Controversial recommendation: American College of Medical Geneticists warns against Alzheimer gene tests

For the Cuartas family and numerous other families around Yarumal, Columbia, middle age brings deep uncertainty. Many people in their 40s begin showing signs of developing Alzheimers disease. This early onset Alzheimers progresses faster than the more common form. It turns children into orphans and grandparents into caretakers.

The Cuartas family what is undoubtedly their extended genetic family in the region carry a mutation that causes the early-onset form of the disease. It's a powerful mutation: you only need one copy of the mutated allele to develop the disease. That's very different from the APOE genes that are associated with the more common late-onset form of the disease. One is a sure thing, the other conveys a risk. And that risk, according to the American College of Medical Genetics and Genomics (ACMG), is too poorly understood to make the test worthwhile.

Earlier this year the ACMG, the academic authority on genetic testing, released guidelines urging consumers to avoid a few specific genetic tests. Among them are the APOE Alzheimer test, the MTHFR test for risk of fatal blood clots and the HFE test for excess iron. Often, people with these mutations never develop these conditions, the ACMG says. So testing for them doesn't offer information that would be useful in making decisions about end of life care or dietary changes, for example. Here's what the ACMG had to say about the Alzheimer-associated APOE genes:

> APOE is a susceptibility gene for later-onset Alzheimer disease (AD), the most common cause of dementia. The presence of an ?4 allele is neither necessary nor sufficient to cause AD. The relative risk conferred by the ?4 allele is confounded by the presence of other risk alleles, gender, environment and possibly ethnicity. APOE genotyping for AD risk prediction has limited clinical utility and poor predictive value.

APOE is the gene most commonly associated with late-onset Alzheimer disease. It codes for the production of apolipoprotein, which transports cholesterol molecules within the brain. Faulty transportation is associated with the build of amyloid beta plaques, the cause of Alzheimers disease.

But there are many other genes that are also associated with developing Alzheimers and a slew of lifestyle factors including alcohol consumption, exercise and diet are also associated. It's also likely that many more genes for Alzheimers disease will be identified. The picture is too complicated for one test to be predictive.

The same goes for the MTHFR gene, but the picture is a little murkier. This metabolic gene codes for the conversion of vitamin B9 and the production of methionine, a vital amino acid. Forty percent of people have a mutated or alternative form of the gene. And while early discoveries of the gene linked it to blood clots and cardiovascular disease, larger follow up studies have disproved that connection. But that uncertainty has left an information void that internet fraudsters are happy to fill writes Carolyn Johnson at

the Washington Post:

> There's a natural human impulse to search for explanations for health problems, and the genome provides a powerful way to deepen that search. But in addition to the genuine promise that the genome brings, it also creates a niche where science can be exploited and vulnerable people seeking answers misled."It's a ripe area for people to claim a scientific basis for stuff that may actually not be true at all, or may have a kernel of truth," said Robert C. Green, a medical geneticist at Brigham and Women's Hospital and Harvard Medical School. "We in genomics and society face a choice. Are genomes going to be so democratized and unregulated that we create an entirely fraudulent industry around them?"

The website Science-based Medicine details the myriad way that MTHFR is linked to disease: adrenal fatigue, diabetes, leaky gut syndrome, cancers. Name a malady, and you can find a website linking it to your MTHFR gene status. If some of those associations prove true in large associate studies, then the gene test might be useful. But until it does the ACMG in essence wants to provide consumer protection to keep people from buying into the idea that their MTHFR gene is causing the harm, and that supplements will make it better.

Unfortunately, it's unlikely that people hawking supplements online are following the ACMG guidelines. They're unlikely to curb their businesses because an academic medical organization claims they're bunk. And the fact that these tests are used to sell bogus medical claims shows how genetics has been assimilated into popular culture. Because the supplement industry is largely unregulated, it can make claims without scientific evidence to back it.

But viewed in a different way, the ACMG guidelines potentially block consumer's access to their own genetic information. If someone thinks that knowing their APOE or MTHFR status will improve their life, help them plan for potential end life care or even just change the vitamins they take, they should be able to do it. Although it seems straight forward, there are many situations in which it turns out consumers don't really own their medical information.

It's particularly confusing in the ACMG case because these are guidelines for both consumers and health care providers. Those providers should understand the predictive value of such tests and be able to correctly describe their utility to their patients. In fact the final recommendation released by the ACMG describes just that. The society recommended that providers not order whole-genome testing without first counseling patients about the possibility of 'incidental findings.' Those are surprises in the genome that pop up when you're testing for other issues, usually to analyze a cancer or look for a genetic basis for another disorder. Those findings can include unexpected paternity results and silent, disease-causing mutations.

The best option for solving both the incidental findings issues and protecting consumers from genetics-based bunk science is a well-educated, science-savvy consumer base. Risk and probability is notoriously difficult for people to grasp, but they will only become more vital as the role of genetics grows in healthcare. Instead of protecting people by keeping them ignorant of their gene status, we should educate

them so they can better understand themselves and make their own decisions.

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