



Frequently asked questions, January 2011

Answers to frequently-asked questions about HD – the first in a regular series of HDBuzz FAQ articles.



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The first in a monthly series of FAQ articles covering hot topics and burning issues in the science behind HD.

What causes Huntington's disease?

HD (Huntington's disease) is caused by a mutation in a person's DNA. Your DNA is basically lots of instructions for building your body and keeping it running. DNA is organized into individual 'recipes' called genes. Each gene is a recipe for one protein (a molecular machine). A mutation in a gene is like a spelling mistake. Some spelling mistakes are harmless, but some result in proteins that don't work properly or are harmful.

The mutation that causes HD was mapped to a specific gene in 1993 - this gene is now called the 'huntingtin' gene, and is abbreviated as 'HTT' or 'HD' or 'IT15'. Knowing the location and nature of the HD mutation has allowed people to be tested for the HD mutation since 1993.

So what's all this about 'CAG'?

Everyone with HD has the same basic type of mutation. It is an expansion of a normal repetitive piece of DNA on chromosome number 4. Chromosomes are long pieces of DNA which are chains of millions of 'bases'. Each base is like letters of the alphabet spelling a word. Every base is one of 4 chemicals (adenine, cytosine, guanine, thymine). These bases are abbreviated as A, C, G or T.

Near the beginning of everyone's HD gene is a repetitive stretch of three letters - CAG. In people without HD, these three bases are repeated fewer than 35 times - usually about 17 times. People with 36 or greater repeats of CAG will develop HD if they live long enough.

Traditionally, CAG is pronounced as three separate letters ('see-ay-gee') rather than as a word.

How does an expanded CAG repeat cause Huntington's disease?

Proteins are made from building blocks called amino acids. The three-base sequence CAG in a gene is an instruction to add an amino acid called glutamine to a growing protein. However many CAG repeats there are in a huntingtin gene, is how many glutamines will be in the finished protein. So, for example, people with 42 CAG repeats produce a huntingtin protein with 42 glutamine blocks at the start.

Scientists have abbreviations for the different amino acids. Glutamine is abbreviated as 'Q', so Huntington's disease is sometimes called a 'polyglutamine disease' or a 'polyQ disease'.

When the huntingtin protein contains too many glutamine blocks, it has a different shape from the normal protein, and behaves differently too. These differences cause the abnormal protein to become harmful to cells, and it's this harmful behaviour that causes cells to malfunction and die.

Malfunctioning and dying neurons (brain cells), and other cells, are what causes the symptoms of HD.

Can you tell when someone will experience symptoms of HD?

If we look at thousands of HD patients, we find that on average, people with longer CAG-repeat lengths tend to have an earlier age of onset of HD symptoms. At the extreme, people with very long repeats have a severe form of HD with childhood onset. This is often called 'juvenile HD' or 'JHD'. HD patients with adult onset have CAG repeat counts that are lower than juvenile HD patients. The average repeat length in HD patients is about 44.

It's important to note that the ability to predict age of onset from CAG-repeat length is not at all accurate. Two people with the same CAG repeat length might start to experience symptoms at very different ages - many years or decades different. Because of this, CAG-repeat lengths are useful for scientific and medical research, but aren't very informative for most people trying to predict their own expected age of onset.

My friend/brother/mom is taking a particular drug for HD - do you think I should?

HDBuzz can't provide personal medical advice. Any decisions about treatment of HD symptoms should be pursued in consultation with your physician.

Unfortunately, no treatment or drug has ever been shown to delay or prevent symptoms of HD in humans.

However, there are **lots** of treatments that can help many of the symptoms of HD, and different people may benefit from different treatments. Ask your HD doctor which treatments, if any, might be helpful for you.

What about supplements? Can you tell me which supplements to use, and how much to take?

No. Lots of people with HD do take supplements like creatine, coenzyme Q and many others, but so far, no supplement has been shown to slow down the disease when tested in a randomized, double-blind placebo-controlled trial (the best kind of scientific trial for answering these questions).

This is not to say that these supplements definitely DON'T work, but merely that they haven't been proven to do so. Until they have, HDBuzz can't recommend any supplement or treatment.

A number of sites on the net provide advice about supplement use for those who wish to consider taking them - HDAC.org and HDlighthouse.org, for example.

What about alternative treatments for HD?

There are a number of individuals and organizations marketing 'alternative' treatments for HD. Many of these like exercise, massage etc. - may be very helpful to many patients.

Other alternative therapies, often marketed as 'cures', include shark cell injections, stem cell injections and dietary supplements. There is no evidence that such treatments are effective for slowing down the progression of HD - and they may actually be harmful. We advise that you speak to a doctor experienced in looking after HD patients before considering any treatment.

Of course, if good scientific evidence is produced that any 'alternative' treatments are effective, you'll hear about it from HDBuzz.

It's worth considering that an 'alternative medicine' which has been proven to work automatically becomes 'medicine'.

Isn't it true that drug companies don't care about HD?

We at HDBuzz believe that drug companies have a critical role to play in developing effective therapies for HD patients. They have the experience and ability to run clinical trials that will prove whether drugs are effective.

In the past, it may have been true that drug companies didn't dedicate many resources to HD. This has changed, and now many drug companies have HD research programs. HDBuzz endorses no individual company or program, and receives no funding from any pharmaceutical company, but we are pleased that both large pharmaceutical companies and small biotechnology companies now have very serious programs and resources dedicated to HD research.

The authors have no conflicts of interest to declare. [For more information about our disclosure policy see our FAQ...](#)

huntingtin protein The protein produced by the HD gene.

PolyQ A description of HD and other diseases that are caused by abnormal expansion of stretches of DNA containing the sequence CAG repeated many times. Too many CAGs in a gene results in proteins with too many 'glutamine' building blocks, and glutamine is represented by the symbol Q.

amino acid the building blocks that proteins are made from

chromosomes Long strings of genes, tightly coiled into packages of DNA inside cells.

Each cell's DNA is stored as 46 chromosomes. The HD gene is on chromosome 4. Each chromosome has two copies, one inherited from each parent.

juvenile HD Huntington's disease where symptoms begin before the age of 20.

CAG repeat The stretch of DNA at the beginning of the HD gene, which contains the sequence CAG repeated many times, and is abnormally long in people who will develop HD

glutamine the amino acid building block that is repeated too many times at the beginning of the mutant huntingtin protein

neuron Brain cells that store and transmit information

placebo A placebo is a dummy medicine containing no active ingredients. The placebo effect is a psychological effect that causes people to feel better even if they're taking a pill that doesn't work.

HDAC histone de-acetylases (HDACs) are machines that remove acetyl tags from histones, causing them to release the DNA they're attached to

HTT one abbreviation for the gene that causes Huntington's disease. The same gene is also called HD and IT-15

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