **CAG repeats** (Cytosine- Adenine- Guanine). We all have CAG repeats but people with HD have more copies of this CAG repeat in one copy of their huntington genes.



U.S. National Library of Medicine

What the CAG Numbers mean:

Normal Range	Intermediate Range	Reduce Penetrance Range	Full Penetrance Range
<ul style="list-style-type: none"> • 26 or fewer CAG repeats • Not at risk for developing HD • Not at risk for passing to children 	<ul style="list-style-type: none"> • 27-35 CAG repeats • Not at risk of developing symptoms of HD • considered unstable so that future generations could be at risk 	<ul style="list-style-type: none"> • 36-39 CAG repeats • may or may not develop symptoms of HD. • considered unstable so that future generations could be at risk 	<ul style="list-style-type: none"> • 40+ CAG repeats • will develop HD symptoms during natural lifespan • considered unstable and 50/50 chance of passing 40+ to children • 60+ CAG repeats is considered Juvenile On-Set HD.

An individual's number of CAG repeats is determined at conception and we wouldn't expect it to change over time.

Paternal Inheritance: While all genders can have or pass on HD, there's an interesting phenomenon that occurs in HD where the gender of the parent you inherit an HD expansion from can impact the age of onset of HD symptoms. If you inherit the HD causing gene from your father the number of the CAG repeats MAY increase whereas if you inherit it from your mother, the number usually remains stable. This is important since we know that the number of these CAG repeats plays a role in the age of onset. In general, the higher the number of CAG repeats, the earlier the onset of symptoms although there are other genetic and non-genetic variables that can play a role in the onset and severity of symptoms.

Types of Genetic Testing for persons 18 and over:

PREDICTIVE TESTING

This testing is completed IF:

*you don't have any symptoms of HD,
you are at risk for HD, AND
you want to know your HD gene status.*

Testing can be an emotional process and you may want to consider some important issues before engaging in predictive testing.

RESOURCE: 10 minute video that explores the basic information about predictive testing:
<https://www.youtube.com/watch?v=4HW5YdgM4zs>



CONFIRMATORY TESTING

This testing completed IF:

*you have symptoms of HD
This includes a comprehensive medical evaluation
your diagnosis and care plan will be discussed
blood test may be drawn at this visit to confirm the diagnosis, and the results will
be shared at your follow-up appointment.*

This can be an emotional process even when you are expecting abnormal results. Your HD professionals can help support and guide you through this process.



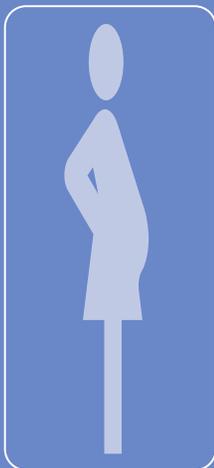
Testing Children under age 18:

At this time the HDSA and the National Society of Genetic Counselors, in conjunction with researchers and clinicians experienced in caring for HD families, do not recommend testing of persons under 18, unless they have symptoms of the condition that require medical treatment.

If a child is suspected of experiencing symptoms of HD (Juvenile Onset Huntington's Disease (JHD)), we strongly encourage you to contact your HDSA Center of Excellence for a medical evaluation to determine if testing is appropriate.

Many families have shared that they want to KNOW if their children carry the gene so they can prepare & plan for their future, while we certainly understand that desire as a parent we are ethically bound to think of the child's right to decide (autonomy) when they are adults themselves. HD is considered an Adult Onset Disease and we know that most adults at risk for HD choose not to have predictive HD DNA testing. We would never test an adult without their consent and making sure their desire to test is NOT influenced or coerced by others. Therefore, the current perspective is that children, once they are of adult age, should have the option of testing or not testing for HD.

Genetic Testing in Pregnancy



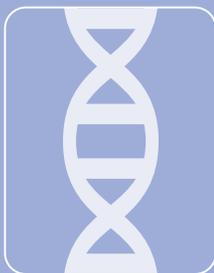
Prenatal Testing

can be done on an unborn fetus to determine if it is carrying the HD gene expansion

This can be a very complex and emotional process so we encourage you to review the issues and procedure with a professional who is knowledgeable in HD.

CVS (Chorionic Villus Sampling) is done typically between 11-13 weeks of pregnancy. A piece of the developing placenta is removed either through a woman's cervix or abdomen using a catheter or needle. This tissue is 99% genetically identical to the fetus so DNA testing can be done for HD status and a result given. CVS carries a risk for miscarriage that can vary slightly from center to center but is usually in the range of 1/500.

Amniocentesis is typically performed between 15-20 weeks of pregnancy. Amniotic fluid that surrounds the baby is removed from the uterus using a thin needle. This fluid contains cells from the baby that can be isolated, grown in the lab, and tested for HD status. Again, amniocentesis carries a risk for miscarriage that can vary slightly from center to center but is usually in the range of 1/500-1/900



PRE-IMPLANTATION DIAGNOSIS (PGD):

This is a way to test an embryo before it's implanted in a woman's uterus.

Using IVF (In Vitro Fertilization) techniques, the egg and sperm are combined outside the woman's body. Once the embryo reaches a certain level of development it can be tested to see if it carries the HD gene expansion. Only embryos that are unaffected with HD are implanted in the woman's uterus. PGD can be done in a way that doesn't disclose the at risk parent's status if unknown.

For more information on PGD please check out [HDFreeWithPGD](#) and [HelpCureHD](#).

To have kids or NOT to have kids:

This is not an easy decision to make and then adding HD into the equation adds some additional questions or concerns. There is NO right or wrong decision, only what is right for you and your partner.

We encourage you to communicate with your partner about desires or concerns about having children and exploring your options together. Please reach out to a genetic counselor or HDSA Center of Excellence for additional discussion and support. All the choices have pros, cons and feelings that you must explore to decide what is best for YOU.

Reproduction Choices:

Natural conception IVF/PGD Prenatal Diagnosis Egg/Sperm Donor Surrogate Adoption Not have children

What is a Genetic Counselor and what do they do?

Genetic counselors

are medical professionals trained in the biology of genetic conditions and counseling.

Their role is to discuss the science and symptoms of genetic conditions with families. They discuss options, outcomes, and risk/benefits in a non-directive, non-judgmental, and supportive approach so YOU can make your own choice about testing, starting a family, etc.



Genetic counseling

is a supportive process where a person or family chooses to talk about genetic information and its impact on the individual and future generations.

The DNA Blood test for HD itself is a straightforward laboratory process, but the implications and emotional aftermath of the results are not as straightforward. HD is RARE and testing can be complex. The emotional burden of results can be very impactful on a person's life and future.

How do I decide to test?

Choosing to test is a PERSONAL choice. A HD genetic counselor, family, trusted friends, or clergy can help you explore all the complexities, concerns, or issues specific to you and your situation. However, the choice to test is ultimately yours alone as it is your genetic information.

SOME (not all) reasons to test:	SOME (not all) reasons to NOT test:
Feeling "stuck" in the uncertainty and unknown; alleviate anxiety	no current treatment to slow progression or cure the disease
Planning for your future (relationships, children, education/career, etc)	Not emotionally prepared for the testing process or results
For future generations (for example, my adult children who are starting families)	Rather have HOPE that I don't have it. Prefer to live life and cope with things as they come.
I'm experiencing symptoms	Privacy, confidentiality or discrimination concerns

There are **NO Right or Wrong Answers** and there are many reasons people choose to test or not test.

What happens in a genetic counseling session?

HD Family History

- referred to as a pedigree/family tree
- who in the family has HD, **how old were they when they started having symptoms, and at age of diagnosis?**

What is your life experience with HD?

- how long have you known about HD risk?
- have you seen or cared for someone with **HD symptoms at different stages of the disease?**

Why test NOW?

- Are you testing for yourself and not feeling pressured by others to do so?
- Is this a good time for you to get this genetic information and process and COPE effectively with it?
- Are there any other major life stressors going on at the same time you are seeking this information? (For example, death of loved one, divorce, pregnancy, or other major life changes)

How would the results change your life?

- what would you do differently if gene positive or if gene negative?
- Potential impact on you current or future relationships, education/career goals, having children, setting life priorities, etc)

How does your family FEEL about you testing?

- Are they supportive or against you testing?
- Are you sharing your desire to test with them?

Privacy & Discrimination Issues

- Insurance & Employment Discrimination is a major concern for many people considering predictive testing for HD.
- Some laws in place for protection include:
 - Health Insurance Portability and Accountability Act of 1996 (HIPAA)*. HIPAA doesn't allow group health insurance providers to create any rule of eligibility for a person or their dependents that discriminates against that person based on any health factor, which includes genetic information.
 - Genetic Information Non-discrimination Act of 2008 (GINA)* provides some security against employment and medical insurance discrimination. GINA does not yet cover life, disability, or long term care insurance, which often concerns people in families with HD. Once a person actually has signs or symptoms of the disease GINA does not apply. GINA doesn't apply to the military, the Veterans Administration, or the Indian Health Service.
 - State of California: Laws and Regulations – California Health and Safety Code Section 124975-124996; State of California: Department of Managed Health Care - Knox-Keene Health Care Service Plan Act of 1975 ; California Insurance Code
 - RESOURCES: Genome.gov; Genetic Home Reference-Overview of genetic discrimination; National Institute of Health – Office of Legislative Policy and Analysis and Council for Responsible Genetics – A non-profit, non-governmental organization that fosters public debate about the social, ethical and environmental implications of genetic technologies.

Commented [MS1]: I can't seem to edit this but maybe it could say: What happens in a genetic counseling session? What will a genetic counselor ask? Or something like that?

Where to go from here?

The diagnosis of HD in an individual or family member can have an immediate or eventual impact on a person's perceptions of themselves, day to day life, and their future goals or plans. Making these adjustments is different for everyone but here at the UC Davis HDSA Center of Excellence we are committed to helping you in this important aspect of your life-bringing hope, meaning, and purpose to your life with HD. We remain available to you at any time. Please do not hesitate to contact us if you have questions or would like to discuss these issues further.

