



PEARL



The Pancreas Education and Research Letter

International Community Unites To Better Define Chronic Pancreatitis

By David C. Whitcomb

In the past, chronic pancreatitis (CP) has been considered a "process of uncertain pathogenesis, unpredictable clinical course, and unclear treatment."¹ The cause was thought to be alcoholism – but most people who drink heavily do not develop chronic pancreatitis, and most people with CP claim to drink only moderately, or not at all! There was no consensus on the definition of CP or diagnostic criteria, and previous definitions were based on what advanced chronic pancreatitis looked like (e.g. "a continuing inflammatory disease of the pancreas, characterized by irreversible morphological change, and typically causing pain and/or permanent loss of function."²) Twenty years ago (1996), the gene causing hereditary pancreatitis was discovered, proving that genetic factors can cause chronic pancreatitis too. This finding triggered new directions in pancreatitis research, and a new definition was needed incorporate new findings, identify chronic pancreatitis earlier and provide guidance to physicians.

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Prospective Observational Study of TPIAT

Beginning in 2016, eight centers will come together to study the procedure of total pancreatectomy with islet autotransplantation (TPIAT) to treat chronic pancreatitis. The University of Minnesota Medical Center, University of Pittsburgh Medical Center, Medical University South Carolina, Baylor Medical Center, University of Chicago, Cincinnati Children's Hospital, John Hopkins Hospital, and Dartmouth-Hitchcock Medical Center will join forces on the study entitled "Advancing Treatment for Pancreatitis: A Prospective Observational Study of TPIAT" (or POST), funded by the National Institute for Diabetes Digestive and Kidney diseases.

Investigators at the collaborating institutions will enroll patients undergoing TPIAT in this observational study, with the goal of working together in order to

define optimal timing of TPIAT, factors that predict success or failure, and overall cost-effectiveness of the procedure. The study will include at least 450 patients whose doctors have deemed TPIAT an appropriate therapy, with careful assessments from the time of surgery through up to 5 years after surgery. We know that TPIAT is not the right treatment choice for every patient with chronic pancreatitis, but doctors still don't know exactly how to predict which patients will respond the best, or how long to wait before considering TPIAT. By joining the forces of multiple major medical centers, this study will be better powered to answer important questions about how to best offer TPIAT to treat those with chronic pancreatitis. If you are interested in learning more about this study, you can contact Peggy Ptacek at the University of Minnesota at vorwa001@umn.edu. ○

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What Are Digestive Enzymes and What Do They Do?



Digestion is the process of breaking down the food you eat so that it can be used by your body.

Did you know that your body prepares to digest each meal shortly before you take that first bite?

As you smell that tasty pizza or that delicious apple, you begin to produce **saliva**. Saliva is the clear, watery liquid in your mouth. At the same time, the pancreas starts to make pancreatic juice to go into the intestine. The salivary gland and the pancreas work in very similar ways for digestion of sugars.

How does saliva begin breaking down food?

Saliva contains very important proteins called **enzymes**. You have many different kinds of enzymes in your digestive system that cut up other molecules in to smaller pieces. You can think of them as little scissors.



Instructions:

- Take some large bites out of the slice of bread and chew without swallowing.
- Keep chewing as it becomes mushy and don't swallow!
- Take note of how the flavor of the bread changes as you chew.
- Swallow or spit out the bread once you figure out how the taste changed.

What Happened?

A digestive enzyme called **amylase** in your saliva began to digest the large starch molecules in your bread. The bread should have tasted sweeter and sweeter as amylase broke down the starch into smaller sugar molecules.

The pancreas produces enzymes that are important for digestion! The pancreas makes amylase, like the salivary gland, but also makes enzymes that digest meat and other things in the meal. The pancreas also makes a lot more enzymes than the salivary gland to finish changing the meal into a liquid, so that it can go into the blood and to different parts of the body.

Sometimes the protein-digesting enzymes that the pancreas makes, such as trypsin, become active in while they are still inside the pancreas – causing the pancreas to start digesting itself. This causes pancreatitis. In hereditary pancreatitis the body cannot control trypsin, causing many attacks of acute pancreatitis and leading to chronic pancreatitis.

Sometimes, people with pancreatitis are not able to make enough enzymes to properly digest their food. This is because the pancreas is sick or injured. These people need to take **pancreatic enzyme pills** so that they can digest their food and absorb important nutrients. ○

Kid's Experiment:

Taste Your Enzymes in Action!

Be sure to ask an adult for permission before performing this experiment.

Time: 5 minutes

What you will need: A slice of white bread and your mouth

Panzanella Bread Salad

Panzanella is a summery Italian salad made with leftover bread. It can be created with rustic white bread or Italian bread, but whole-wheat provides you with more slowly digested carbohydrates, which won't spike your insulin levels as much as white bread will.



Ingredients:

- 5 ripe tomatoes (any combination of red, orange, and yellow), cut into large chunks
- 4 cups day-old, crusty, whole-wheat French or Italian bread, cut into bite-size chunks
- 1 English cucumber, peeled and seeded, cut into large chunks
- 1/2 cup red onion, very thinly sliced and then cut into 1- to 2-inch pieces
- 1/4 cup fresh basil leaves, torn into small pieces

- 1/4 cup extra-virgin olive oil
- 2 tablespoons fresh lemon juice
- 1/8 teaspoon fine sea salt and pepper to taste

Preparation:

Combine all ingredients in a large ceramic or other nonreactive bowl. Cover and let marinate for 1 hour to overnight (up to 12 hours). Do not refrigerate. Serve at room temperature. Makes 8 servings. ○

International Community Unites

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In 2013 the President of the European Pancreas Club (EPC) and International Association of Pancreatology (IAP) invited Professor David C Whitcomb MD, PhD, of the University of Pittsburgh and UPMC to develop an international consensus on a better definition of chronic pancreatitis. He invited an international team of experts in pancreatic disease to develop a new consensus document, published in Spring 2016 (<http://www.ncbi.nlm.nih.gov/pubmed/26924663> – to access, click "Full text links" on the top right of the web page).

A good definition of something has two parts. (A) what it is (the essence), and (B) what it looks like (the characteristics). The old definition only included "B", at the end-stage of the disease. Physicians need to recognize what the cause is within each patient (part "A"), and prevent the end-stage features (part "B").

The new mechanistic definition is: (A) "Chronic pancreatitis is a pathologic fibro-inflammatory syndrome of the pancreas in individuals with genetic, environmental and/or other risk factors who develop persistent pathologic responses to parenchymal injury or stress."³ In addition, (B) "Common features of established and advanced CP include pancreatic atrophy, fibrosis, pain syndromes, duct distortion and strictures, calcifications, pancreatic exocrine dysfunction, pancreatic endocrine dysfunction and dysplasia."³

The new mechanistic definition should be very useful for several reasons. First, it presents chronic pancreatitis as a process that begins without symptoms and progresses in multiple ways to end-stage disease over a number of years. Second, it helps researchers to focus on specific problems such as fibrosis, pancreatic insufficiency, diabetes, pain and cancer risk, and how these different problems may be interrelated. Third, it aids in developing better ways to detect early chronic pancreatitis. Finally, it enables Precision Medicine by helping the physician understand the underlying cause in individual patients (early diagnosis), to predict what will happen without treatment (prognosis) and to guide therapy (treatment).

During the summer of 2016 three international conferences held in Liverpool, England (EPC meeting), in Pittsburgh, PA (PancreasFest) and in Sendai, Japan (IAP) will begin applying medical and scientific knowledge to the new Mechanistic Definition so the physicians and scientist from around the world can help solve the mysteries of chronic pancreatitis together. ○

References

- ¹ Steer ML, Waxman I, Freedman S. Chronic pancreatitis. *New England Journal of Medicine*. 1995;332(22):1482-90.
- ² Sarner M, Cotton PB. Classification of Pancreatitis. *Gut*. 1984;25(7):756-9.
- ³ Whitcomb DC, Frulloni L, Garg P, Greer JB, Schneider A, Yadav D, et al. Chronic pancreatitis: An international draft consensus proposal for a new mechanistic definition. *Pancreatology*. 2016;16:218-24.

HAPPENINGS: Congratulations to Dr. Whitcomb

May 21, 2016, San Diego, CA. Congratulations to **David C. Whitcomb, MD, PhD, AGAF**, Professor of Medicine, Cell Biology & Physiology, and Human Genetics at the University of Pittsburgh for winning the 2016 Research Mentor Award from the Pancreatic Disorders Section of the American Gastroenterology Association Institute (AGAI) Counsel. The award recognizes an individual for his or her achievements as an outstanding mentor in a specific area of research. Professor Whitcomb served as Chief, Division of Gastroenterology, Hepatology and Nutrition at the University of Pittsburgh for 17 years. He is now the founding Director, Precision Medicine Service, UPMC, Pittsburgh, PA. He continues to manage a major research laboratory, provide inpatient consulting services and serve as Editor-in-Chief of *Clinical and Translational Gastroenterology*, a Nature Publishing Group journal and official journal of the American College of Gastroenterology. The AGAI conferred a Research Mentoring Award twice previously: to John A. Williams MD, PhD (2012) and to Eugene P. DiMagno, MD (2014). The AGAI is the largest gastroenterology organization in the world.

The award was presented during the 2016 annual meeting of the four major societies during Digestive Diseases Week (DDW). ○



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The Hereditary Pancreatitis Study

The Hereditary Pancreatitis Study is an ongoing research study at the University of Pittsburgh. The goal is to gather information that may be used, in the future, to improve treatment and help clinicians make better clinical decisions.

Have you participated in this research study in the past and are over the age of 18? If so, we want to ask you some new online questions on health and quality of life. If you are interested, please contact **Celeste Shelton, MS** for more information by calling 412-864-2826 or our toll-free number at 1-888 PITT-DNA/1-888-748-8362, or by email at cas186@pitt.edu. She will confirm your enrollment in the research study and provide you with an individualized link to the web-survey. For those unable to take the new survey online, a paper form is available. Thank you to all of our current and past participants for helping us to better understand hereditary pancreatitis! ○

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