

Minimally Invasive and Novel Therapeutics (M.I.N.T.)
September 13th- 15th 2023

The necrosis is gone...now what?

Outpatient management of patients with complex necrotizing pancreatitis

Yasmin Hernandez-Barco, MD

Director of the MGH Pancreas Center

Division of Gastroenterology, Massachusetts General Hospital

Instructor, Harvard Medical School



Disclosures

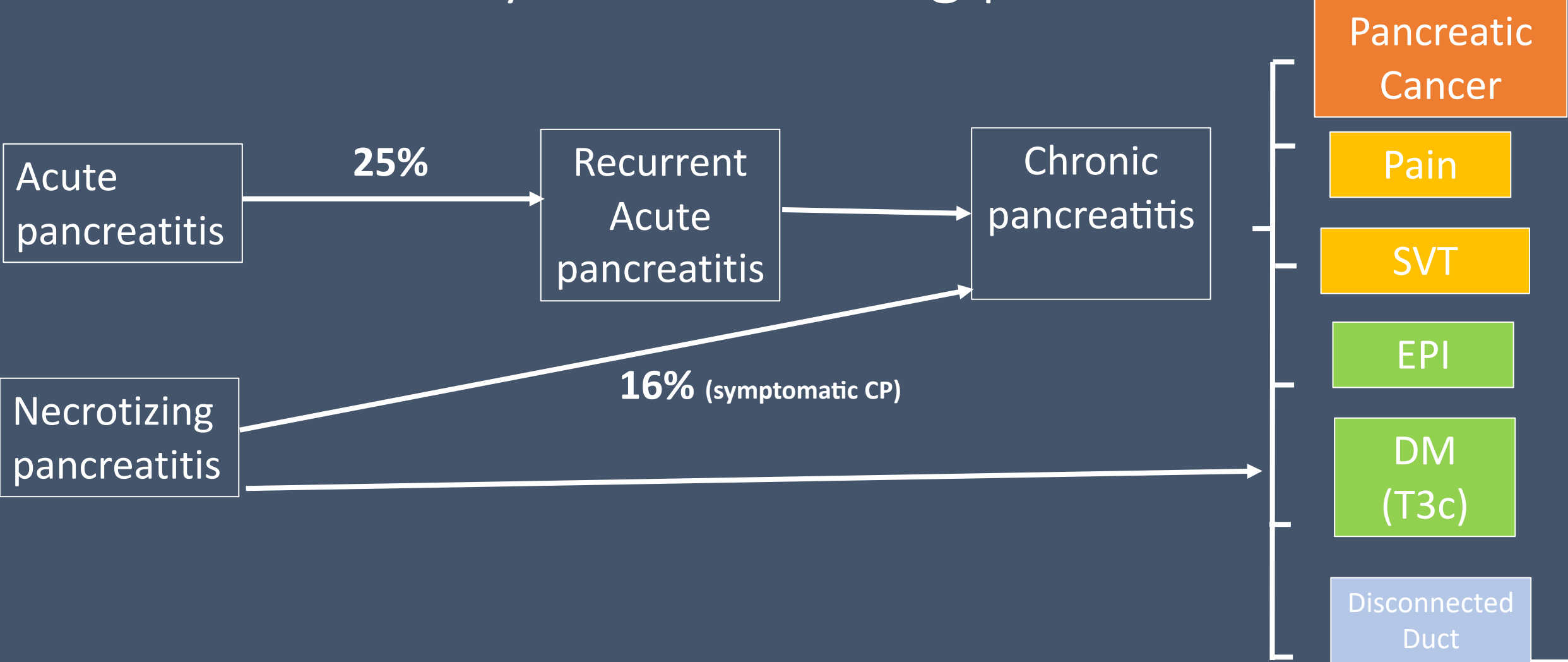
- Nestle Health Science, Aimmune – Scientific Advisory Board for the development of the PACT-CP registry
- Honorarium for Grand Rounds and other CME talks
- Research funding for PACT-CP (Chronic pancreatitis patient registry); Nestle Health Science

Learning Objectives

- 1) Evaluate the etiology for necrotizing pancreatitis
- 2) Understand how to monitor patients for long term complications from necrotizing pancreatitis
 - a. Exocrine pancreatic insufficiency
 - b. Diabetes
 - c. SVT
 - d. Disconnected duct syndrome
 - e. Strictures
 - f. Pain management approach
- 3) Review the management of these long-term complications



Natural History of Necrotizing pancreatitis



Confirming the Etiology of Necrotizing Pancreatitis

1. **Alcohol (28%)**
2. **Gallstones (45%)**
3. **Hypertriglyceridemia (5.8%)**
4. **Post-ERCP**
5. Hypercalcemia
6. Medications
7. Toxins (ie- tobacco, cannabis)
8. Genetic mutations (SPINK, CFTR, PRSS1, CTRC) - <35 years
9. Anatomical (PDA, structural)
10. Infections
11. Autoimmune (extremely rare cause of necrosis)
12. Idiopathic

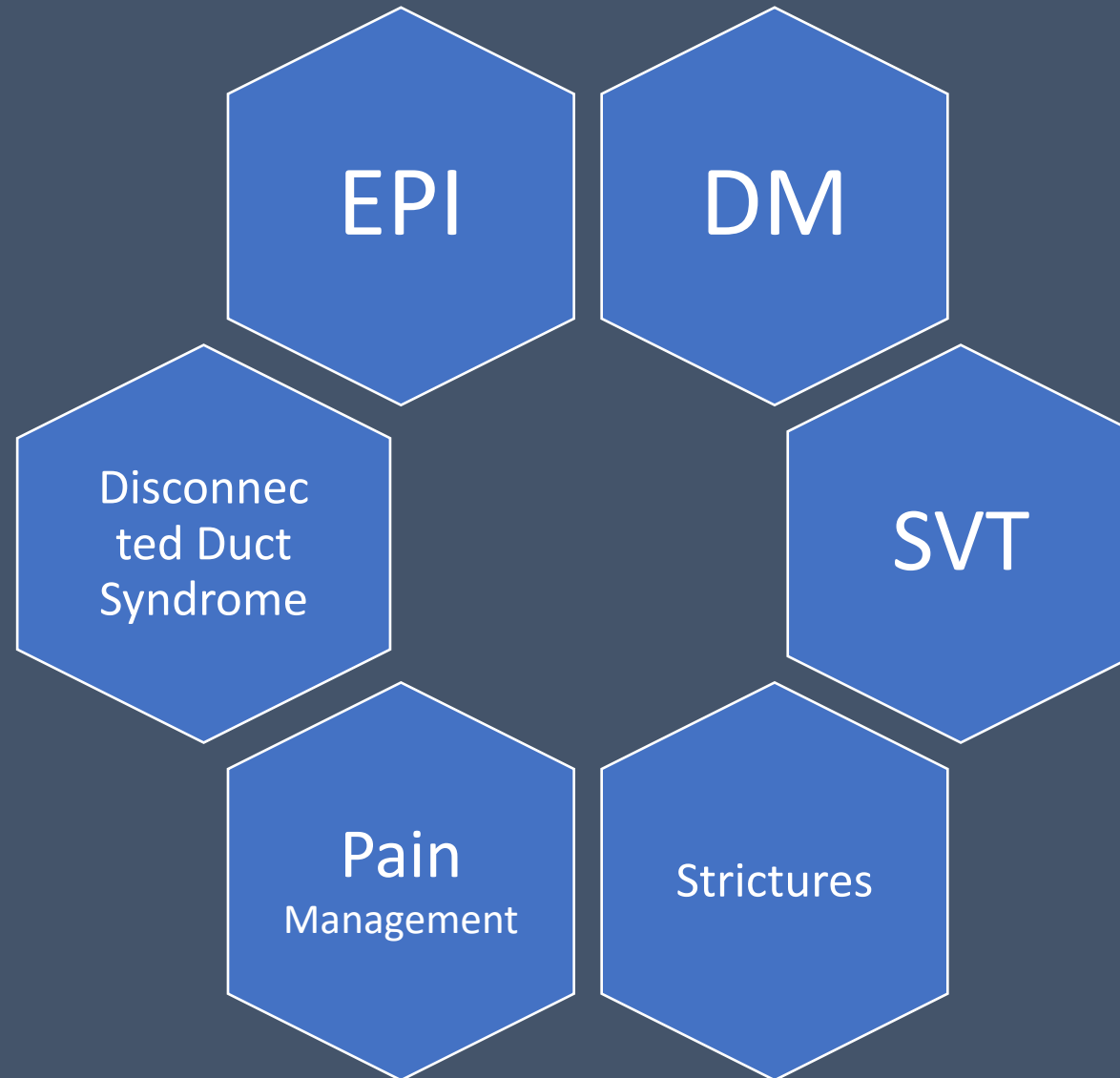


Preventing Recurrence of Pancreatitis

- Cholecystectomy for gallstone pancreatitis
 - Mild – prior to discharge
 - Severe – ensure surgical appointment made or perform biliary sphincterotomy
- Remove toxins/risk factors
 - Smoking and alcohol counseling
- Hypertriglyceridemia
 - Glycemic control
 - Endocrine follow-up
- Idiopathic
 - GI follow-up



Monitoring Complications



Exocrine Pancreatic Insufficiency

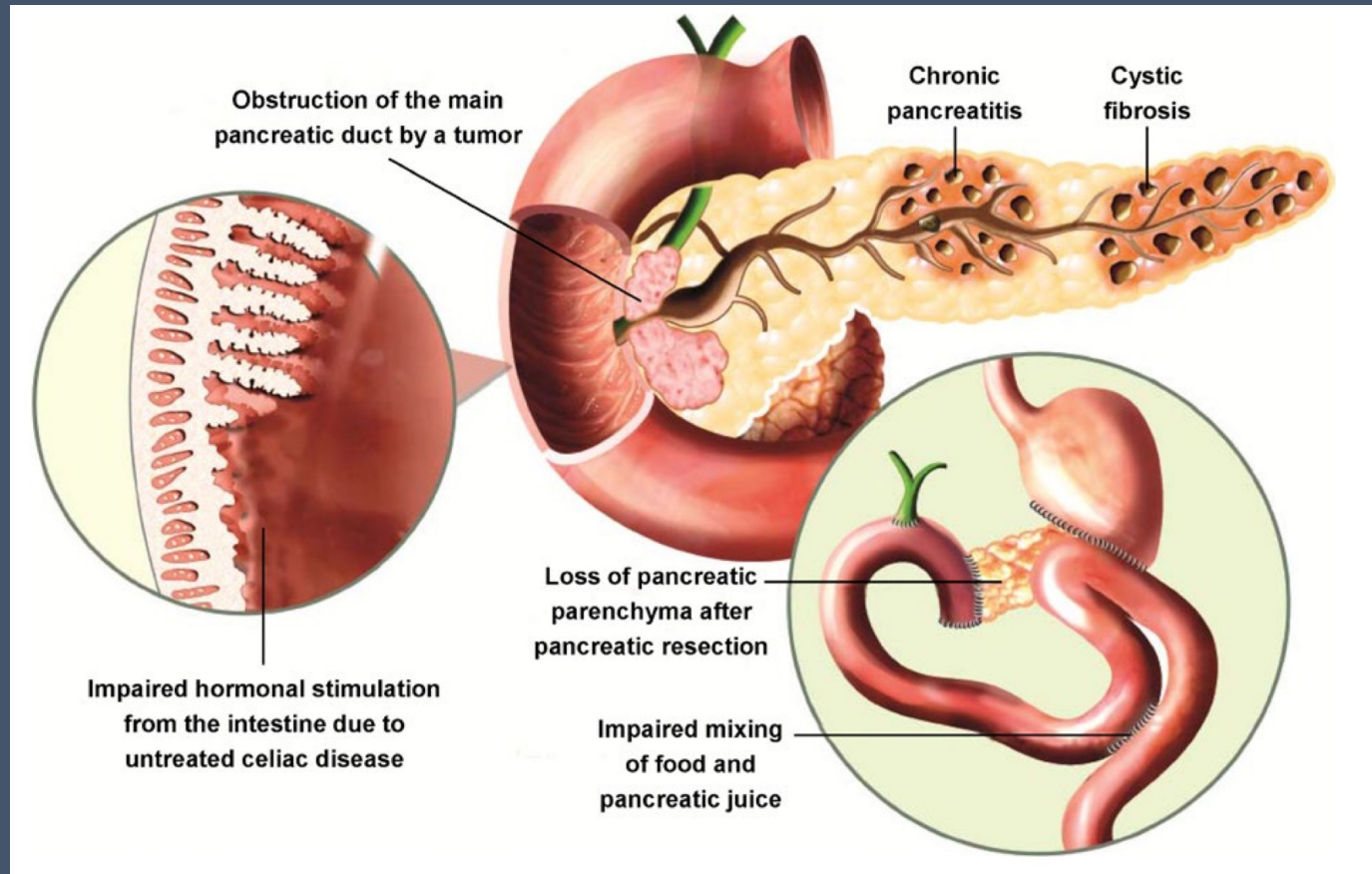


Prevalence of exocrine insufficiency

- Meta-analysis:
 - 32 studies – 1,495 patients
- Tests – fecal fat or fecal elastase
 - mean follow-up, 36 months after pancreatitis
- Exocrine insufficiency
 - 25% of all patients
 - higher risk in alcoholic pancreatitis
 - higher risk in necrotizing pancreatitis



Pathophysiology: Normal digestion vs. EPI



Exocrine
Lipase
Protease
Amylase



EPI Disease burden

- Prevalence in the general population is difficult to establish
- ~200,000 patients with chronic pancreatitis
 - 15% of patients with EPI at time of diagnosis
 - 35–75% risk of developing EPI over course of disease
- **45% of patients with NP will develop EPI over first 5 years**

MALNUTRITION

MALDIGESTION
(nutritional &
symptomatic)

MALABSORPTION
(nutritional &
symptomatic)



Screening tools

1

Screen for symptoms of steatorrhea, weight loss, bloating or other maldigestion

2

Stool based testing with fecal elastase with 72-hour fecal fat

3

Micronutrient deficiencies: Vitamin A, E, D, K, B12, zinc, copper, selenium, folate and iron

4

DEXA scan to screen for metabolic bone disease

Treatment and Monitoring

ALL patients with pancreatic necrosis need to be started on PERT

- Following diagnosis, a robust assessment of nutritional status, diet and lifestyle should be performed
- The role of the registered dietician cannot be under-emphasized
- Regular follow-up to monitor compliance and response is needed to achieve optimal results

Metabolic needs
Nutritional status
Dietary intake
Alcohol & smoking
Metabolic issues
Concomitant disease



Pancreatic Enzyme Replacement Therapy (PERT)

Medication	Available lipase strengths (USP)	Formulation
Pancreaze	2600 • 4200 • 10,500 • 16,800 21,000 • 37,000	Hard gelatin capsule with enteric coated microtablets
Zenpep	3000 • 5000 • 10,000 • 15,000 • 20,000 25,000 • 40,000	Enteric Coated spheres
Viokace	10,444 • 20,880	Non-enteric coated tablet
Creon	3000 • 6000 • 12,000 • 24,000 • 36,000	Enteric Coated spheres
Pertzye	4000 • 8000 • 16,000 • 24,000	Bicarbonate buffered enteric-coated microspheres



PERT dosing and timing

- PERT should treat the meal, not the patient
- PERT should be consumed at the start of a meal which contains protein or fat
- Split dosing likely leads to improved absorption
- Limited guidelines on dosing of PERT in the US, but dose should be a minimum of 1000 units/kg/meal (minimum 40,000 Units per meal)
- Side effects such as nausea, abdominal cramping, abdominal bloating, diarrhea, and constipation may occur with PERT



Treatment Monitoring

- Monitoring of symptoms (including via patient tracking tools):
 - Weight stabilization/gain
 - Improved steatorrhea and diarrhea
 - Reduced post-prandial bloating, pain and flatulence
- Does not uniformly improve pain, bloating, nausea
- Fecal elastase not affected by PERT and should not be used as a response marker
- Patients with pancreatic necrosis can be periodically assessed for ongoing need for PERT



Failure of PERT?

- Is PERT underdosed?
- Is the timing of PERT sub-optimal?
- Inadequate acid suppression?
- Surgical anatomy or issues with GI dysmotility leading to PERT asynchrony?
- Are there underlying GI disorders contributing to symptoms which are inadequately treated?



Endocrine Dysfunction



Prevalence of endocrine dysfunction

- 1,102 patient – first episode of acute pancreatitis
- Prevalence of diabetes within 12 months
 - ~20%-after acute pancreatitis
 - 4-9%-in general population
- Risk of diabetes not related to
 - Etiology, age or gender
- INCREASED risk with Severe AP

With Necrosis	Without Necrosis
37%	11%

SCREENING: A1c at the time of clinic visit and annually



Splanchnic Venous Thrombosis (SVT)



- Up to 25% of patients with AP develop SVT and up to 45% of those with NP develop SVT
- Anticoagulation can be considered if acute clot and no evidence of collaterals for 3-6 months
- Anticoagulation is probably NOT indicated for splenic vein thrombosis



Anatomical Complications

Strictures

- symptomatic disconnected pancreatic duct syndrome (27-49%)
- biliary stricture (16%)
- Gastrointestinal fistula (8%)
- pancreatic duct stricture (5%)
- duodenal stricture (5%)



Disconnect Duct Syndrome

- Diabetes risk
- Persistent intractable pain
- Recurrent pancreatitis
- Formation of pseudocysts/collections

Disconnec
ted Duct
Syndrome

Endoscopy
or Surgical
Colleagues

Pain Approach



1. Confirm whether or not pain is anatomical
2. Smoking and alcohol cessation is imperative
3. Proton pump inhibitor therapy to prevent PUD
4. Psychological assessment
5. Determine if primary pain, visceral hypersensitivity or centralization
6. Lyrica or other neuromodulators such as Cymbalta or gabapentin
7. Tramadol
8. Pain management referral
9. WHO Pain ladder



Take Home Message

- Pancreatic necrosis leads to damage of a significant portion of the pancreas
- Necrotic collections are either endoscopically or surgically treated or resorb and lead to fibrosis of the damaged parenchyma over time
- The etiology of necrotizing pancreatitis should be carefully evaluated and preventative measures implemented when possible
- Patients are at increased risk of a series of complications most commonly exocrine pancreatic insufficiency and diabetes
- All patients with NP should be started on PERT
- All patients should be screened and monitored for diabetes



Take Home Message

- All patients should be initiated on proton pump inhibitors to prevent penetrating ulcer disease
- Anticoagulation for splanchnic vein thrombosis is controversial
- Disconnected duct syndrome should be approached by a multidisciplinary team and interventions directed at underlying symptoms
- Pain is complex and anatomical reasons for pain should be evaluated

Necrotizing pancreatitis is complex disease, which requires multidisciplinary care.

Thank you!

Happy to take questions



Yhernandez-barco@mgh.Harvard.edu