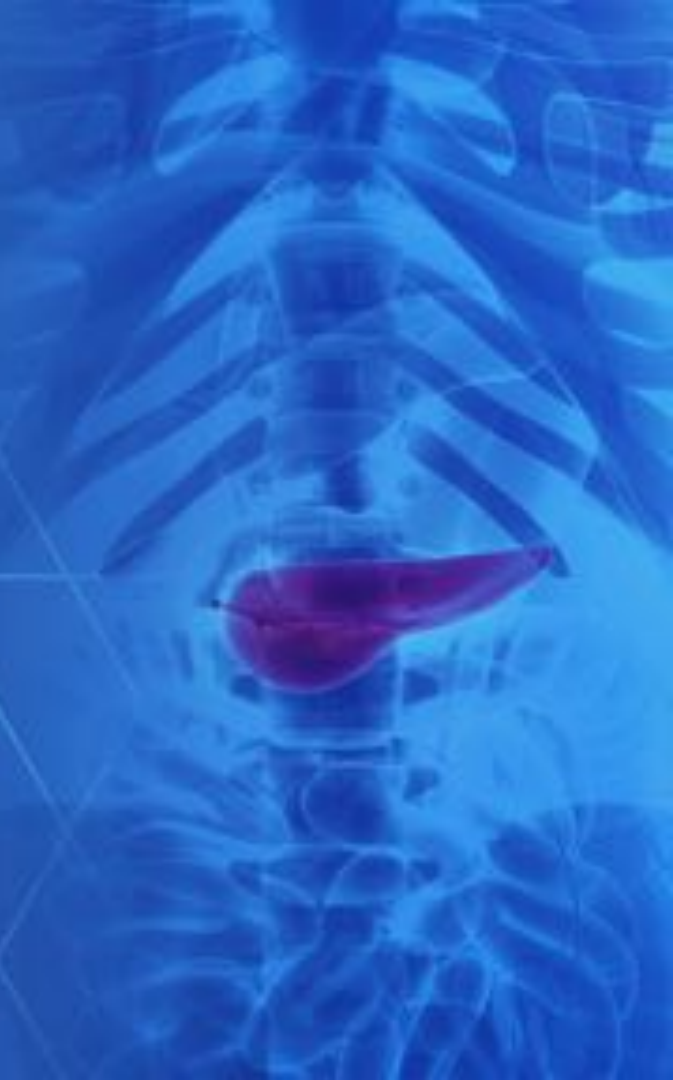


2018 CAPER Collaborative Alliance for
Pancreatic Education and
Research

PANCREAS ACADEMY



jointly provided by the New Mexico Medical Society (NMMS) through the joint
providership of Rehoboth McKinley Christian Health Care Services (RMCHCS)
and the Collaborative Alliance for Pancreatic Education and Research.





Exocrine Pancreatic Insufficiency Diagnosis, Treatment & Treatment Failure

Andres Gelrud, MD

Director, Pancreatic Disease Center

Miami Cancer Institute, Baptist Health System

Gastro Health



Conflict of Interest:

Abbvie Pharmaceutical. Consultant and Lectures on PERT. Grant support PERT.

Boston Scientific. Consultant Pancreatic Stents

Introduction – Exocrine Pancreas

- Normal function
- Associated conditions with exocrine insufficiency
- Making the diagnosis
- Indications and dosing for pancreatic enzyme replacement therapy (PERT)
- Why they “fail”

The “Normal Pancreas”

- Pancreatic enzyme secretion varies with content and volume of meal ingested ¹
- Average lipase unit per meal = 720,000 lipase U
- Exocrine pancreatic insufficiency occurs with 90% of enzyme output is diminished ^{2,3}

(1) Keller J, Layer P. Human pancreatic exocrine response to nutrients in health and disease. *Gut*. 2005.

(2) Dimagno et al. *NEJM* 1973

(3) Ferrone M, Raimondo M et al. *Panc Enz Pharmacotherapy*. *Pharmacotherapy* 2007

Exocrine Pancreatic Insufficiency (EPI)

Primary EPI (parenchymal disease):

Reduced enzyme synthesis

Secondary EPI (normal parenchyma):

Ductal obstruction or

Poorly synchronized enzyme release

Associated Medical Conditions (primary EPI)

- Chronic Pancreatitis
- Other genetic conditions
 - CFTR
 - PRSS1
- Other inherited disorders of the pancreas
- Occasionally after severe acute pancreatitis
- Others “systemic” conditions:
 - IBD, Diabetes, Celiac disease, VHL

Associated Medical Conditions (secondary EPI)

- Tumors obstructing the main pancreatic duct
- Pancreatic surgical resection (partial / total)
- Other surgeries: distal gastrectomy or gastric bypass surgery
- Short bowel syndrome
- Others “systemic” conditions:
 - Celiac disease, Gastrinoma, Autoimmune Pancreatitis

EPI and Pancreatic CA

Pancreatology. 2015 Jun 23. pii: S1424-3903(15)00594-3. doi: 10.1016/j.pan.2015.06.003. [Epub ahead of print]

Invited review: Pancreatic exocrine insufficiency following pancreatic resection.

Phillips ME¹.

- 42-45% of patients undergoing pancreaticoduodenectomy (PD) experience EPI pre-operatively
- The post-operative incidence is 56-98% in PD, and 12-80% following distal and central pancreatectomy.

EPI and Pancreatic CA



National
Comprehensive
Cancer
Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Pancreatic Adenocarcinoma

Version 2.2015

NCCN.org

weight loss, and malnutrition.⁵³⁸ Oral pancreatic exocrine enzyme replacement therapy is recommended for patients with pancreatic cancer who have symptoms of exocrine enzyme deficiency. Because pancreatic exocrine insufficiency occurs in up to 94% of patients undergoing pancreatic surgery,^{539,540} therapy may be initiated without diagnostic tests. Enteric-coated mini-microspheres containing

Symptoms of fat Malabsorption

Am J Gastroenterol. 2010 Dec;105(12):2680-6. doi: 10.1038/ajg.2010.325. Epub 2010 Aug 24.

High prevalence of low-trauma fracture in chronic pancreatitis.

Tignor AS¹, Wu BU, Whitlock TL, Lopez R, Repas K, Banks PA, Conwell D.

Pancreas. 2016 Mar;45(3):355-61. doi: 10.1097/MPA.0000000000000381.

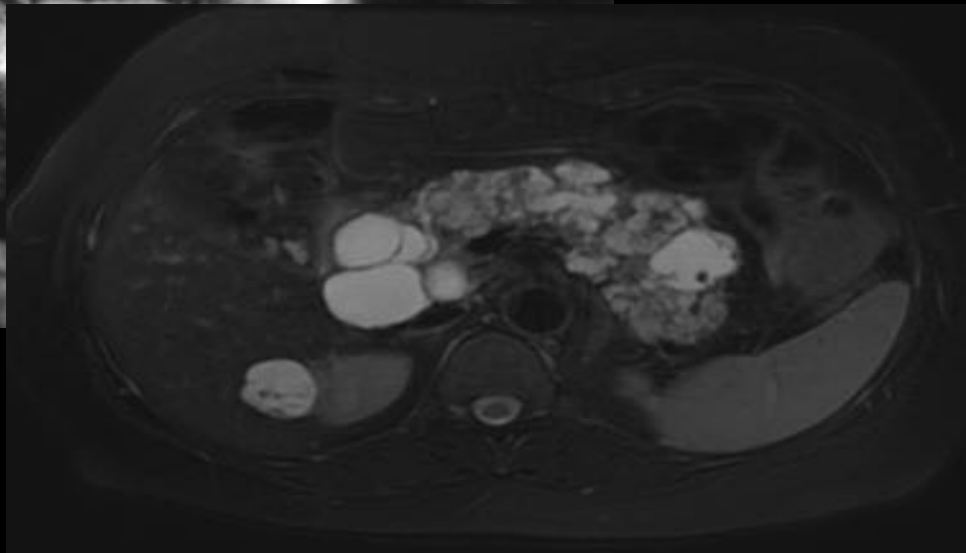
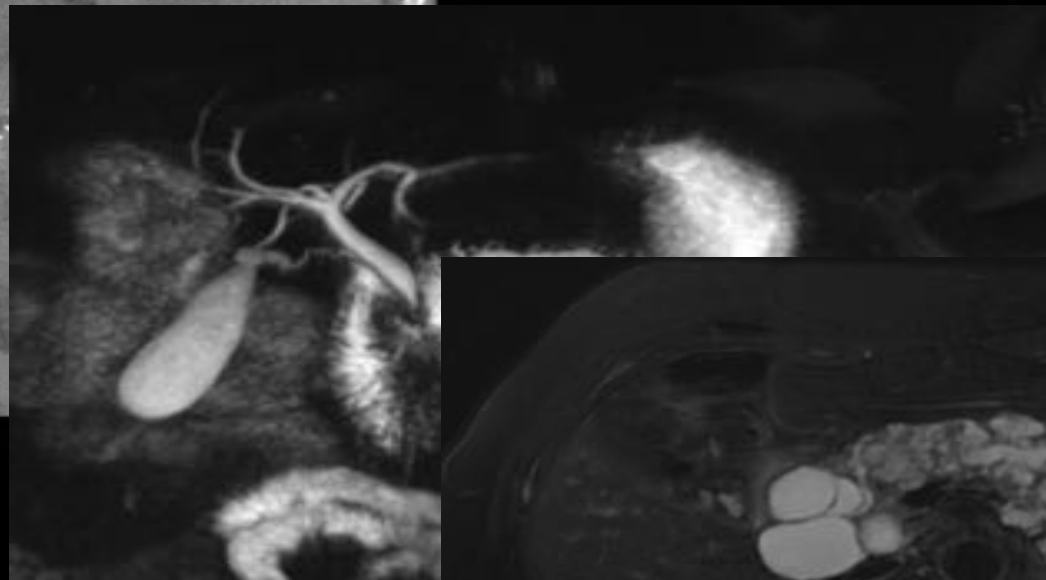
Chronic Pancreatitis and Fracture: A Retrospective, Population-Based Veterans Administration Study.

Munigala S¹, Agarwal B, Gelrud A, Conwell DL.

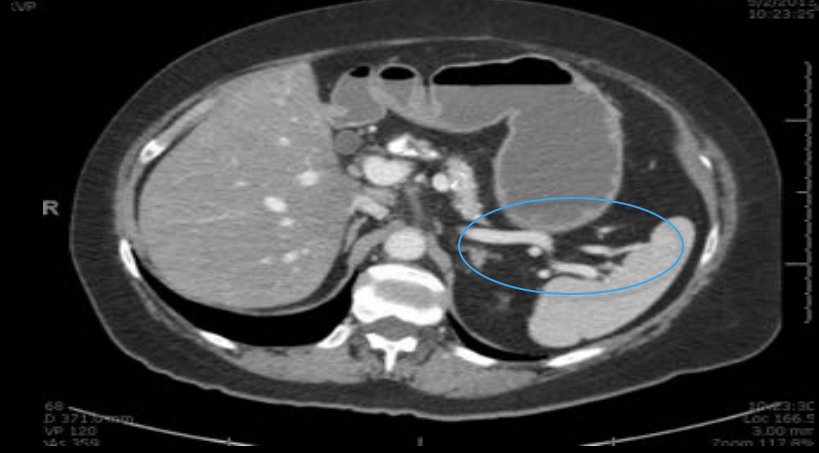
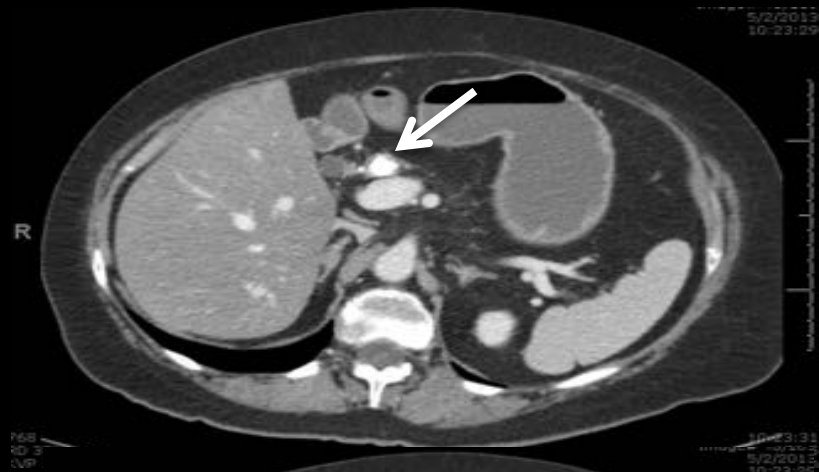
Consider Exocrine Pancreatic Insufficiency

- Symptoms: Foul smelling stools, bloating, gas, weight loss, and steatorrhea
- Clinically relevant maldigestion occurs earlier than the appearance of overt symptoms ¹
- Personal experience: night time bowel movements & always ask the significant other

(1) Dumasi V et al. Fat malabsorption screening in CP. Am J Gastro 2004



Abdominal CT Scan



Making the Diagnosis

- Fecal elastase
- 72 hour fecal fat (w calculation of CFA)
- Elevated 13C – mixed triglyceride breath test
- Clinical response to PERT
- Suspect EPI with the following labs:
 - Low: Hb; albumin, pre-albumin or elevated HgA1c, Vit A, D, E, K

(1) Domingues Munoz FE1 AJM 1995

(2) Leeds JS et al. The role of FE1 in detecting EPI. Nat Rev Gastron Hep 2011

(3) C13 Mixed TG breath test . Clin Gastro and Hep 2007

(4) Lindkvist et al. Pancreatology 2012

Steatorrhea



Goals of Pancreatic Enzyme Use

- Restore normal / close to normal digestion of proteins, fat and carbohydrates
- Alleviate symptoms of exocrine pancreatic insufficiency
- Maintain normal nutrition

Current FDA Approved Enzymes

Name	Dosages Available			Approximate Cost per 10,000 Units of Lipase*	Manufacturer and Contact Information
	Lipase Units	Protease Units	Amylase Units		
Creon®	3,000	9,500	15,000	\$4.30	Abbott Laboratories www.creon.com (800) 241-1643
	6,000	19,000	30,000	\$2.39	
	12,000	38,000	60,000	\$2.11	
	24,000	76,000	120,000	\$2.02	

May 2009

August 2009

April 2010

March 2012

March 2012

May 2012

CREON®
approved

ZENPEP®
approved

PANCREAZE®
approved

VIOKACE™
approved

ULTRESA™
approved

PERTZYE™
approved

Name	Dosages Available			Approximate Cost per 10,000 Units of Lipase*	Manufacturer and Contact Information
	Lipase Units	Protease Units	Amylase Units		
Zenpep®	3,000	10,000	16,000	\$4.59	Aptalis Pharma US, Inc. www.zenpep.com 1-800-950-8085
	5,000	17,000	27,000	\$2.64	
	10,000	34,000	55,000	\$2.40	
	15,000	51,000	82,000	\$2.25	
	20,000	68,000	109,000	\$2.26	
	25,000	85,000	136,000	\$2.37	

How Much Should We Prescribe ?

Whitcomb DC et al. Pancrealipase delayed release cap for EPI due to CP or Pancreatic Surgery: a double blind randomized trial. Am J Gastro 2010



72,000 lipase units per meal

36,000 lipase units per snack

Coefficient of fat absorption (CFA) measured

How Much Should We Prescribe ?

Whitcomb Study Am J Gastro 2010

Both CFA (>86%) and CNA significantly improved compared to placebo $p < 0.0001$

Adverse reactions:

Glycemic control; abdominal pain; flatulence; frequent bowel movements

68 yo F recently diagnosed with EPI, started on PERT every 8 hrs. Now with persistent steatorrhea. Picture of the most recent BM ...



What is the Best Time to Take Enzymes ?

N = 24 all pt's with documented steatorrhea

Prospective, randomized, 3 way crossover study

Highest efficacy → Enzymes consumed throughout the meal

Second highest efficacy → just after meals

Lowest efficacy → just before meals

Why Does Treatment Therapy Fails ?

- Under treatment
 - Start low and increase approach
- Compliance with therapy and schedule
 - Too many too frequent
- Discontinue alcohol and / or smoking
- Underlying motility disorder (after surgery)
- Consider superimposed: bacterial over growth; giardia celiac disease

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Why Does Treatment Therapy Fails ?

- Under treatment
- Compliance with therapy and schedule
- Discontinue alcohol and / or smoking
- **Underlying motility disorder**
 - Possible Rx: NJ feeding tube vs PEG or PEJ vs Medical TPN (discouraged)
 - IF rapid transient consider: lomotil; Imodium; tincture of opium
- Consider superimposed: bacterial over growth; giardia; celiac disease

Why Does Treatment Therapy Fails ?

- Under treatment
- Compliance with therapy and schedule
- Discontinue alcohol and / or smoking
- Underlying motility disorder
- **Consider superimposed: bacterial over growth; giardia; celiac disease; super imposed infection**

Work up: Stool analysis (O&P, C diff, Giardia Ag)

Possible Rx: Empiric treatment for bacterial overgrowth

Pancreatic Enzymes: Challenges

- Do we have the right amount of enzymes for the particular meal
- Size of the pills, “to big” → compliance
- To many → compliance
- Synchronization / GI motility
- Concomitant use of acid inhibition (PPI)

Conclusion

Patients who suffer from EPI due to pancreatectomy, dosage should be individualized based on clinical symptoms, degree of steatorrhea, and fat content in the diet, lack of clinical response should trigger work up for other medical conditions



Home » Nutrition and PERT » Role and Benefits of Pancreatic Enzyme Replacement Therapy (PERT) » Animation: Understanding Nutrition and the Role and Benefits of PERT

Module Content

Role and Benefits of Pancreatic Enzyme Replacement
Therapy (PERT)

Animation

Expert Videos (3)

Patient Videos (2)

Slide Show

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Understanding Nutrition and the Role and Benefits of PE...

***"Understanding Nutrition and
the Role and Benefits of Pancreatic
Enzyme Replacement Therapy
(PERT)"***

*Please note: This animation represents a visual interpretation
and is not intended to provide, nor substitute as,
medical and/or clinical advice.

▶ ⏪ 0:02 / 4:00





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Miami Cancer Institute

BAPTIST HEALTH SOUTH FLORIDA

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agehrud@gastrohealth.com

