

# CHRONIC PANCREATITIS

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# OUTLINE

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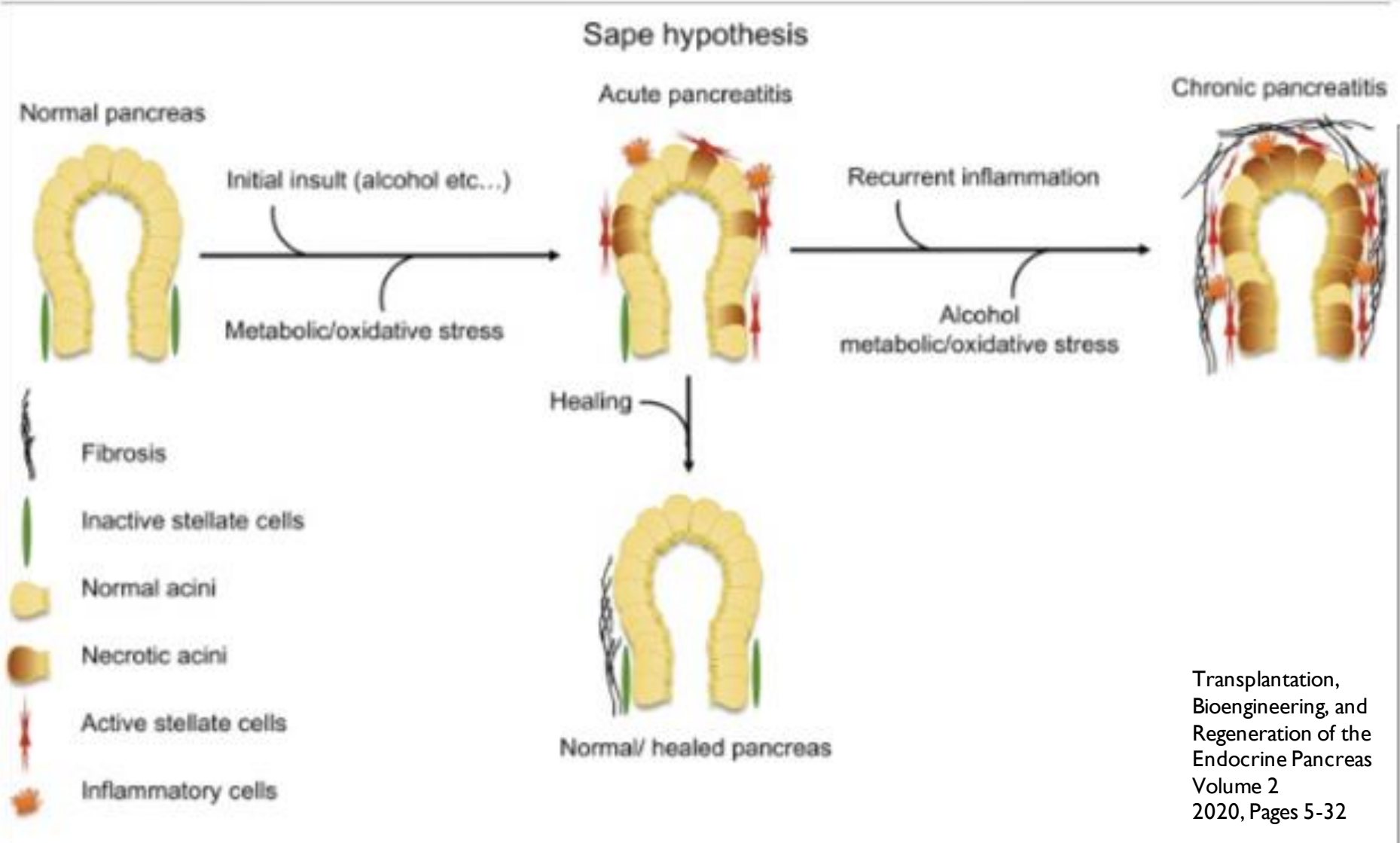
- Pathogenesis
- Etiology
- Diagnosis
- Treatment

# PATHOGENESIS

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- **Necrosis-Fibrosis Hypothesis**(Comfort and colleagues 1946)
- **Protein-Plug(Stone/Ductal Obstruction) Hypothesis**(Multigner et al, 1985; Sarles, 1986)
- **Oxidative stress theory**(Braganza 1983)
- **Toxic-Metabolic theory**(Bordalo and colleagues 1977)
- **Primary duct hypothesis**(Cavallini 1993)
- **Sentinel Acute Pancreatitis Event Hypothesis**(Whitcomb 1999)
- **Sustained Intraacinar Nuclear Factor-kB Activation**

# SAPE HYPOTHESIS



Transplantation,  
Bioengineering, and  
Regeneration of the  
Endocrine Pancreas  
Volume 2  
2020, Pages 5-32

# ETIOLOGY

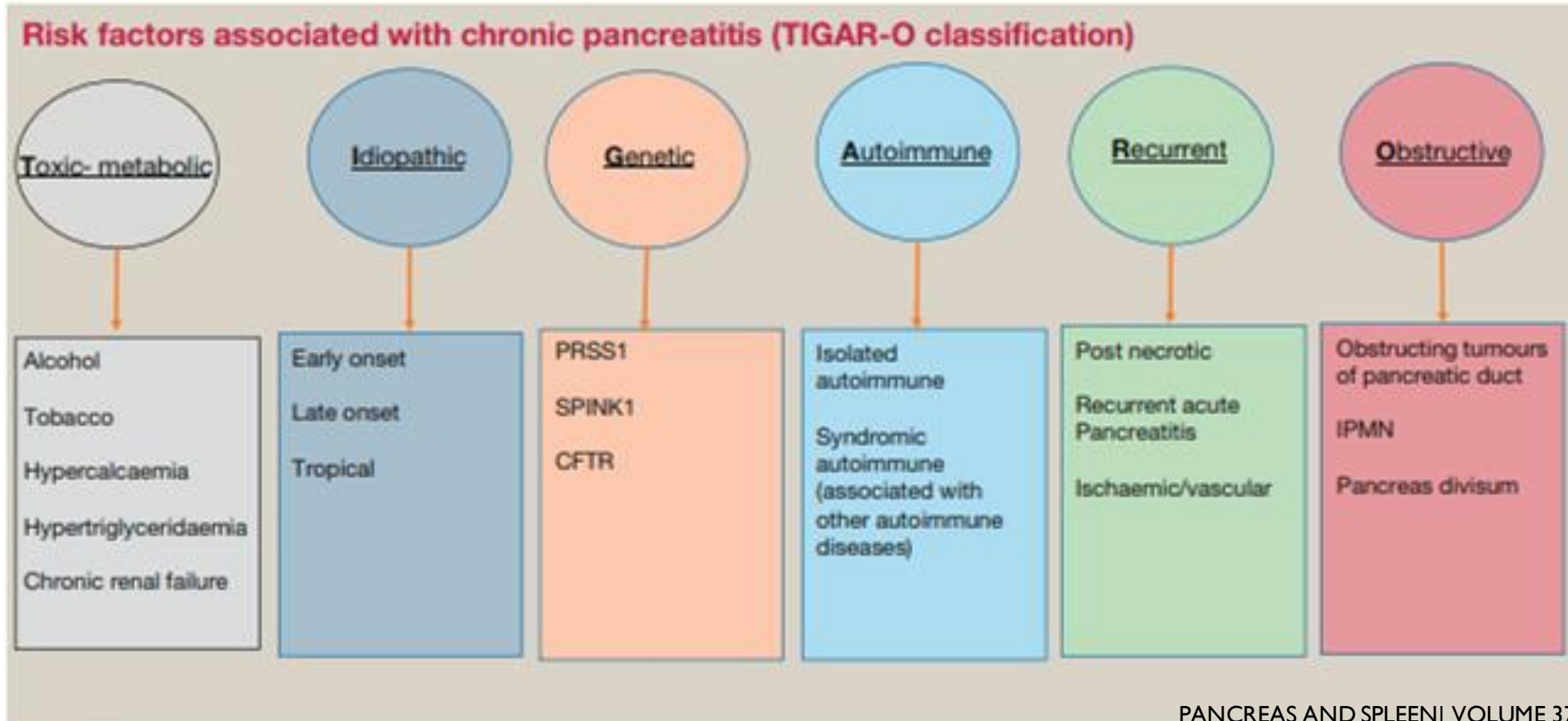
**TABLE 57.1** Etiopathogenesis of Chronic Pancreatitis

Etiology/Mechanism of Injury	Pathogenesis
<b>Toxic-Metabolic</b>	
Alcohol ingestion (genetic mutations)	Protein plug obstructive hypothesis
Tobacco	Toxic-metabolic hypothesis
Hypercalcemia (hyperparathyroidism)	Necrosis-fibrosis
Lipoprotein lipase deficiency	Oxidative stress (detoxification insufficiency)
Apolipoprotein CII deficiency	
Chronic renal failure (uremia)	
Protein deficiency	
Trace-element deficiency	
Dietary toxins	
Medicinal products (phenacetin)	
<b>Idiopathic</b>	
Early onset	Necrosis-fibrosis
Late onset	Protein plug
Tropical form ( <i>SPINK1</i> mutations)	
Tropical calcific pancreatitis	
Fibrocalculous pancreatic diabetes	
Unknown cause (likely genetic or hereditary)	

**TABLE 57.1** Etiopathogenesis of Chronic Pancreatitis

Etiology/Mechanism of Injury	Pathogenesis
<p><b>Genetic/Hereditary</b></p> <p>Autosomal dominant mutations, cationic trypsinogen gene (<i>PRSS1</i>)</p> <p>Autosomal recessive mutations: <i>SPINK1</i>, cationic trypsinogen (codons 16, 22, 23)</p> <p>Cystic fibrosis transmembrane conductance regulator (<i>CFTR</i>) defects</p> <p><math>\alpha_1</math>-Antitrypsin deficiency</p>	<p>Necrosis-fibrosis</p>
<p><b>Autoimmune/Immunologic</b></p> <p>Viral infection</p> <ul style="list-style-type: none"> <li>Hepatitis B</li> <li>Coxsackievirus</li> </ul> <p>Autoimmune diseases</p> <ul style="list-style-type: none"> <li>Primary autoimmune pancreatitis</li> <li>Associated with Sjögren's syndrome, Crohn's disease, ulcerative colitis, or primary biliary cirrhosis</li> </ul>	<p>Large duct</p>
<p><b>Recurrent and Severe Acute Pancreatitis</b></p> <p>Vascular disease</p> <p>Ischemia</p> <p>Postradiation therapy</p>	<p>Necrosis-fibrosis</p>
<p><b>Obstructive Mechanical Causes</b></p> <p>Pancreas divisum with insufficient accessory papillae</p> <p>Annular pancreas</p> <p>Papillary stenosis</p> <p>Ductal scarring</p> <p>Malignant pancreatic duct stricture (pancreatic, ampullary, or duodenal carcinoma; mucinous duct ectasia)</p> <p>Duodenal obstruction (diverticulum, duodenal)</p> <p>Stricture of pancreatic duct after severe acute pancreatitis or trauma</p> <p>Stones</p> <p>Sphincter of Oddi dysfunction</p> <p>Cholelithiasis</p>	<p>Stone and duct obstruction</p> <p>Protein plug</p>

# TIGAR-O CLASSIFICATION



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Figure 1

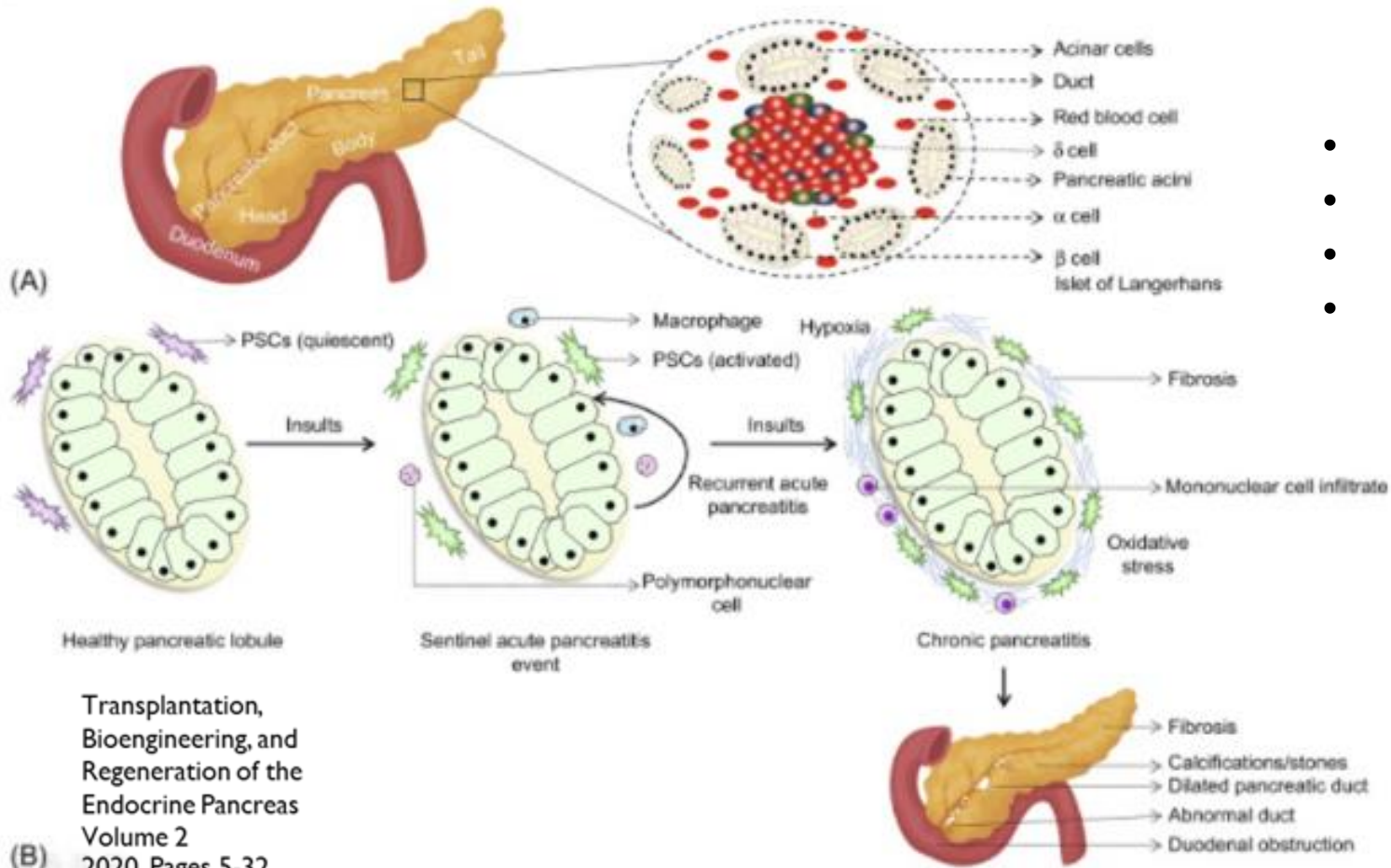
# DIAGNOSIS

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- Definition
  - Continuing inflammatory disease of the pancreas characterized by irreversible morphologic changes that typically cause abdominal pain and/or permanent impairment of pancreatic function



# PRESENTATION



- Abdominal pain
- Fat malabsorption  Steatorrhae
- Pancreatic Exocrine Insufficiency
- Endocrine insufficiency

Transplantation,  
Bioengineering, and  
Regeneration of the  
Endocrine Pancreas  
Volume 2  
2020, Pages 5-32

(B)

# STAGE OF CHRONIC PANCREATITIS

**TABLE 57.2** Stages of Chronic Pancreatitis: Typical Clinical and Morphologic Pictures, Pancreatic Function, and Recommended Diagnostic Procedures

Stage	CLINICAL PICTURE		Morphology	Pancreatic Function	Diagnostics
	Pain	Complications			
A: Early	Recurrent acute attacks	No complications	Morphologic changes detectable with imaging procedures directed to pancreatic parenchyma and ductal system	Normal pancreatic endocrine and exocrine function	EUS, ERP/MRP, CT, secretin
B: Moderate	Increasing number of attacks and increased intensity	Pseudocysts, cholestasis, segmental portal hypertension	Progradient morphologic changes detectable in several imaging procedures	Impairment of pancreatic function in several degrees, but rarely steatorrhea	Transabdominal US, ERP/MRP, EUS, CT, fasting blood glucose, oral glucose tolerance test
C: Advanced	Decreasing pain ("burnout" of the pancreas)	Pseudocysts, cholestasis, segmental portal hypertension	Calculi	Marked impairment of pancreatic function, more often steatorrhea than in other stages; diabetes mellitus	Transabdominal US, ERP/MRP, CT, FE-1, fasting blood glucose, oral glucose tolerance test

CT, Computed tomography; ERP, endoscopic retrograde pancreatography; EUS, endoscopic ultrasound; FE-1, fecal elastase 1; MRP, magnetic resonance pancreatography; US, ultrasonography.

# COMPLICATION

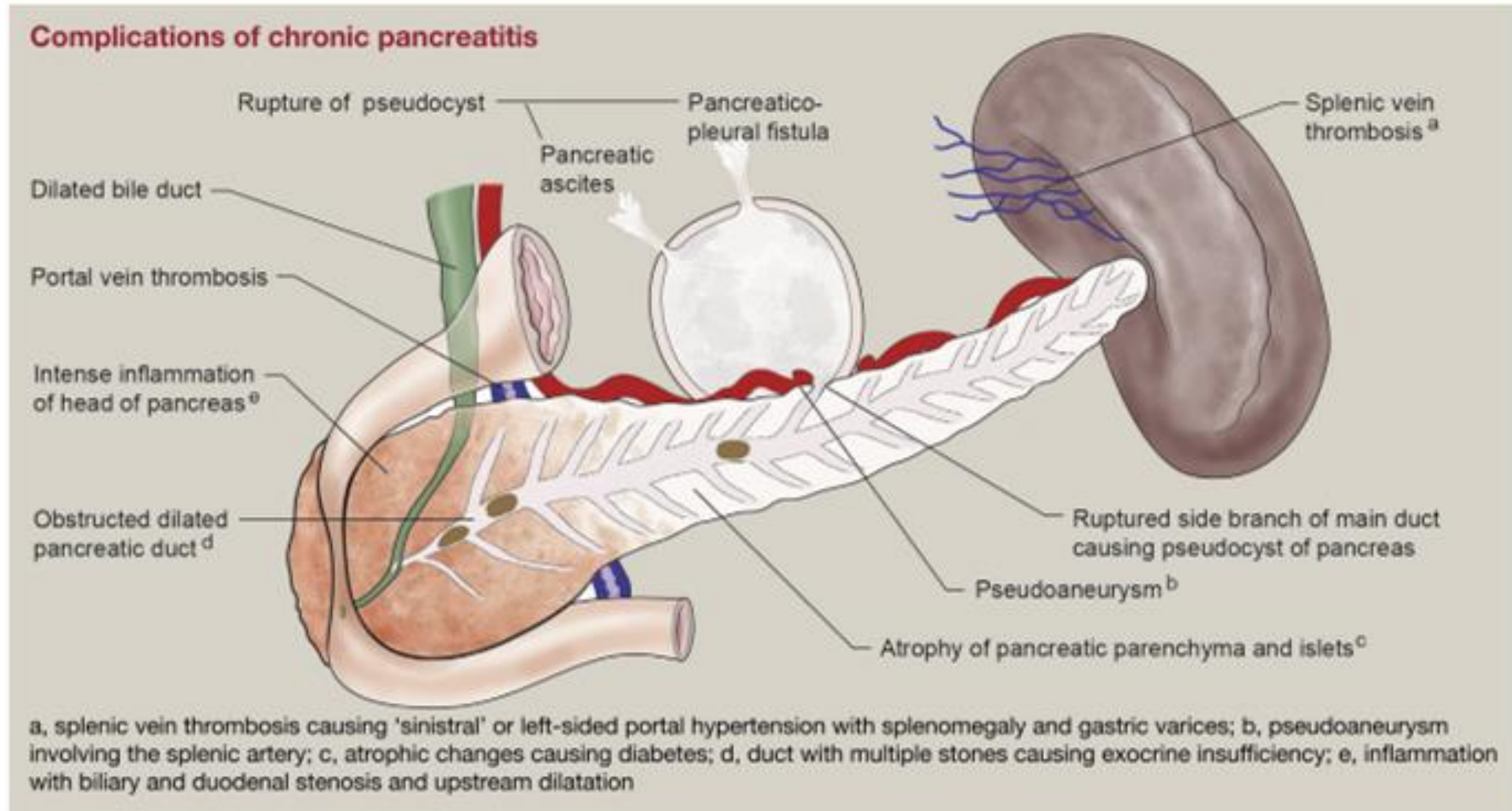


Figure 2

R. Ravindran, Surg Oxford 2019

# IMAGING METHODS

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- Plain Abdominal Radiography
- Transabdominal Ultrasonography
- Computed Tomography
- Endoscopic Retrograde Pancreatography
- Endoscopic Ultrasonography
- Magnetic Resonance Imaging and Cholangiopancreatography

# PLAIN ABDOMINAL RADIOGRAPHY

- 30-40% in Advance CP

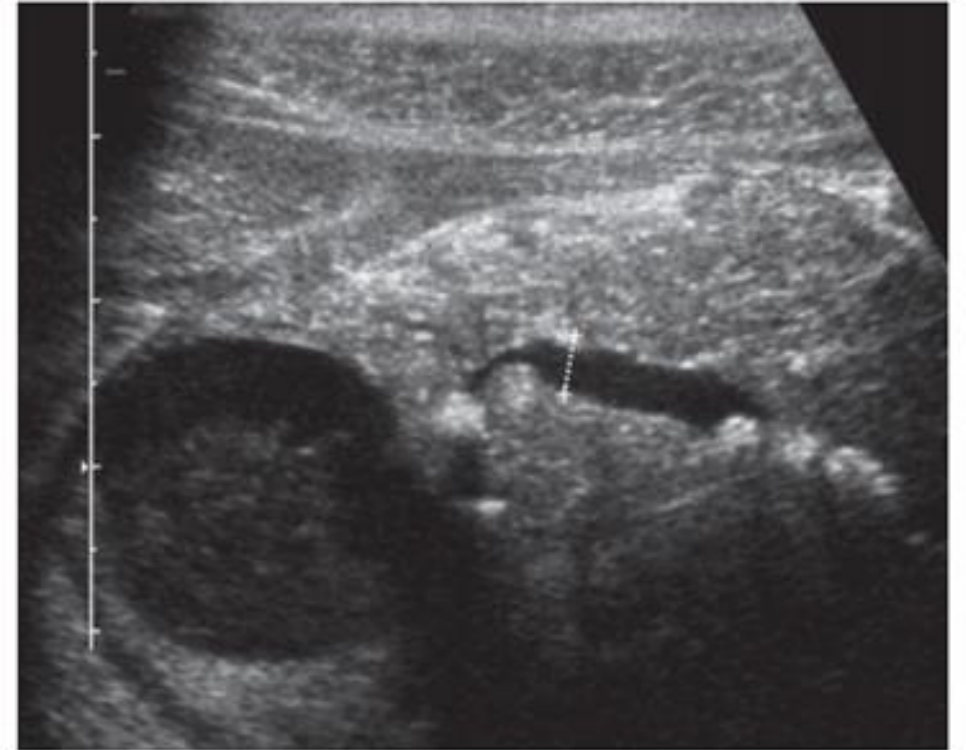
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**Figure 3** Plain X-ray of the abdomen showing diffuse calcification of the pancreas with advanced chronic pancreatitis.

# TRANSABDOMINAL ULTRASONOGRAPHY

- 48%-96%(Advance CP)
- Irregular contour (lobulation)
- Pancreatic duct dilation and irregularity of the main pancreatic duct
- Loss or reduction of pancreatic parenchyma echogenicity (echo-poor or echo-rich)
- Cysts or cavities
- Pancreatic calcifications



**FIGURE 57.6.** Transabdominal ultrasound showing typical changes of chronic pancreatitis. Note the multiple intrapancreatic calcifications and the dilated pancreatic duct. A large pseudocyst is also present in the region of the head of the pancreas.

# COMPUTED TOMOGRAPHY

- 80%
- Main pancreatic duct and secondary ductule dilation
- Intraductal calcifications
- Gland atrophy
- Cystic lesions

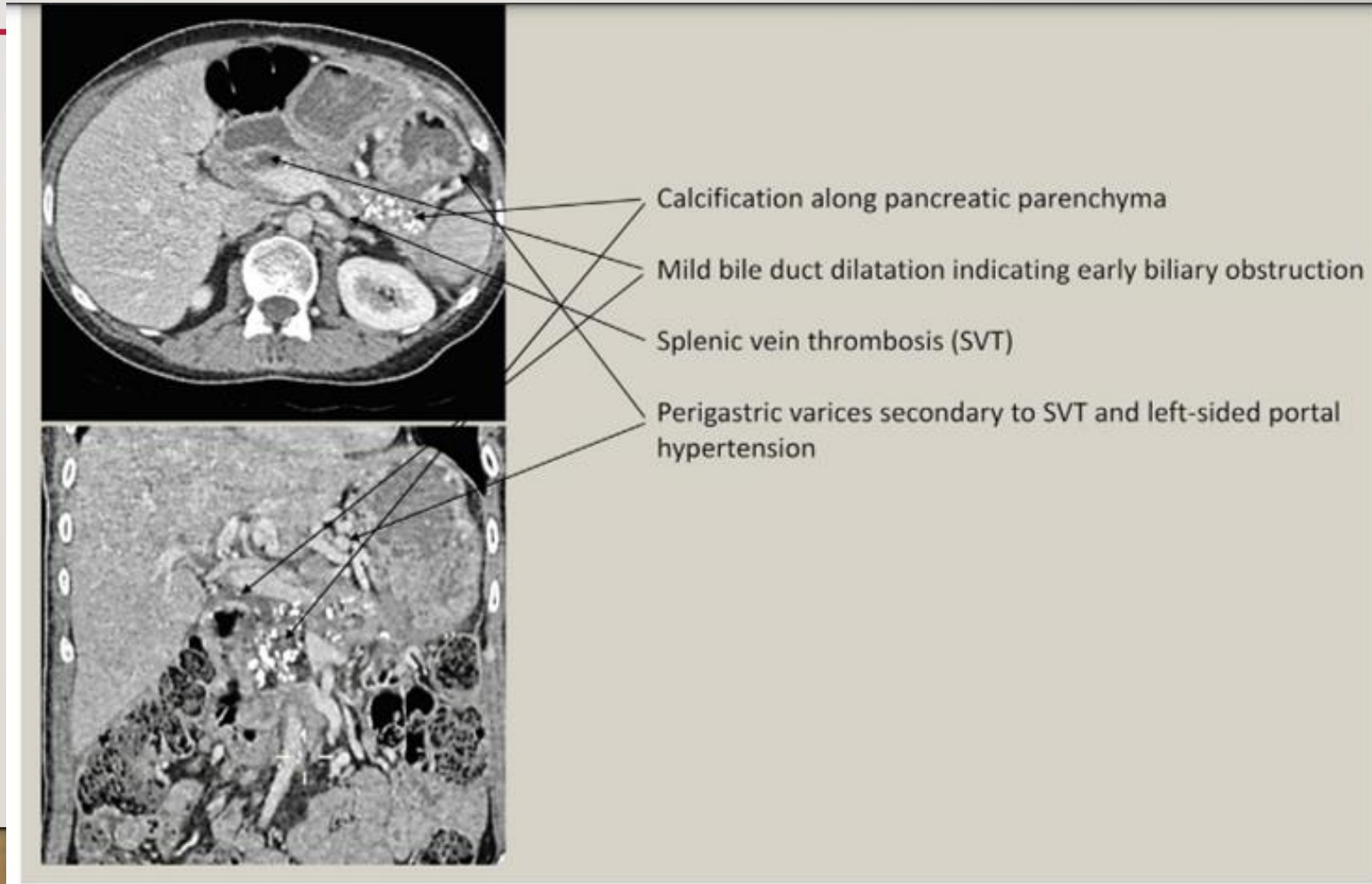


Figure 4 Axial and coronal reconstruction of a CT scan of a patient with chronic pancreatitis.

# ENDOSCOPIC RETROGRADE PANCREATOGRAPHY

**TABLE 57.4 Cambridge Criteria of Chronic Pancreatitis**

Stage	Typical Changes
Normal	Normal appearance of side branches and main pancreatic duct
Equivocal	Dilation or obstruction of less than three side branches; normal main pancreatic duct
Mild	Dilation or obstruction of more than three side branches; normal main pancreatic duct
Moderate	Additional stenosis and dilation of main pancreatic duct
Severe	Additional obstructions, cysts, and stenosis of main pancreatic duct; calculi

From Axon AT, et al: Pancreatography in chronic pancreatitis: international definitions. Gut 25:1107-1112, 1984.



This endoscopic retrograde cholangiopancreatography (ERCP) shows advanced chronic pancreatitis. The pancreatogram has blunting of the lateral branches, dilation of the main pancreatic duct, and filling defects consistent with pancreatolithiasis. The cholangiogram also shows a stenosis of the distal bile duct and a dilated biliary tree.



# ENDOSCOPIC ULTRASONOGRAPHY

## Rosemont criteria for chronic pancreatitis

Major Criteria	Minor Criteria
<p><i>Major Criteria A</i></p> <p>Hyperechoic foci with posterior acoustic shadow</p> <p>Lithiasis in main pancreatic duct</p>	<p>Cysts</p> <p>Ductal dilation greater than 3.5 mm</p> <p>Irregular Wirsung Duct</p> <p>Dilation of secondary branches greater than 1 mm</p> <p>Hyperechoic walls of Wirsung duct</p>
<p><i>Major Criteria B</i></p> <p>Honeycomb pattern of lobularity</p>	<p>Fibrous tracts</p> <p>Hyperechoic foci without posterior acoustic shadow</p> <p>Lobularity without honeycomb pattern</p>

## EUS diagnosis for Chronic Pancreatitis based on Rosemont criteria

I. CP diagnosis	<p>A. 1 major A criteria + <math>\geq 3</math> minor criteria</p> <p>B. 1 major A criteria + major B criteria</p> <p>C. 2 major A criteria</p>
II. CP suggestive	<p>A. 1 major A criteria + <math>&lt; 3</math> minor criteria</p> <p>B. 1 major B criteria + <math>\geq 3</math> minor criteria</p> <p>C. <math>\geq 5</math> minor criteria (anyone)</p>
III. Undetermined for CP	<p>A. 3 to 4 minor criteria, no major criteria</p> <p>B. Major B criteria just or with <math>&lt; 3</math> minor criteria</p>
IV. Normal	2 minor criteria, no major criteria

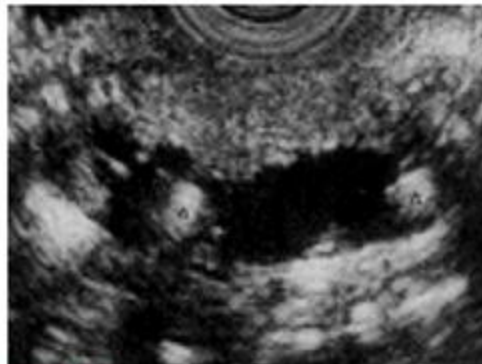


FIGURE 57.13. Endoscopic ultrasound in 54-year-old patient with chronic pancreatitis as a result of alcohol abuse. Note the marked

Gastroenterologist July 2018

# MAGNETIC RESONANCE IMAGING AND CHOLANGIOPANCREATOGRAPHY

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- Evaluate for periductal fibrosis
- Ductal dilation with ectasia and side-branch abnormalities
- Intraparenchymal cyst formation
- Pancreatic duct strictures and stones leading to obstructed outflow
- Especially useful to detect early parenchymal changes suggestive of CP

# TESTS OF EXOCRINE PANCREATIC FUNCTION

- Faecal Elastase (PE-I)

PEI/Pancreatic Function	Faecal Elastase
Normal	>500ug
Suboptimal	200-500ug
Mild - Moderate	100-200ug
Severe	<100ug

- Mild PEI → reduced secretion of one or more enzymes with normal bicarbonate concentration
- Moderate PEI → reduced enzyme output and bicarbonate concentration but normal faecal fat excretion
- Severe PEI → reduced enzyme output and bicarbonate concentration plus steatorrhea

Clinical and Experimental  
Gastroenterology 2011;4  
55-73

# TREATMENT

## I. Confirm Diagnosis

### Make a correct diagnosis

- Appropriate history
- Corroborating imaging tests
  - MRI/MRCP
  - EUS
  - CT
- Functional tests if imaging tests equivocal
  - Tube-based secretin test
  - Endoscopic-based secretin test
- Assess for alternative diseases and complications and treat if present
  - Pancreatic cancer or IPMN
  - Pseudocyst
  - Bile duct obstruction
  - Duodenal obstruction

Schwartz  
11<sup>th</sup> ed

# TREATMENT

## 2. Medical therapy

### Medical therapy

- Measure pain severity, character, and impact on QOL
- Refer for formal structured smoking and alcohol cessation programs
- Counsel on good nutrition and initiate supplementation with vitamin D and calcium
  - Baseline bone mineral density testing
- Provide information on local and national support groups
- Initiate analgesics (starting with Tramadol)
  - Increase dose and potency slowly as required
- Initiate adjunctive agents in those with persistent pain or requiring higher dosages or potency of narcotics
  - Pregabalin, Gabapentin
  - SSRI
  - SSNRI
  - Tricyclic antidepressants
- Assess for evidence of coexistent exocrine or endocrine insufficiency and treat if present
  - Fecal elastase or serum trypsin
  - HgB A1C or GTT
- Initiate steroids if autoimmune pancreatitis

Schwartz  
11<sup>th</sup> ed

# PERT

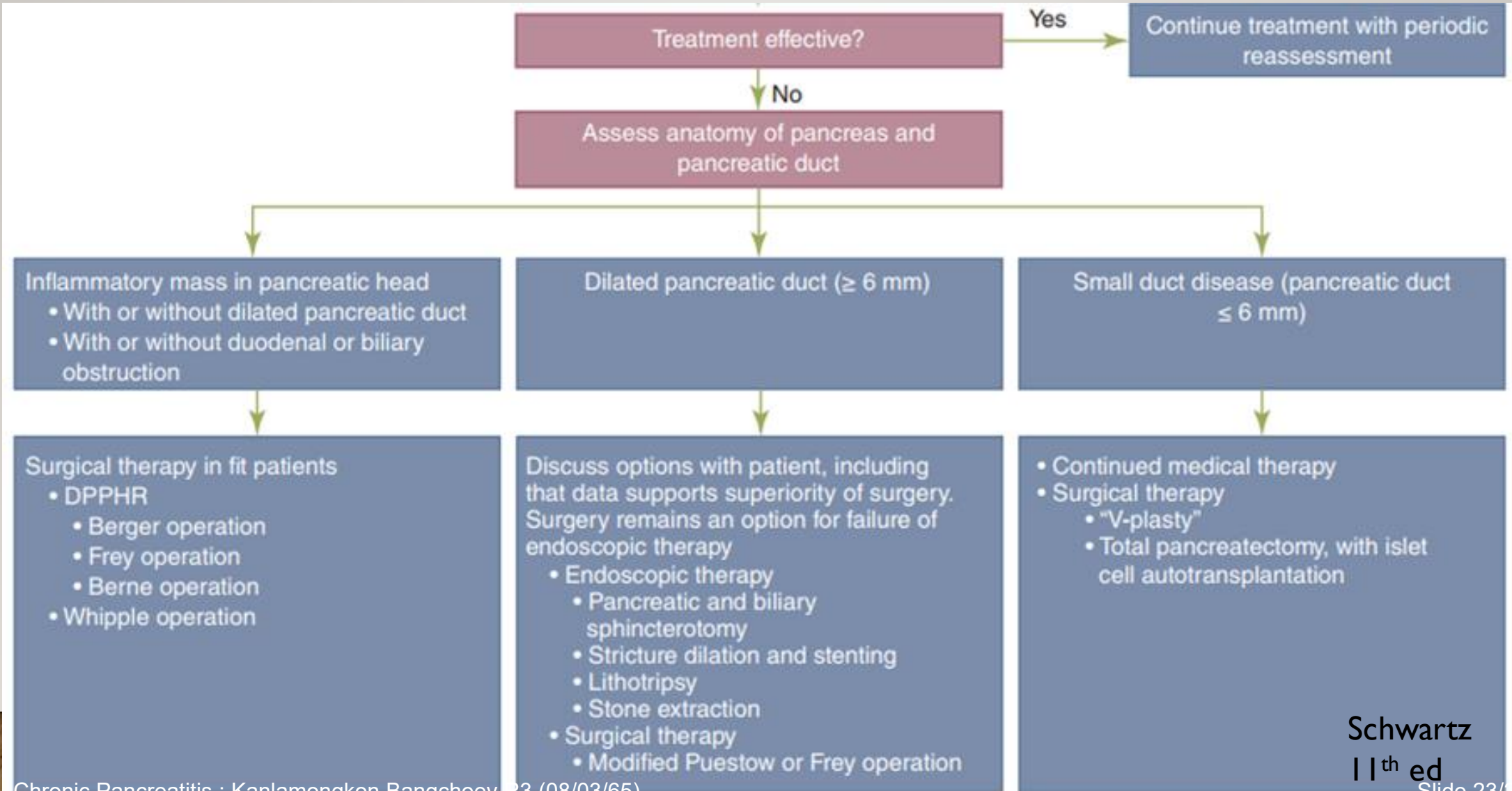
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- 20,000 to 40,000 units as a starting dose for a meal
- 10,000 to 20,000 lipase units for a snack

## Pancreatic Enzyme Replacement Therapy (PERT)



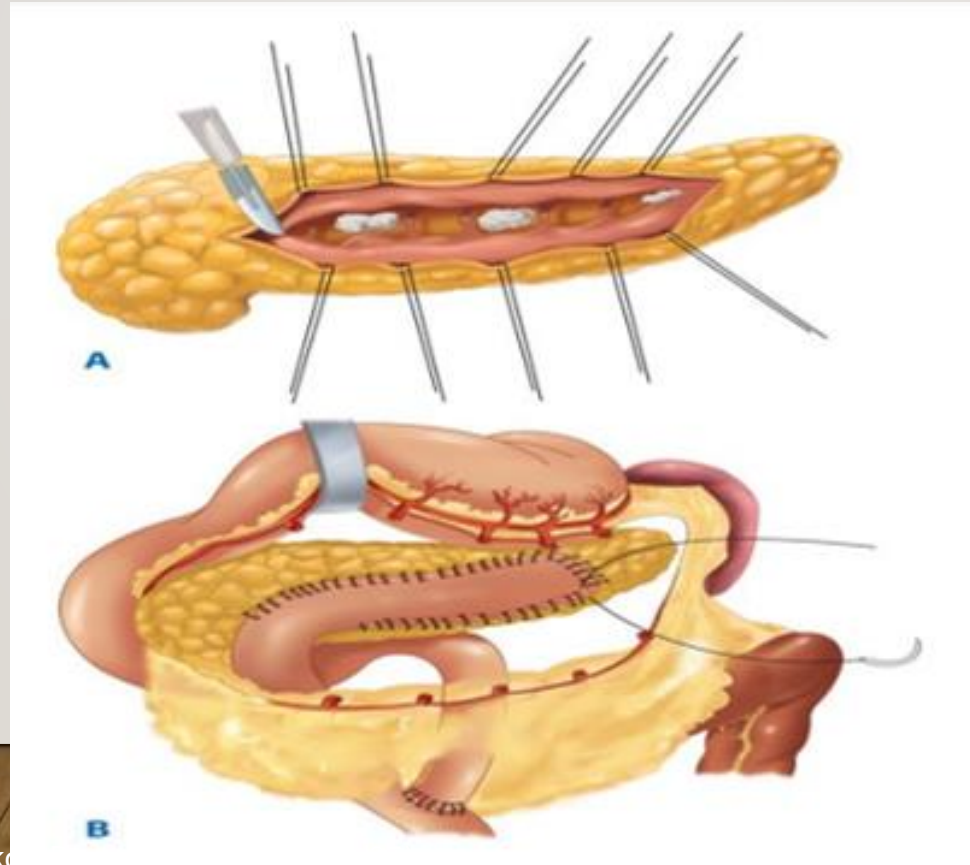
# TREATMENT



# DRAINAGE PROCEDURE

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- Modified Puestow's Operation (Partington & Rochell's procedure)

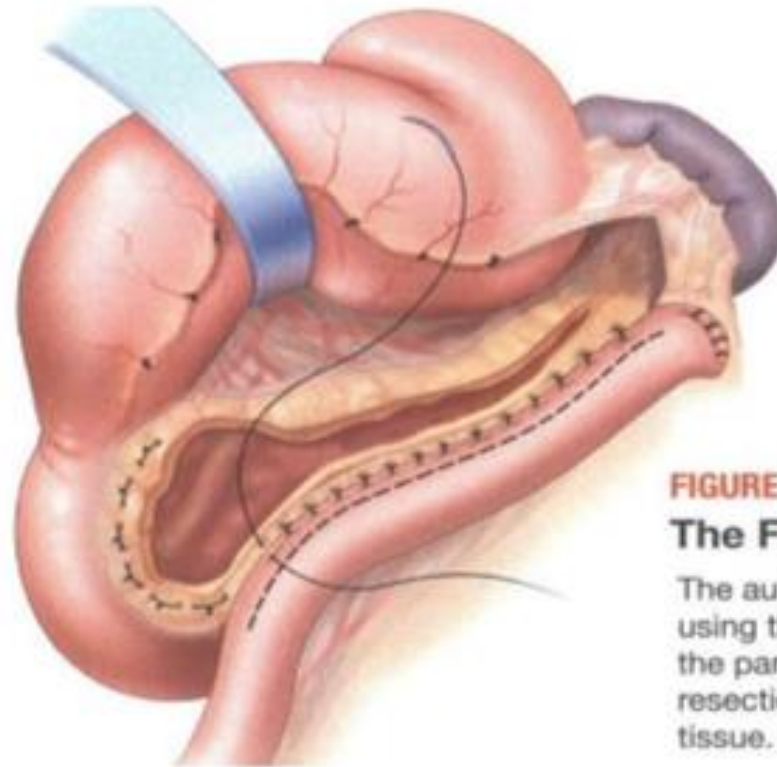




# DRAINAGE PROCEDURE

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- Frey's Operation



**FIGURE 1**

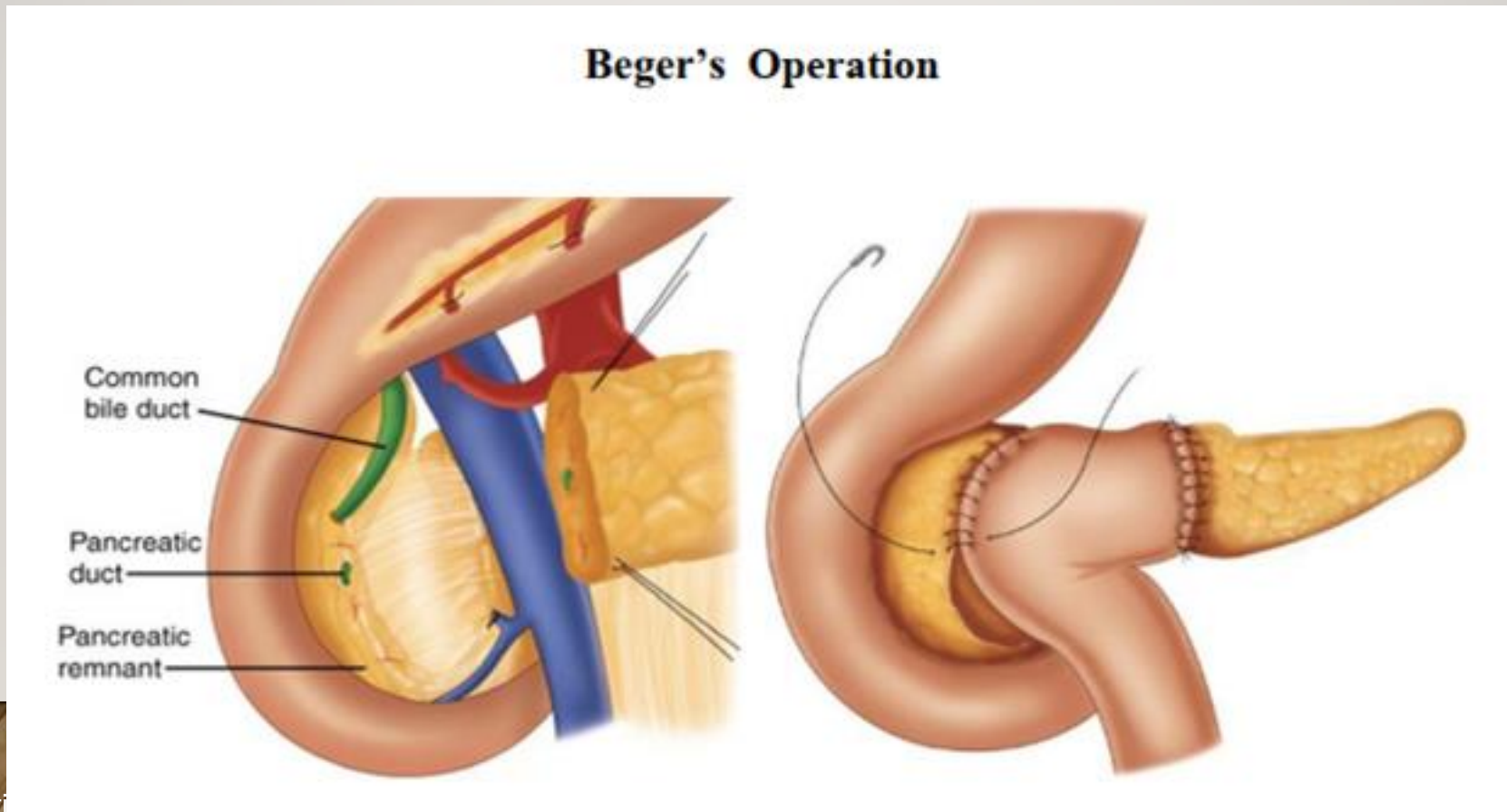
## **The Frey procedure**

The authors prefer this approach using the longitudinal opening of the pancreatic duct and conization resection of diseased pancreatic tissue. (Illustrations by Rob Flewell)

# RESECTION PROCEDURE

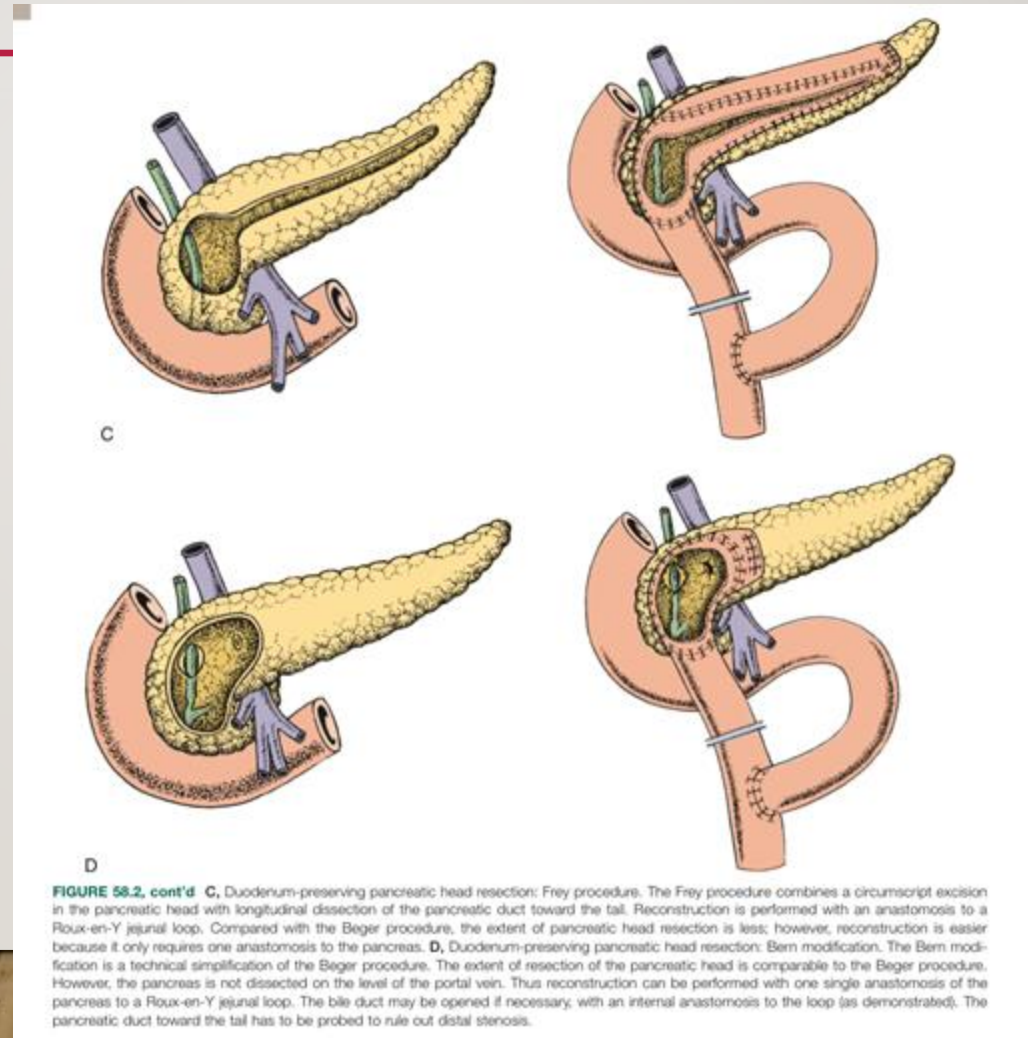
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- Beger's Operation



# RESECTION PROCEDURE

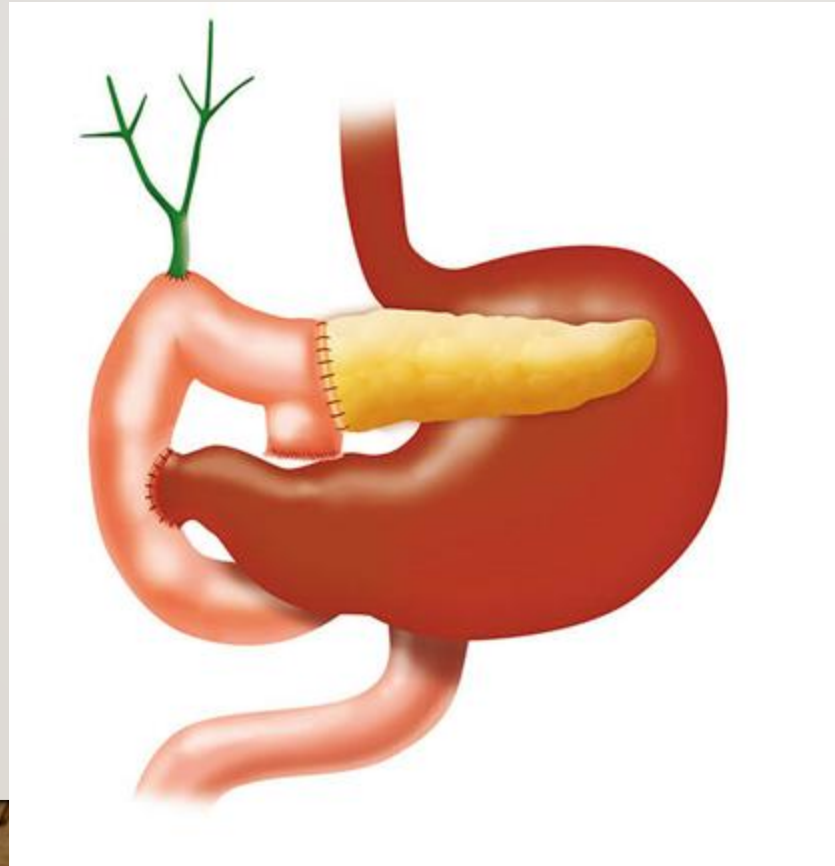
## Bern's Operation



# RESECTION PROCEDURE

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## Whipple Operation



# RESECTION PROCEDURE

- V-Shape excision

