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Genetic Tests May Prevent Drug Reactions

By GENE JOHNSON, Associated Press Writer

SEATTLE — Medical experts say genetic tests offer hope for people whose bodies have trouble processing certain drugs. In theory, such tests might help prevent some of the 100,000 deaths and the more than 2 million serious drug reactions in the United States every year.

The Mayo Clinic's psychiatry and psychology department has used genetic tests for two years to predict bad drug reactions, and other departments are beginning to use them as well, said Dr. David Mrazek, the department's chairman. He called it a giant step forward from the "dinosaur position" of prescribing drugs by trial-and-error.

For most of her life, Eileen Marshall's trips to the dentist offered the prospect of sweating, itching and a racing heart.

Her affliction wasn't a case of nerves before the drill. It was a genetic inability to process Novocain, something she learned last summer when she took a DNA test offered by Seattle-based Genelex Corp.

"I've never really taken medications, but when I've had to take little amounts, like at the dentist, I've always had adverse reactions," the 54-year-old Olympia resident said. "I just figured that this is what people feel when they get Novocain."

DNA analysis can identify any number of potential health problems. More than half the population is believed to have detectable genetic variations that affect the eight to 10 enzymes in the liver responsible for breaking down most drugs.

Varying levels of the enzymes affect how long a drug stays in the system. A buildup in the body can lead to a bad reaction; if it passes through too quickly, it may be

ineffective. If someone has a genetic variation of the enzyme known as CYP2D6, for example, that person may have trouble with antidepressants, antipsychotics and certain heart drugs.

Though some research institutions and clinics may test their patients, Genelex is among the few companies that market such tests to the public. For \$600, it will provide a genetic profile for drug processing and, if the patient is on medication, recommend dosages and alternatives. Someone taking the antidepressant Paxil who metabolizes CYP2D6 poorly might be told to take about two-thirds of the standard dose.

Besides antidepressants and antipsychotics, Genelex tests for enzymes needed to process many painkillers and anti-inflammatories, such as Celebrex and Aleve, as well as some heart, seizure and diabetes drugs. It takes about two weeks to get the results after patients ship in a blood sample. Some insurance companies are starting to cover the test, said Genelex founder Howard Coleman.

"The patients we get are ones that have had a long history of problems," Coleman said. "One of the reasons they come to us is mainstream medicine has been unresponsive. The doctors have been looking at them like they're hypochondriacs. This explains why they have a problem."

One such patient was Margery Dussing, a 67-year-old grandmother of 16 from Syracuse, N.Y. Though she had been taking Verapamil to control her blood pressure, her doctor told her it was still too high, and in the fall of 2003 he upped her dosage.

The result, she said, "was nine months of hell." Her blood pressure and diabetes spiraled out of control, and with doctors giving her more medicine, things only got worse. At one point she was hospitalized. At another, she was told to go home and stay in bed for three days.

"The doctors yelled at me. They thought I was neurotic," Dussing said. "And I was very angry, because I wasn't neurotic. I went from doctor to doctor to doctor. I was freaking out. When I picked up a pill, I'd think, what's it going to do?"

Finally, she saw an article mentioning Genelex. She took the test last June.

"All these drugs I had been on, it said I was a poor metabolizer for these and I shouldn't be taking them," she said. With the results in mind, her doctors prescribed a very low dose of the antidepressant Celexa, which calmed her and lowered her blood pressure.

"It's been such a load off my mind," she said. "I feel like a new person."

Shirley Roberts, 45, of Orange Park, Fla., said that if she had taken such a test sooner, she would have known she couldn't properly process Prozac and Paxil. Instead, she endured more than a year of fatigue, rashes, irregular heartbeats and other side effects -- including, most seriously, liver damage.

"I don't want anyone to have to go through what I've gone through," said Roberts, who took Genelex's test last summer.

The field, called pharmacogenetics, remains in its infancy. In fact, it's so little known that the Pharmacogenetics Diagnostic Laboratory at the University of Louisville's School of Medicine has posted an introductory fact sheet on its Web site, urging patients to show the information to their doctors.

The National Institutes of Health launched its Pharmacogenetics Research Network in 2000. Dr. Rochelle Long, the network's director, said that while the tests can help predict many adverse reactions, it may be several more years before they can predict more subtle, complex reactions -- such as those involving multiple enzymes.

"Doing a test isn't hard; it's interpreting the results that's hard," she said. "You have to figure out what a variant means in terms of other drugs the person may be taking, age, nutrition, other variants they may have. People have to weigh and assemble all these factors. It's not as simple as a pregnancy test."

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