



# PEARL



The Pancreas Education and Research Letter

## New Diagnostic Approaches Prove Useful in Pancreatic Cancer Evaluation

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Pancreatic cancer is one of the most concerning cancers because it is hard to detect and difficult to treat unless it is caught very early when it can be treated by surgery. Physicians struggle with making the correct diagnosis in many cases because a "shadow" on a CT scan could be an early cancer or just a small scar.

Physicians and researchers at the University of Pittsburgh have developed a new method to help physicians distinguish between normal cells, pre-cancerous cells, and cancer. The new method uses



endoscopic ultrasound (EUS), which is an ultrasound probe attached to the end of an endoscope (instrument used to visualize the inside of hollow organs). The advantage of EUS is that specially trained and skilled gastroenterologists can position the ultrasound probe within an inch or two of the suspicious shadow.

A special needle can then be placed directly into the suspicious area and a sample of cells or fluid can be withdrawn (this is called a fine needle aspirate or FNA).

The new way to analyze cells was developed by Sydney Finkelstein, MD, a pathologist from the University of Pittsburgh and the founder of Redpath Integrated Pathology. The new method examines tumor suppressor genes which act to limit the growth of cells. When tumor suppressor genes are not working properly, cells can grow uncontrollably, which is a central characteristic of cancer cells. This new method, called "LOH analysis" detects pre-cancerous and cancerous cells based on the loss of one or more tumor suppressor genes. Now, for the first time, physicians can identify both cancerous and pre-cancerous cells in the pancreas and make decisions on how to best prevent the development and spread of cancer.

A team from the Pancreas and Biliary Center of Excellence at the University of Pittsburgh evaluated this new approach in a series of patients who were suspected of

having cancer. The results of combining LOH analysis with ERCP (using tiny brushes to catch cells from possible growths in the pancreatic duct or bile duct) or EUS (using FNA) markedly improved the accuracy of each diagnosis. The results of these studies have been presented to the medical community in the journals listed below. This work represents a major breakthrough in the fight against pancreatic cancer. ○

### References:

- Khalid A, et al. Use of microsatellite marker loss of heterozygosity in accurate diagnosis of pancreaticobiliary malignancy from brush cytology samples. *Gut* 2004;53(12):1860-5.
- Khalid A, et al. The role of pancreatic cyst fluid molecular analysis in predicting cyst pathology. *Clin Gastroenterol Hepatol* 2005;3(10):967-73.

## Hereditary Pancreatitis Study: Moving Forward

As research on Hereditary Pancreatitis has advanced, we have improved the questionnaire for the Hereditary Pancreatitis Study. We would like to have as many individuals as possible fill out the new questionnaire. Doing so will ensure that the research team has the best information possible in order to search for a treatment or cure for this disease. If you and/or family members have already enrolled in our study (or want to participate) and would be willing to complete our new, updated questionnaire, please call our toll free number at **1-888-PITT-DNA** and speak with one of our coordinators. We would also like to thank everyone who has already returned our new questionnaire. ○

On the Internet:  
[www.pancreas.org](http://www.pancreas.org)

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

## What is Chronic Pancreatitis?

When we hurt ourselves – for example, scrape or cut our hand, we have an *injury* – and our body has to heal itself. If we bleed, our body makes a scab over the cut area on the hand. After a few weeks, the hand may look perfectly normal, as if it had never been hurt or injured, or a *scar* may have formed over the area where there was an injury. Bigger cuts and more serious injuries tend to make scars that can be there for a lifetime. Sometimes, it is difficult to know if an injury will leave a scar or if a person will heal back to normal.

In a similar manner, if the pancreas gets injured or *inflamed* (as happens when one has "*acute pancreatitis*" – please see the last *Kids' Corner* in **PEARL** volume 1 number 3), the body has to work to heal the pancreas. Often, the healing process leaves a perfectly normal pancreas. However, at other times, the pancreas is left with scars.

As with scars on the skin, scars within the pancreas tend to stay for a person's entire life. This *long-term* scarring within the pancreas is known as *chronic pancreatitis*.

Many people have scarring in their pancreas and do not know it. Often, a person feels perfectly well. The scarring may be seen if the person has x-rays such as a CT scan (computer tomography). X-rays and other specialized tests are also used to make the diagnosis of chronic pancreatitis.

Other people **do** have problems and symptoms when they have chronic pancreatitis. Some people have pain.

This pain can be a little or a lot, only at certain times (such as after eating) or all the time. People with very bad pancreas pain often need the help of a special team of doctors and nurses that are specialists in dealing with pain (a "pain clinic") to help with the pain. A person may take pain medications or pancreatic enzymes (special digestive proteins the pancreas makes) to try to make the pain better.

For some people, the pancreas can have so much scarring that it cannot make the proteins that it is supposed to, and these people may develop the two major problems of chronic pancreatitis:

- They are unable to digest food properly. (The pancreas makes the digestive proteins needed to obtain the calories that are in food – and calories are the fuel for the body). They lose the undigested food in the stool (their poop), especially fatty food. The stool may be very large, look oily or greasy and be hard to wipe off or hard to flush down the toilet. The person may be very hungry and eat more than before but still lose weight. When this happens, a person is said to have "*exocrine insufficiency*" and must be given pancreatic enzymes (special pills) to help digest food properly.
- They start to have trouble controlling their blood sugar. This is called *diabetes mellitus*. A person may lose weight, feel thirsty, and drink a lot. This can cause the person to urinate (pee) a large amount. If a person develops diabetes, he or she must start to take special injections (shots) of "insulin," which is a special protein that the pancreas normally makes when it is healthy. Sometimes, if their pancreas is still making some insulin, a person can take a pill to lower their blood sugar instead of taking shots of insulin.

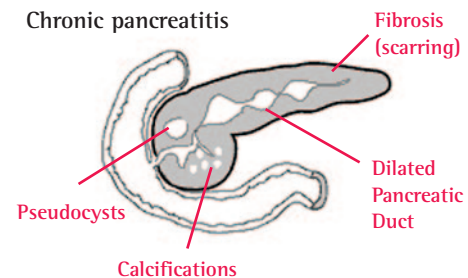
A person can live many, many years with chronic pancreatitis – but taking care of any pain, digestion problems, and diabetes becomes very important. ○



Normal pancreas



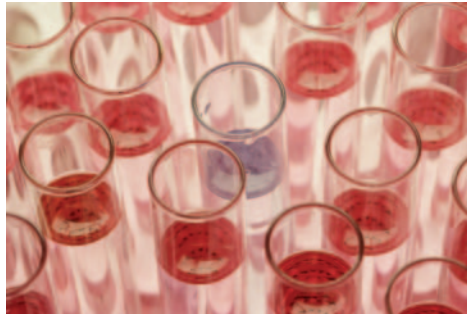
Chronic pancreatitis



This diagram shows some of the differences between a normal pancreas and a pancreas with chronic pancreatitis. A pseudocyst is a collection of liquids that can not drain from the pancreas. Pseudocysts can be seen with either acute or chronic pancreatitis. A calcification is a scar that can form after the pancreas is injured. It is a sign of chronic pancreatitis. A dilated pancreatic duct is another sign of chronic pancreatitis. As chronic pancreatitis progresses, the pancreas often begins to look smaller as scar tissue (or fibrosis) replaces the working pancreatic tissue.

## Blood and Tissue Studies of Patients Lead to Important Discoveries

The most important advances in understanding human pancreatitis over the past half century have come from studies on the blood and tissue of patients who have volunteered to join research studies. Many hundreds of people with pancreatic disorders and their friends and relatives have donated blood samples and supplied information on their health. Some of these individuals who were having surgery on their pancreas donated a piece of it for further studies. The results from these studies are being published in *Gut*.



One study focused on a 93-year-old man from a family with hereditary pancreatitis who had the hereditary pancreatitis gene (i.e. a cationic trypsinogen gene mutation), but had never experienced any symptoms of acute or chronic pancreatitis in his entire life. Upon his death from unrelated causes, his family donated his pancreas to research. This pancreas was compared with other pancreas samples with known chronic

hereditary pancreatitis, alcoholic chronic pancreatitis, and those without pancreatitis.

The results of this and other studies show that environmental factors, rather than genetic factors alone, determine when each attack of acute pancreatitis occurs. Furthermore, it raises hope that medications or other strategies may one day be able to limit or eliminate attacks of pancreatitis.

Studies in people who have developed chronic pancreatitis are especially important because laboratory animal studies could not have led to the same breakthroughs. Indeed, a big thank you must go out to each patient who has gone the extra mile to advance our knowledge of these pancreatic diseases either by accurately completing a questionnaire, giving a blood sample, or even donating a piece of their pancreas. ○

## Hereditary Pancreatitis Clinic at the University of Pittsburgh

We are happy to announce that David Whitcomb, MD, PhD will be taking over the Hereditary Pancreatitis (HP) clinic from Veronique Morinville, MD following her departure from the University of Pittsburgh to return to her home in Canada. The purpose of the clinic is to offer a detailed, one-time assessment of entire families who have known or suspected HP. The clinic will include a thorough medical history and physical examination of all family members who wish to be assessed, a discussion of management issues, recommendations for further treatment, and a session answering the family's questions. A genetic counselor, Erin Fink, MS, will collect a family history and discuss how HP runs in families, explain inheritance risks for family members, and talk about available testing options, if appropriate. Since the clinic will only provide a one-time consultation, the family's primary care physician and/or pediatrician will receive a detailed letter summarizing the clinic visit, findings, and any management suggestions. The goal of this clinic is to help families with HP to better understand their condition and medical management options, and to learn about recent

research findings. Family members may also be given the opportunity to participate in ongoing research studies. If you are interested in the Hereditary Pancreatitis Clinic, you may contact our Pancreatic Studies Office for more details: 1-888-PITT-DNA. ○

### *Au Revoir...*

Veronique Morinville, MD completed her one-year advanced fellowship in the Pancreatic Studies Office in December and returned to McGill University in Montreal, Quebec, Canada where she will be finishing her fellowship in Gastroenterology. During her time here, she conducted a clinical trial evaluating the safety of a medication that may stop or decrease the inflammation and pain experienced by people with hereditary pancreatitis (HP). She also saw patients in the hereditary pancreatitis clinic at the University of Pittsburgh Medical Center. We greatly appreciate the hard work that Dr. Morinville has done this past year with us and wish her much success in her future endeavors. ○



## Ask Dr. Whitcomb

### Dear Dr. Whitcomb:

*After battling pancreatitis for nearly seven years with hospital admissions almost monthly, I was sent to see Dr. Adam Slivka at the University of Pittsburgh Medical Center. He noticed that my calcium levels were slightly elevated and found that I had a parathyroid tumor which caused my elevated calcium levels. Surgery was performed to remove my parathyroid and I have not had a pancreatitis attack in over two years! Does calcium cause pancreatitis and do you think that my pancreatitis has been cured?*

**Answer:** Elevated calcium levels are an unusual, but well documented cause of acute pancreatitis. High calcium levels in the blood can increase the amount of calcium found in the cells of the pancreas that make digestive enzymes. Trypsinogen, the master digestive enzyme, is activated by high levels of calcium. Once activated, trypsinogen turns on other digestive enzymes. When the digestive enzymes are active in the pancreas, they can injure it and cause inflammation, which we recognize as pancreatitis. The parathyroid gland controls blood calcium levels. If too much parathyroid hormone is released because of a tumor, the blood calcium levels will be high and could trigger pancreatitis. If the tumor was removed, then you should not have another attack of acute pancreatitis.

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](mailto: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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