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No more guessing games

Good news for those being prescribed an antidepressant: There's an easier way to determine the one that will work for you BY DIANA BALLON



ENTERING THE

sixth-floor laboratory at the Centre for Addiction and Mental Health (CAMH) in downtown Toronto one crisp fall day, I feel like I'm walking into the future of DNA testing. The post-doc students I have already met with have briefed me about the test I will be taking, posed a series of questions about my history of antidepressant use, and administered a depression test to assess my mood. Now I'll give three vials of blood—and, in four to six weeks, I will find out the results, which I hope will help my psychiatrist to prescribe an antidepressant that will work even better for my anxiety.

Since I was 30, I've been taking a low-dose antidepressant, and I'm grateful for it. Now 47, I'm a freelance writer, an editor and a married mom of two. Before taking medication, I couldn't maintain a job or a relationship for more than a few months. While my depression was never extreme enough to land me in hospital, fighting the ravages of anxiety was exhausting—I had obsessive-compulsive disorder in childhood, and later was diagnosed with "generalized anxiety disorder," or worrying all the time. I knew life could be better, and thanks to Celexa (citalopram), and now CipraleX (escitalopram), it has been. But has either of those antidepressants been the best choice for me?

I'm hoping to find out. Because I have few side effects on CipraleX, and it seems to be working well enough (I still get really anxious, but I'm no longer seriously depressed), the results are unlikely to be transformative. But it'll be interesting to see if science—a DNA test—will confirm this is the right medication for me. The study, developed by Dr. Daniel

J. Mueller, head of CAMH's pharmacogenetics research clinic, is just one effort by researchers to make prescribing less random. Right now it's a guessing game that involves trying different antidepressants without a way to predict what will work. This study is relatively modest; so far the DNA test has been performed on about 80 people, and analyzes two liver enzymes. But another study, which began in January this year, will involve thousands of people and will look at brain genes as well, says Dr. James Kennedy, director of the neuroscience research clinic at CAMH.

Though many people do benefit from antidepressants, "there's not one single, reliable and specific variable that a prescriber can depend on to know the appropriate treatment," says Dr. Roger S. McIntyre, head of the mood disorders psychopharmacology unit at the University Health Network in Toronto. There's really no way of knowing how an

individual will react to a given medication unless they've tried it before. In other words, it's often a long and difficult process of trial and error.

About 16 percent of women and 11 percent of men will experience clinical or major depression at some point in their lives. Many will take antidepressants: Some will take one or two types over a lifetime; others six, seven or eight in an effort to find relief. There are 24 antidepressants on the market in Canada—common ones like Cipralex (escitalopram), Zoloft (sertraline), Paxil (paroxetine), Prozac (fluoxetine) and Effexor (venlafaxine) are just a few examples. Some people will have no side effects to whichever one is prescribed; others will have many side effects from that same drug. Moreover, what works for one person might not work for another. So finding a way to personalize drug prescribing would be somewhat of a revolution.

How you metabolize is key

Genetic testing is a first step in personalized medicine, the idea being that treatment can be tailored to the individual, rather than relying on a one-size-fits-all treatment. (Of course, mood is affected by non-genetic factors as well, such as stressful life events. But genes do play a role.) The DNA test I'm taking will look at two liver enzymes, CYP2D6 and CYP2C19, to analyze how quickly, or how slowly, I metabolize antidepressants. If it finds I metabolize them slowly, it means I would suffer more side effects than if I metabolized them quickly. That's because the drug would stay in my system longer.

Therefore, I wouldn't need as high a dose, or I might need a different medication. If the test shows I am a fast metabolizer, that would mean my liver would process a particular drug too quickly—so while I'd be unlikely to have side effects, I'd also be unlikely to benefit because the drug wouldn't stay in my system long enough. Or, of course, I could be a normal metabolizer, meaning what I've been taking is fine.

For anyone who is severely depressed, not having the right medication or dosage means they end up suffering longer; if they are suicidal, the repercussions could be fatal. The wrong medication or dosage could also result in needless side effects, which could include insomnia, weight gain, low libido and dizziness. Knowing what kind of metabolizer you are can be particularly important for certain groups. For example, up to 30 percent of those of African descent are fast metabolizers, and up to 50 percent of Japanese people are intermediate metabolizers, so their processing is impaired but closer to normal than the slow and fast metabolizers, according to Mueller. (Up to 10 percent of Caucasians are slow or intermediate metabolizers.)

The new standard?

Mayo Medical Laboratories in Rochester, Minn., has been doing DNA testing since 2003 to determine how people will tolerate certain antidepressants. As they develop their testing strategy, they have been gradually introducing additional genes so the lab now looks at a panel of both liver and brain genes. (CAMH's study is unique in that it is the first for a mental health facility versus a general

hospital.) There are also about a dozen U.S. companies from which consumers can buy genetic test kits, but experts say the manufacturers often overestimate the benefits to consumers. Also, since the results go to the individual and not a doctor, the results can be misinterpreted and the individual won't necessarily know how to decide next steps.

Dr. David Mrazek is a child and adolescent psychiatrist and a professor at the Mayo Clinic School of Medicine. He thinks the kind of testing CAMH and Mayo are doing will become the standard of practice, in large part because the price will be a non-issue. "About 10 years from now, we'll be able to do complete genomic testing of all of a patient's gene structure for under \$1,000." Mrazek anticipates that, one day, everyone's genome will be known at birth, maybe even before. The work, he says, will be to make sense of this information.

For now, the people who want DNA testing tend to be the ones who have had bad reactions to antidepressants. They would feel better if they knew before starting a medication that they would be able to tolerate it. But more and more people will likely be interested in having this kind of information.

According to IMS (a privately held company that provides pharmaceutical information and consulting services for the healthcare industry globally), Canadian pharmacists filled some 40.2 million prescriptions for antidepressants in 2011.

"As the public becomes more educated, there will be higher demand for the doctor to have this information, and patients will demand to have this test done because it protects them," Kennedy says.

And the effects of this kind of testing for people with depression? "I call it a small revolution in how drugs are prescribed," Kennedy says. He can only speak for Ontario, but estimates that making these tests available would save that province's healthcare system about \$11 million a year—with fewer doctor's visits, side effects, unnecessary visits to intensive care and infections developed from stays in hospital.

Several weeks after my DNA test, I get the results. In some ways, it's anticlimactic: I'm a normal metabolizer, which isn't so surprising, since I haven't had significant side effects from Cipralex, nor from the Celexa I have also taken. I've been fortunate.

I don't like to have to rely on an antidepressant, and I worry about still-unknown long-term effects, but I'm indebted to these medications: I have gotten better. While one of my biggest life struggles is knowing that, at least for now, I need an antidepressant to keep me from sliding into serious depression, I'm grateful a drug exists, and that it works. □



Learn about the pros and cons of some common antidepressants at besthealthmag.ca/sept2012.

The CAMH DNA study is free, and participants receive \$90. Anyone in Canada can take the test if their doctor recommends to CAMH that they can. Be aware that it requires three visits to CAMH in Toronto.