PEaRL

The Pancreas Education and Research Letter

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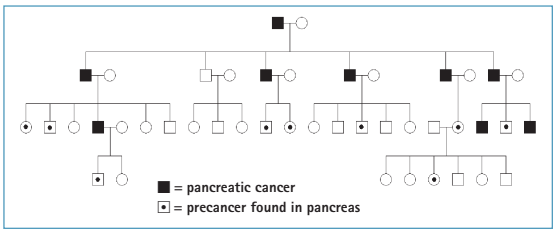
Major Breakthrough in Pancreatic Cancer Research

A major research breakthrough in the genetics of pancreatic cancer was just announced. The research is a joint effort between researchers in the laboratories of Teresa Brentnall, MD, of the University of Washington, Seattle, Washington and David Whitcomb, MD, PhD of the University of Pittsburgh, Pittsburgh, Pennsylvania as well as several other contributing institutions. The discovery, which is reported in December 12, 2006 issue of *PLoS Medicine* (www.plosmedicine.org), reported that harmful changes called mutations in the **palladin** gene can cause familial pancreatic cancer.

Palladin is a gene that instructs proteins to make the skeleton of a cell, holding the cell in the shape of a cylinder or a block. Normally, cells are organized in sheets or other types of orderly groups that give structure to organs. When Palladin is mutated, the pancreatic cells become cancerous more quickly than normal. They take on new forms and begin moving out of the pancreas. This may be one reason why pancreatic cancer metastasizes or spreads so quickly. In additional experiments, researchers discovered that the Palladin gene is also abnormal in randomly occurring pancreatic tumors that we term "sporadic." This discovery could also prove to be valuable in other types of cancer research.



The discovery of the palladin gene would not have been possible without the participation of this large family.

It is well known that pancreatic cancer is a leading cause of cancer-related death in the United States. Less clear is why some people get pancreatic cancer while others do not. Perhaps this new discovery will be important in learning how to prevent pancreatic cancer or to treat early cancers so that they do not spread.

An equally important part of this major discovery was that the research was largely funded by the donations of individuals to the investigators' laboratories or through pancreas research foundations.* Clearly, the contributions of individuals with a concern for this disease are making a significant difference. ❍

**Lustgarten Foundation, The National Pancreas Foundation, the Wayne Fusaro Pancreatic Cancer Research Fund, the Gene and Mary Ann Walters Fund for Pancreatic Cancer Research, and the Canary Foundation.*

Genetic Studies on Pancreatic Cancer

Major breakthroughs, like the one described for palladin, require the strong support of individuals and families. We are continuing to enroll individuals in our Pancreatic Adenocarcinoma Gene-Environment Risk (PAGER) registry and study. We are currently seeking individuals to participate in a study of familial pancreatic cancer who either:

- Have had at least two relatives diagnosed with pancreatic cancer or
- Have themselves been diagnosed with pancreatic cancer and have had at least one relative who has been diagnosed with pancreatic cancer

Participation includes completing a questionnaire and providing a blood sample. If you are interested in participating, please call our toll-free phone number **1-888-PITT-DNA**. Additionally, we are now collecting blood samples from individuals who previously participated in our familial pancreatic cancer registry. If you previously participated but did not provide a blood sample and are willing to provide one now, please call our toll-free phone number **1-888-PITT-DNA** for additional information.

If you wish to be a partner of the PAGER studies through financial gifts of any amount, checks may be made payable to **UPCI/Pancreatic Cancer Center** and sent to: Development Department, UPMC Cancer Pavilion, Suite 1B, 5150 Centre Avenue, Pittsburgh, PA 15232.

Gifts may also be made by credit card by calling 412-623-4700. Please mention that you would like your gift to support the UPCI/ Pancreatic Cancer Center. 100% of your donation will go directly to pancreatic cancer research. Your support will be greatly appreciated by everyone who is dedicated to the prevention and cure of pancreatic cancer. ❍

On the Internet:
www.pancreas.org

Toll-Free Phone:
1-888-PITT-DNA
(1-888-748-8362)

Kids' Corner

Can You Live Without a Pancreas?

Think about what you do when you do not have a fork and you are eating. You find another way to eat your food without a fork, right? If you do not have a pancreas, you have to do the same thing – find another way to replace the pancreas's jobs. The pancreas has three main jobs that need to be replaced if the pancreas is removed.

First, the pancreas has special cells called islet cells that make insulin and other special proteins that help control blood sugar. This is called the "endocrine function" of the pancreas. When the endocrine function of the pancreas does not work, a person is said to have diabetes and has trouble controlling his or her blood sugar. Some of the endocrine function of the pancreas can be replaced by taking shots of insulin. Diabetes caused by removing the pancreas is more difficult to control than most other causes of diabetes because shots of insulin do not replace the other special proteins that help insulin control blood sugar levels.

Second, the pancreas has areas called "acini" that make special proteins called enzymes *(see the last Kids' Corner, volume 2 number 2)* which are needed to break down food so the body can use the nutrients found in the food. This is called the "exocrine function" of the pancreas. If the exocrine function of a person's pancreas does not work (exocrine insufficiency), the person will not be able to digest and use his or her food for energy or to grow. The unused food is lost in his or her stool (poop), which may look greasy, be very large, and hard to flush down the toilet. The exocrine function of the pancreas can be replaced by taking pancreatic enzyme pills with every meal or snack.

Third, duct cells in the pancreas create a liquid that is made of water and "sodium bicarbonate," a unique type of salt which is also called baking soda. The fluid helps flush the digestive enzymes out of the pancreas. Sodium bicarbonate mixes with acid from the stomach and changes it into table salt and water. Changing stomach acid into table salt and water helps in two ways. First, most digestive enzymes do not work well when there is a lot of stomach acid in the intestines, so bicarbonate helps digestive enzymes do their job by changing stomach acid into salt and water. Second, it is safer to have table salt and water passing through the intestines than having the strong stomach acid. If the pancreas does not make sodium bicarbonate, digestive enzymes will not break down food very well and the stomach acid can damage the lining of the small intestine, causing an ulcer (a sore). Pills called acid blockers are needed to stop the stomach from making a lot of acid if the pancreas is not making enough sodium bicarbonate.

As long as a person takes pancreatic enzyme pills with each meal, insulin shots to control his or her blood sugar, and acid blockers to control his or her stomach acid, it is possible to live a long time without a pancreas. ❍

New Studies Show That Vitamin D Reduces Pancreatic Cancer Risk

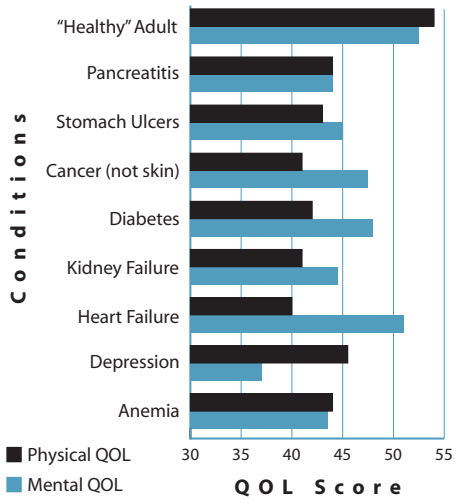
Two large, new studies looked at both men and women and how their intake of vitamin D might affect the possibility of their developing this highly fatal cancer. Over 45,000 men ages 40 to 75 years and over 75,000 women ages 38 to 65 years were followed for approximately 15 years and a total of 365 pancreatic cancer cases occurred. The men and women were surveyed on their intake of a large number of foods and nutritional supplements. The studies demonstrated that people who had the highest vitamin D intake (from both food and vitamin pills) of greater than or equal to 600 IUs (international units) cut their risk of developing pancreatic cancer by a little bit more than 40%. When the researchers looked only at food intake and omitted vitamin pills from their data, the trend towards decreased risk was still evident but not as strong. These findings were also more evident in men than in women. You can get vitamin D from sunlight exposure as well as from vitamins, eggs, fatty fish like salmon, and, most easily, from fortified cereals. ❍

Skinner, HG, Michaud DS, Giovannucci E, et al. Vitamin D intake and the risk for pancreatic cancer in two cohort studies. Cancer Epidemiol Biomarkers Prev 2006; 15(9)

A Study of Chronic Pain and Quality of Life in Individuals With Pancreatitis

This past year, data was collected from the Hereditary Pancreatitis (HP) study and the North American Pancreatitis Study 2 (NAPS2) in order to study the relationship between chronic pain and quality of life (physical and mental well-being) in individuals with pancreatitis. Data from a total of 344 individuals who had filled out new versions of the questionnaires were used for this study.

Comparing Physical and Mental Quality of Life (QOL)



One of the most important findings of the research was that the majority of individuals with both sporadic and familial pancreatitis reported severe and constant pain levels and a resulting low quality of life. Individuals with familial pancreatitis reported lower physical and mental quality of life than individuals with sporadic pancreatitis. Individuals with pancreatitis had a lower mental and physical quality of life when compared to individuals from the general population. The physical and mental quality of life of individuals with pancreatitis was also compared to the quality of life of individuals with other health conditions. Individuals with depression have the only published mental health score that is lower than individuals with pancreatitis.

Individuals who reported experiencing severe and constant pain have lower quality of life than those who had mild or moderate pancreatitis-associated pain. These results show that quality of life is a useful tool for identifying patients with pancreatitis who are in need of support services because this population experiences a considerable decline in quality of life compared with the general population. By identifying individuals with significant pain, medical professionals treating pancreatitis can identify patients that need additional assistance in coping with the psychological factors that are likely linked to quality of life in terms of mental health.

The results of this study became my thesis, which I have successfully defended. I have since graduated with my masters in genetic counseling. Thank you to all of the participants of the HP and NAPS2 studies for your time and participation in research on pancreatitis. I would also like to take this opportunity to thank the members of the HP and NAPS2 research teams at the University of Pittsburgh, including David C. Whitcomb, MD, PhD, M. Michael Barmada, PhD, Erin Fink, MS, Beth Elinoff, RN, MPH, CCRC and Janette Lamb, PhD. This research project would not have been possible without their time and hard work.

For additional questions or comments please feel free to contact me: Megan Marshall, MS, at mmarsha2@wpahs.org ❍

Welcome

In July, the Pancreatic Studies Office welcomed the arrival of **Dr. Dhiraj Yadav, MD, MPH.** Dr. Yadav is originally from India, where he attended medical school. He completed a residency in Internal Medicine and a fellowship in Gastroenterology at New York Medical College. He then went to the Mayo Clinic in Minnesota for a year of advanced training in Clinical Pancreatology. In addition, Dr. Yadav has completed a Masters in Public Health (Epidemiology) from the University of Arkansas. Prior to joining the University of Pittsburgh, Dr Yadav was on faculty at the University of Arkansas for Medical Sciences and Central Arkansas Veterans Healthcare System in Little Rock, AR. We are very excited to add Dr. Yadav to our pancreatic studies research team where he will help us in evaluating the causes of pancreatitis. ❍

Ask Dr. Whitcomb

I carry the R122H mutation in the hereditary pancreatitis gene (cationic trysinogen, PRSS1), but I have never had symptoms of pancreatitis. Do I still have a 40% chance of developing pancreatic cancer?

Answer: Studies have shown that anyone who has chronic pancreatitis has an increased risk of developing pancreatic cancer regardless of the reason they developed chronic pancreatitis. Thus, the high risk of pancreatic cancer in individuals with hereditary pancreatitis is due to having chronic pancreatitis, not from carrying the mutation in the hereditary pancreatitis gene. It is thought that the risk of pancreatic cancer is actually due to the environment that pancreatitis creates in the pancreas. Individuals who begin to have attacks of pancreatitis later in life have a lower lifetime risk of developing pancreatic cancer. It has been found that individuals with hereditary pancreatitis have about a 2.5% chance of developing pancreatic cancer 30 years after they first develop symptoms, about a 15% chance of developing pancreatic cancer 50 years after their first symptoms, and about a 40% chance of developing pancreatic cancer 70 years after their first symptoms of pancreatitis. Thus, a person who developed their first symptoms of pancreatitis when they were 20 years old will have a lower risk of pancreatic cancer when they are 50 years old than a person who developed their first symptoms in early childhood.

Individuals who carry a mutation in the hereditary pancreatitis gene but have never had pancreatitis (called asymptomatic carriers) do not have an increased risk of developing pancreatic cancer. However, care must be taken before an individual assumes that they have never had pancreatitis. Some individuals experience less painful and less frequent pancreatic attacks that may be attributed to food poisoning or the flu.

If you have any questions for Dr. Whitcomb about the pancreas or management of pancreatic diseases, please e-mail the newsletter at **askpearl@pitt.edu**. We want to share the answers to your questions each PEARL publication in order to help educate everyone about pancreatic disease. ❍

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