

WE'VE GOT THE HD GENE! BUT WHAT DOES IT MEAN?

By Dr. Nancy S. Wexler

Finding the gene means that we have the CAUSE of Huntington's Disease in our hands! Something has gone wrong with the HD gene, and now we can concentrate on understanding exactly how the HD gene makes someone sick. And we can now focus solely on the cure!

IS THIS THE CURE?

Not yet. But this is a MAJOR MILESTONE on the road to the cure. It is a HUGE STEP FORWARD in knowing what goes wrong in HD. Like malaria, TB, polio and other diseases, when scientists find the cause of a disorder, they can begin designing and targeting treatments that get at the root of the problem. So new treatments and even possibly a cure are likely to stem from this discovery, but we cannot predict exactly when.

A cure is our goal and we will not stop working until we have one!!

WHAT IS THE HUNTINGTON'S DISEASE GENE?

The HD gene is brand new. Nothing similar to it has ever been discovered before in animals or plants. We still need to learn exactly what the HD gene makes normally and what it makes in people with HD.

We know that the HD gene is in almost every cell of the body — like all genes — but it may be setting up its "manufacturing plants" in only a few places, like the brain, for example. We need to find out in which cells of the body the HD gene is "turned on" and working. Scientists are studying these questions intensively right now and we should have some answers soon.

WHAT IS DIFFERENT ABOUT THE HD GENE?

DNA is made up of four chemicals: A for adenine, T for thymine, G for guanine, and C for cytosine. These four letters make up the genetic alphabet and spell out commands for exactly what the body is to make. Sometimes, certain letters will repeat over and over again. This can be completely harmless, or, if the repetitions get to be too many, can be very harmful.

At one end of the HD gene, the letters CAG repeat many times, like



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a "molecular stutter." In a person *without* HD, CAG can be repeated between 11 and 34 times. In someone *with* HD, CAG is repeated over and over again between 42 and 86 times.

WHAT DOES HAVING TOO MANY REPEATS DO TO THE HD GENE?

Good question. We don't know yet. We don't know how these repeats affect the gene or its functioning, but we should know soon.

IS THERE ANY OVERLAP BETWEEN THE "NORMAL" RANGE OF REPEATS AND THE HD RANGE?

There very well might be. Scientists are checking right now to find out.

DOES THE NUMBER OF REPEATS YOU HAVE IN YOUR GENE AFFECT WHEN YOU WILL BEGIN TO SHOW SYMPTOMS?

Preliminary evidence suggests that, in general, the more CAG is repeated — the longer the string — the earlier in life the disease appears. The shorter the string, the later the disease onset. But the correlation is NOT tight enough to give a person information about when the disease will start. People with juvenile onset have the longest strings of anybody.

CAN THE LENGTH OF THE STRING EXPAND OR CONTRACT FROM GENERATION TO GENERATION?

Yes, the string can expand and con-

tract. The string definitely expands to create juvenile onset. It also seems to be able to get shorter. Maybe we can learn what shortens the string and try to shorten it ourselves.

WHO FOUND THE HD GENE?

The Huntington's Disease Collaborative Research Group! The Collaborative Group consists of six research teams including over 50 scientists in the US and Great Britain [see page 3]. Together, they have hunted for the Huntington's Disease gene for ten years. They always kept before them the knowledge of the genetic clock ticking away in family members and this propelled them to their successful finish. They were kept together and guided by a magnificent Advisory Committee (see page 7) of the Hereditary Disease Foundation.

WHO ELSE FOUND THE GENE?

The Families! All of you who gave tissue samples. All of you who gave information. All of these precious materials were used and will continue to be used. You took matters into your own hands and you prevailed!

We also owe a huge debt of gratitude to the families of Venezuela. Critical families in Venezuela finally revealed the HD gene. Just as in 1983, when the HD gene was first localized, these Venezuelan families have contributed a priceless gift to all of us.

WHAT IS THE NEXT STEP?

Celebrate! We don't yet know what the gene does, but we have the tools to find out. We will soon have a more accurate predictive test. But if you find out that you carry the HD gene, the answer now will be the same as it was before. So think hard before you leap into testing, and talk to many knowledgeable people beforehand.

We don't have the cure yet. BUT WE WILL! The scientists working on HD are brilliant and passionately committed to finding a cure. We will prevail — if everybody helps.

OK cure — we're on the way!

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