

THE GENETICS OF MIGRAINE



What About My Kids?

Migraine sufferers often express their concern that they will pass on their affliction to their children.

Sally (Bethesda, Maryland):

Jim, the man I eventually married, is a wonderful guy, a great husband and father, but after our first date I wasn't so sure we were going to work out. Midway through the movie we were watching he told me he wasn't feeling well and asked me to help him get back to his apartment. We'd taken the Metro, but he didn't think he could manage the walk to the Cleveland Park station, just a couple of blocks away. I got us a cab, and on the way to his apartment he vomited twice in the back seat. He was having a migraine, he told me. He was very embarrassed. And he looked terrible.

This scenario was repeated a half dozen times over the next few months; we'd be enjoying ourselves, and then within just a matter of minutes we'd have to leave the restaurant, club, party, etc. On one particularly memorable occasion we were celebrating Valentine's Day at my place, feeding each other chocolate-dipped strawberries by candlelight, when he suddenly vaulted from the bed and spent the next half-hour over the toilet in my bathroom. Not the most romantic of evenings.

I have migraine myself and found it easy enough to sympathize, but I knew the disorder could be inherited. When we got married, I worried that between us we would pass on to any children we had such a gigantic genetic dose of migraine that it



could really affect their lives.

Sure enough, our six year old daughter has always been extremely prone to car-sickness, and now she's beginning to complain of headaches. She loves school and is a good student, but three times last month I was called away from work to bring her home early due to her "sick headaches".

We're ready to have a second child now, but I'm worried what we might pass on to that child in the way of migraine. Would we be dooming him or her to a life compromised by frequent attacks of crippling migraine?

MIGRAINE & GENETICS: THE FACTS

- Genetic predisposition is not synonymous with clinical expression.
- Some portions of the inherited genome are static (e.g. bb=blue eyes throughout one's life)
- Some portions of the genome are dynamic (e.g. from family member to family member, the clinical expression of a genetic predisposition to migraine may vary widely)
- ...and even in the given individual, the clinical expression of his/her genetic predisposition to migraine changes over time
- Throughout our lives, what we experience will influence how much or how little our genetic predisposition migraine is expressed symptomatically; Epigenetics!

THE ORIGIN OF MIGRAINE

Blood Vessel or Brain? For much of the last half of the 20th century, migraine was assumed to be a vascular headache. For whatever mysterious reason (as the theory went), in the arteries of the head would dilate inappropriately to cause attacks of throbbing, sickening pain. Treatment was directed at preventing the arteries from dilating or, in the case of acute attacks, at constricting the dilated vessels.

Starting in the 1980s, there began to accumulate ever more convincing evidence that this so-called “vascular hypothesis” was oversimplified or even inaccurate. We now believe migraine to be a brain disorder, with the recurrent headaches and associated symptoms of migraine reflecting a genetically hypersensitive brain. Either spontaneously or in response to various environmental stimuli, internal (eg, drop in estrogen level at menses) or external (eg, change in barometric pressure), genetically primed brain cells-neurons-fire off and trigger a series of electrochemical events that result in...an attack of migraine.

THE MIGRAINE GENE

If migraine is a genetic disorder, great! We’ve mapped the human genome, so why not just go find the cursed gene that causes all this misery and fix it!

Would that it were so simple. Unfortunately, we already have identified no fewer than 47(!) genetic permutations that each are capable of producing the symptoms we refer to as “migraine”, and more such mutations undoubtedly are to come. To complicate matters further, genetic predisposition is not synonymous with clinical expression; in two children who possess the same genetic “load” for migraine, one may experience little or nothing in the way of migrainous symptoms, while for the other migraine will be an all-pervasive and life-long adversary.

EPIGENETICS

Why this striking difference in two genetically similar individuals? At least in part the answer lies in epigenetics. Although the genetic hand of cards we are dealt at conception remains with us unchanged throughout our lives, what we experience in life-what we do and what is done to us-will influence how that hand is played. In our pair of youngsters with an equal genetic predisposition for migraine, for example, research performed by Dr. Gretchen Tietjen and her colleagues at the University of Toledo has demonstrated that the child subjected to emotional neglect will experience the onset of migraine at an earlier age and a higher likelihood of eventually

developing chronic migraine. In short, your genome is the piano, your epigenome is the pianist and you are the music they combine to produce.

SO...WHAT ABOUT MY KIDS?

- 1 It's important to remember that migraine's clinical course varies widely from one person to another, even between family members; your migraine is unlikely to be your mother's migraine.
- 2 Related to this variability, simply having a genetic predisposition to migraine does not doom one to a lifetime spent in darkened rooms, suffering from relentless headache.
- 3 There are worse chronic disorders to have than migraine; rarely does migraine cause irreversible physical harm, and the arsenal of effective therapies for dealing with migraine is already large and rapidly continuing to expand.

Finally, if it's any consolation to you as a migraineur, this is a disorder that has been with humankind for no less than 5,000 years. If migraine conveyed only harm and nothing in the way of benefit, would not the sweeping broom of evolution and natural selection have whisked it away long ago? While it's not easy to recall when in the throes of an acute migraine, perhaps there's something about this peculiar disorder which marks you as a special contributor to the tribe's common good.

