Personalized Medicine

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Study targets possible genetic risk for fibromyalgia

Fibromyalgia is a chronic pain syndrome that is difficult to diagnose and treat. The fibromyalgia syndrome (FMS) affects millions of people in the United States. Fibromyalgia is among the most common conditions treated by rheumatologists and physical medicine specialists.

FMS is characterized by widespread muscle pain, sleep disturbance, fatigue, and morning stiffness. The pain is often described as "migratory", in that it tends to move around the body. This makes FMS especially difficult to diagnose. The fact that there are no diagnostic tests that physicians can rely on to confirm the diagnosis or follow the course of the condition simply adds to the challenge of diagnosing and treating FMS. In fact, for many years there was considerable disagreement among clinicians over the issue of whether fibromyalgia was even "real."

Jonathan Reeser, M.D., Ph.D.

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Research Foundation

From the Director

Cathy McCarty, Ph.D.

Welcome to the third Personalized Medicine Research Project (PMRP) newsletter. Please note on the back page that we have two new additions to the PMRP Community Advisory Group. I am delighted to welcome Rev. Mark Krueger and Nancy Kaster.

And "thank you" to Sally Lang who served with excellence and commitment for five years as Administrative Secretary for the Center for Human Genetics and the PMRP until accepting a promotion in the Central Division of Marshfield Clinic.

We welcome Marion Naugle into the position of Administrative Secretary. She joins us from the Pittsville School District.

PMRP continues to receive national attention. Michael Caldwell, M.D., Ph.D., Russell A. Wilke, M.D., Ph.D., and I were invited to participate in a workshop held in Bethesda, Maryland, in December 2006 to discuss "Understanding the Genetic Basis of Medication Safety." This workshop was jointly sponsored by the Food and Drug Administration and the National Institutes of Health. Dr. Caldwell talked about the research being done at Marshfield Clinic to improve dosing for the drug warfarin, a blood thinner, through the use of genetic testing. Dr. Caldwell and colleagues recently received a large grant from the Agency for Healthcare Research and Quality to test their new dosing algorithm for warfarin in the Clinic.

The PMRP was asked to join the Pharmacogenetics Research Network (PGRN) as an Affiliate Member (http://www.pharmgkb.org/views/project.jsp?pId=49). The mission of the PGRN is to advance knowledge of the genetic basis for variable drug responses. As described in a previous newsletter, Dr. Wilke is the Principal Investigator in Marshfield on a multi-center PGRN study to assess the role of genetics in LDL (bad cholesterol) response to lipid-lowering medications. A number of PGRN members, as well as the Project Officer from the National Institute of General Medical Sciences, visited Marshfield in July 2006. We look forward to more collaborations with the PGRN.

At-home genetic tests can have unintended consequences

At-home genetic testing is easy to administer, relatively inexpensive – and potentially harmful to your health.

An increasing number of entrepreneurs are marketing tests that can show susceptibility to numerous diseases. They are riding a wave of genetic discoveries that have been reported since scientists published the complete map of all human genes four years ago.

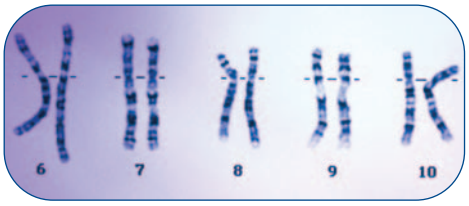
But even assuming the tests are valid, skeptics in the health care profession are concerned that online companies don't have the expertise to properly explain the often-complicated results.

"Results are given to the patient and can be interpreted out of context in the absence of genetic counseling," said Philip F. Giampietro, M.D., Ph.D., director, Marshfield Clinic Medical Genetics Services.

The American College of Medical Genetics (ACMG) is concerned that science is running ahead of public policy. The ACMG states that genetic testing should be provided only through a qualified health care professional, and that, "the use of genetic 'home testing' kits is potentially harmful. Potential harms include inappropriate test utilization, misinterpretation of test results, lack of necessary follow-up and other adverse consequences."

Christina Zaleski, M.S., is a certified genetic counselor at Marshfield Clinic, one of only about 2,500 genetic counselors in the United States. Zaleski offers this hypothetical scenario to illustrate potential problems with home testing:

A woman has a family history of multiple people with blood clots and strokes. She is in her mid-20s and wants to take oral contraceptives, but knows that if she has Factor V Leiden, she shouldn't because of the increased risk of clotting problems. (Factor V Leiden is the most common hereditary blood coagulation disorder in the United States.) She pursued at-home testing and received normal results. She now assumes that she is at low risk for clots and proceeds with using oral contraceptives.



HOWEVER, the patient was tested for only one of about a dozen inherited clotting factors. She merely assumed Factor V Leiden caused the clots in her family. She may have tested herself for the wrong condition. It could still be very dangerous for her to take oral contraceptives if she carries other clotting susceptibility genes.

"If the woman in this scenario had genetic counseling first, we would gather medical records on her affected family members and discover what condition the family has," Zaleski said. "Many genetic and environmental factors contribute to clots. In this case she misinterpreted the results and her own follow-up could be quite dangerous to her health."

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Genetic counseling is available at Marshfield Clinic. Outreach services are available in Wausau, Lakeland and Eau Claire. Telehealth is also available for many situations. For information, please contact Marshfield Clinic Medical Genetic Services, 1-877-216-8535.

ONLINE: A family history is the simplest, most cost-effective way to begin to understand your family's health risk. A Family Health History Worksheet is available at: http://www2.marshfieldclinic.org/family_history/MCFamHealthHistory.pdf.

Diet survey shows area residents light on dairy products

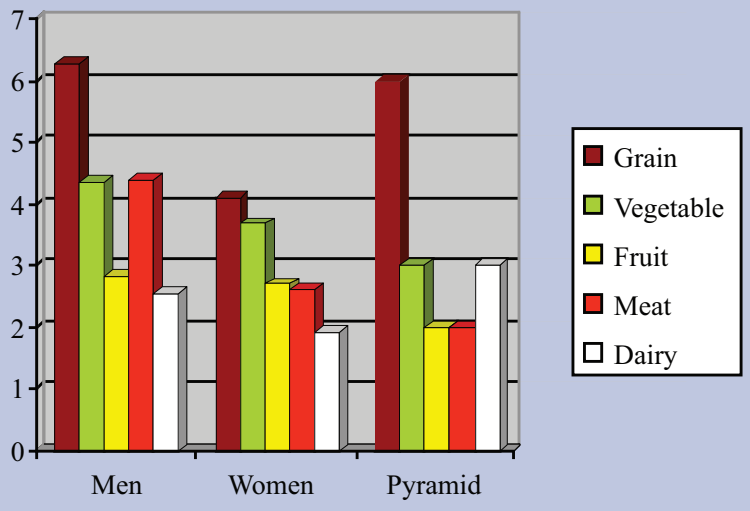
Residents in the heart of America's Dairyland report that they consume less than they should from an important segment of the food pyramid – dairy products.

This is but one bit of information gleaned from a survey of approximately 1,800 Personalized Medicine Research Project participants, who filled out questionnaires on diet and physical activity.

The long-term objective of the project is to study the interaction of environment (diet and exercise) and genes, and their impact on body weight.

Completed questionnaires returned so far indicate that both men and women with a desirable body weight fall short of the 3 daily servings of dairy products recommended as a minimum. Women also fall short in the grain consumption category. Both men and women exceed the minimum in meat, fruit and vegetables. On average, most people in the U.S. don't consume the recommended amounts of fruits and vegetables, so PMRP participants are doing better than the general population, which is good news, said co-investigator Laura Coleman, Ph.D., R.D.

To learn more about the food pyramid, go to http://www.mypyramid.gov/.



- Comparison of average daily servings for men and women in PMRP (based on Diet History Questionnaire) with Food Guide Pyramid recommendations.
- Pyramid servings are minimum recommended number of servings per day. Actual individual recommendations are based on caloric intake.
- Mean servings shown are for individuals with a desirable body weight.

Are men really listening?

Do men listen as well as women? "No," according to results of a study of PMRP participants. The study focused on participants' understanding of the PMRP concept — information that is explained to participants by research coordinators at the time of enrollment. The objective was to identify factors that predict understanding of study elements.

Bottom line? Men didn't score as well on the study questionnaire, which means that research coordinators will need to take more time informing males and older individuals about project details so that they are making truly informed decisions about study participation.

A manuscript detailing the results, "Informed consent and subject motivation to participate in a large, population-based genomics study: the Marshfield Clinic Personalized Medicine Research Project," was published in the journal Community Genetics. Lead author was PMRP Director Cathy McCarty, Ph.D. Co-authors with Marshfield connections included Philip F. Giampietro, M.D., Ph.D., and Diane Austin.

We keep growing

The PMRP had enrolled 19,350 subjects as of Jan. 7, 2007. Enrollment is open to anyone age 18 and older living in Abbotsford, Arpin, Auburndale, Blenker, Chili, Colby, Dorchester, Granton, Greenwood, Hewitt, Loyal, Marshfield, Milladore, Pittsville, Spencer, Stratford, Thorp, Unity or Vesper. Contact the PMRP at 1-888-334-2232 or 715-389-7733.

Did you know?

In 1991, Wisconsin passed the first law to prevent genetic discrimination in health care and employment.

Humans are 99.9% alike genetically.

DNA is present in every cell in our bodies except red blood cells.

All of the 10 leading causes of death, except injury, are thought to have some genetic component to them.

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Study targets possible genetic risk for fibromyalgia

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Principal Investigator Jonathan Reeser, M.D., Ph.D., has begun a research project designed to evaluate a possible genetic risk factor for fibromyalgia. Using data from the Personalized Medicine Research Project, the study will explore whether the prevalence of a gene called apolipoprotein E4 (APOE4) is higher in people with fibromyalgia than in people with no history of the disease. The APOE4 gene also is a marker for Alzheimer's disease and cardiovascular disease.

Dr. Reeser decided to investigate the APOE4 gene because the gene has also been found to be associated with poor outcomes from head trauma. Although no specific genotype has thus far been definitely associated with fibromyalgia, previous epidemiologic studies have suggested that there is a distinct genetic component to the syndrome. Furthermore, there is increasing evidence to suggest that fibromyalgia results from a defect in the processing of pain signals by the central nervous system, and APOE4 is thought to play an important role in central nervous system function.

The study is just getting underway. "The long-term goal of this research team is to identify clinically useful genetic and biochemical markers for the fibromyalgia syndrome," Dr. Reeser said.

Presently, FMS is a diagnosis of exclusion – meaning that other conditions that could result in similar symptoms must be ruled out before the diagnosis of fibromyalgia can be made with confidence. Consequently, patients often experience frustrating delays in arriving at an understanding of the cause of their perplexing list of symptoms. Based upon prior studies, we know that women tend to be diagnosed with the syndrome more often than men (by a 9:1 ratio), but the reasons for this disparity are not entirely clear.

Dr. Reeser hopes that by "gaining a foothold" in our understanding of the genetics of FMS, we may be able to pave the way for further research that will yield additional information that in turn may enhance our ability to care for people who suffer from fibromyalgia.

Presently, the treatment of fibromyalgia focuses on symptom management, and typically includes a combination of patient education and counseling, regular exercise, and medication.

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