

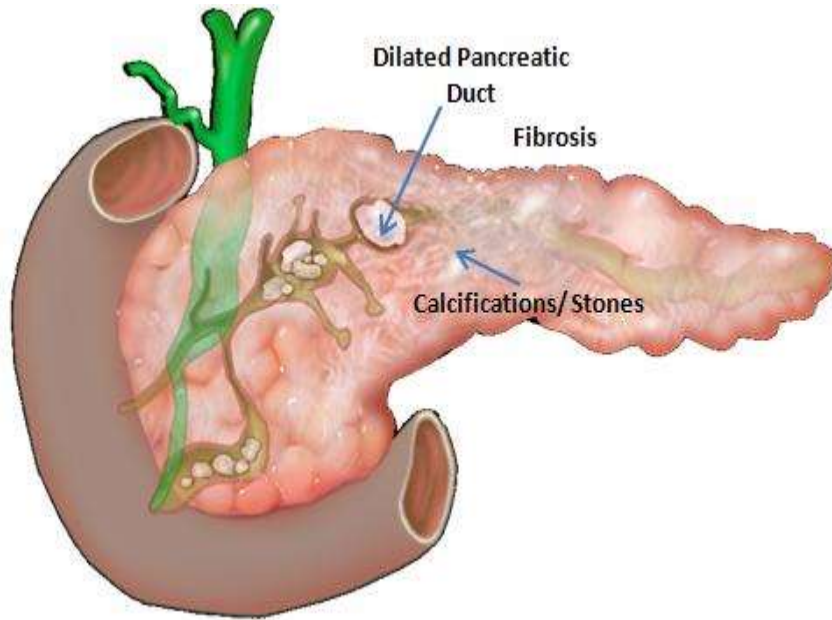
Supportive module 2: Basics of diagnosis, treatment  
and prevention of major gastroenterological diseases

# Chronic Pancreatitis

LECTURE IN INTERNAL MEDICINE FOR IV COURSE STUDENTS

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# Plan of the Lecture



- Definition
- Epidemiology
- Mechanisms
- Classification
- Clinical presentation
- Diagnosis
- Treatment
- Prognosis
- Prophylaxis
- Abbreviations
- Diagnostic guidelines

# US MLE TEST

## **Pancreatic disorders**

Acute Pancreatitis

Chronic Pancreatitis

Annular Pancreas

Pancreatic Pseudocysts

**Qbank (0 Questions)**

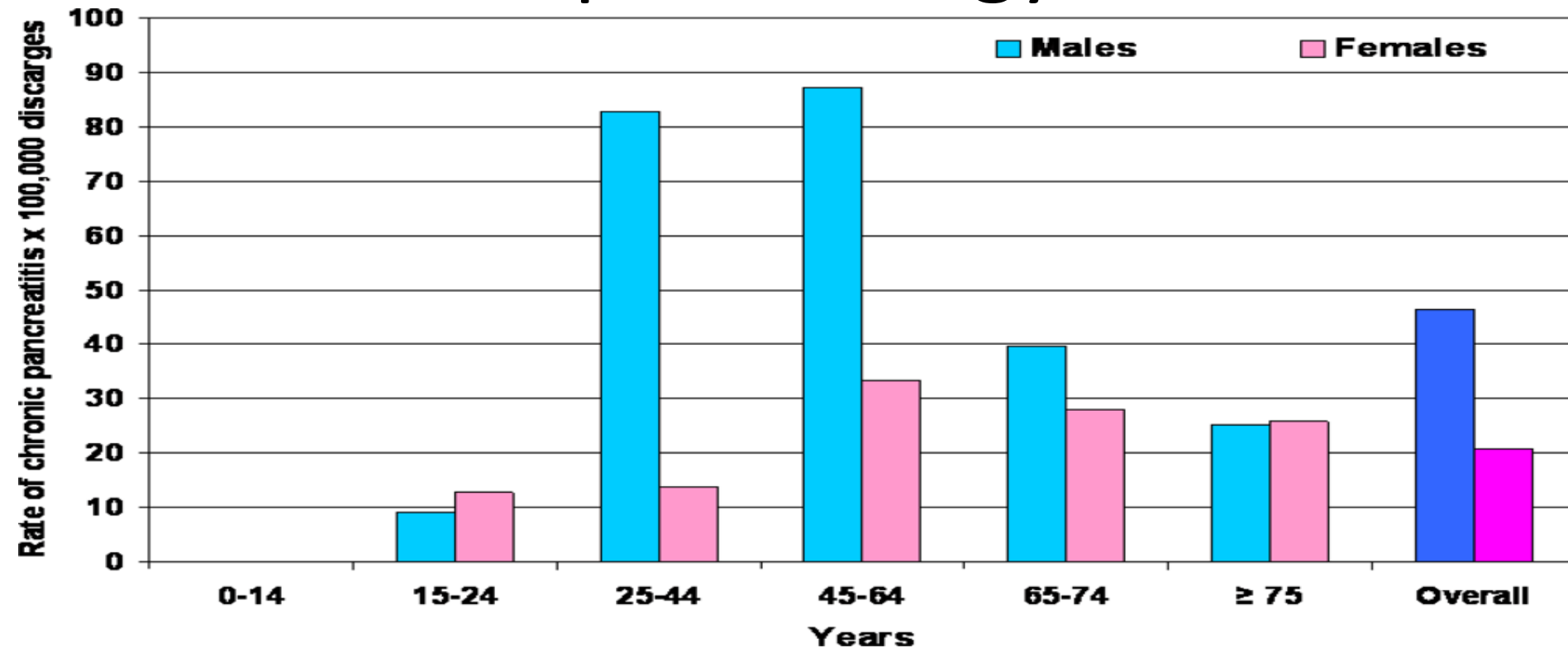
# Definition

Chronic pancreatitis (CP) is characterized by chronic progressive pancreatic inflammation and scarring with pancreatic parenchymal calcifications, dilations of pancreatic ducts, stones and pseudocyst irreversibly damaging the pancreas function by various etiological factors with usually recurrent upper abdominal pain or as constant and disabling pain and/or pancreatic exocrine and endocrine insufficiency.

# Epidemiology

- The annual incidence of CP is 5 to 12 per 100,000 persons, the prevalence is 50 per 100,000 persons
- The prevalence of CP was 42/100000 in the USA, 26/100000 in France, 22/100000 in Japan, and 114-200/100000 in India (the highest), respectively
- In China, an investigation on 2008 patients with CP from 22 hospitals from 1994 to 2004 showed that the incidence was 13/100000 and an increasing trend was seen.

# Epidemiology



Rate of patients discharged from the Italian hospitals in the year 2005 having the diagnosis of chronic pancreatitis and stratified according to gender and age.

# Risk Factors & Etiology 1

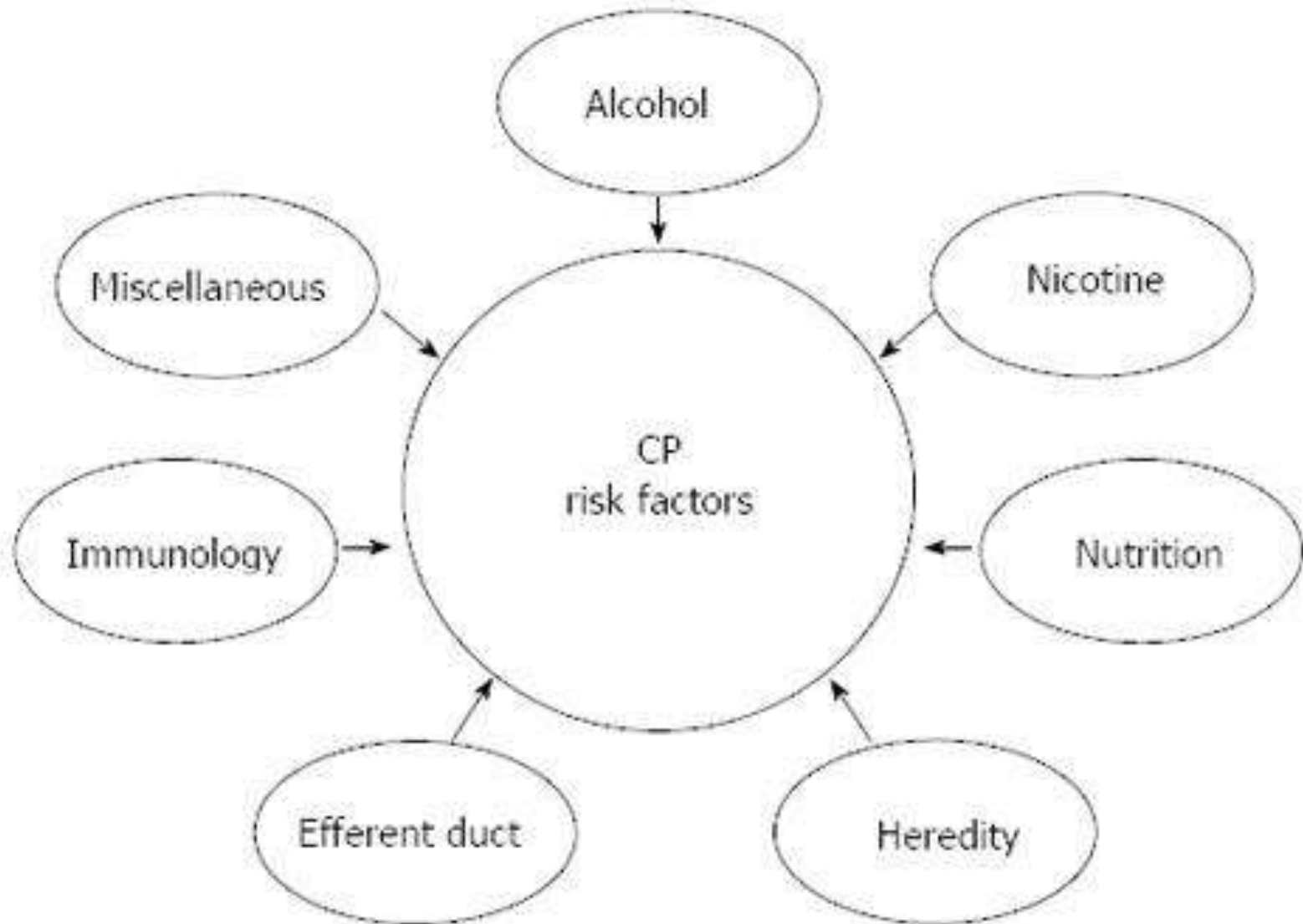
- In the Western world CP is commonly associated with excessive consumption of alcohol
- About 20% of cases are considered idiopathic CP
- About 10% of cases are associated with duct obstruction, trauma, cystic dystrophy of the duodenal wall, hyperparathyroidism, hypertriglyceridemia, autoimmune deviations, etc.
- Other important aspects are the role of cigarette smoking on CP evolution

# Risk Factors & Etiology 2

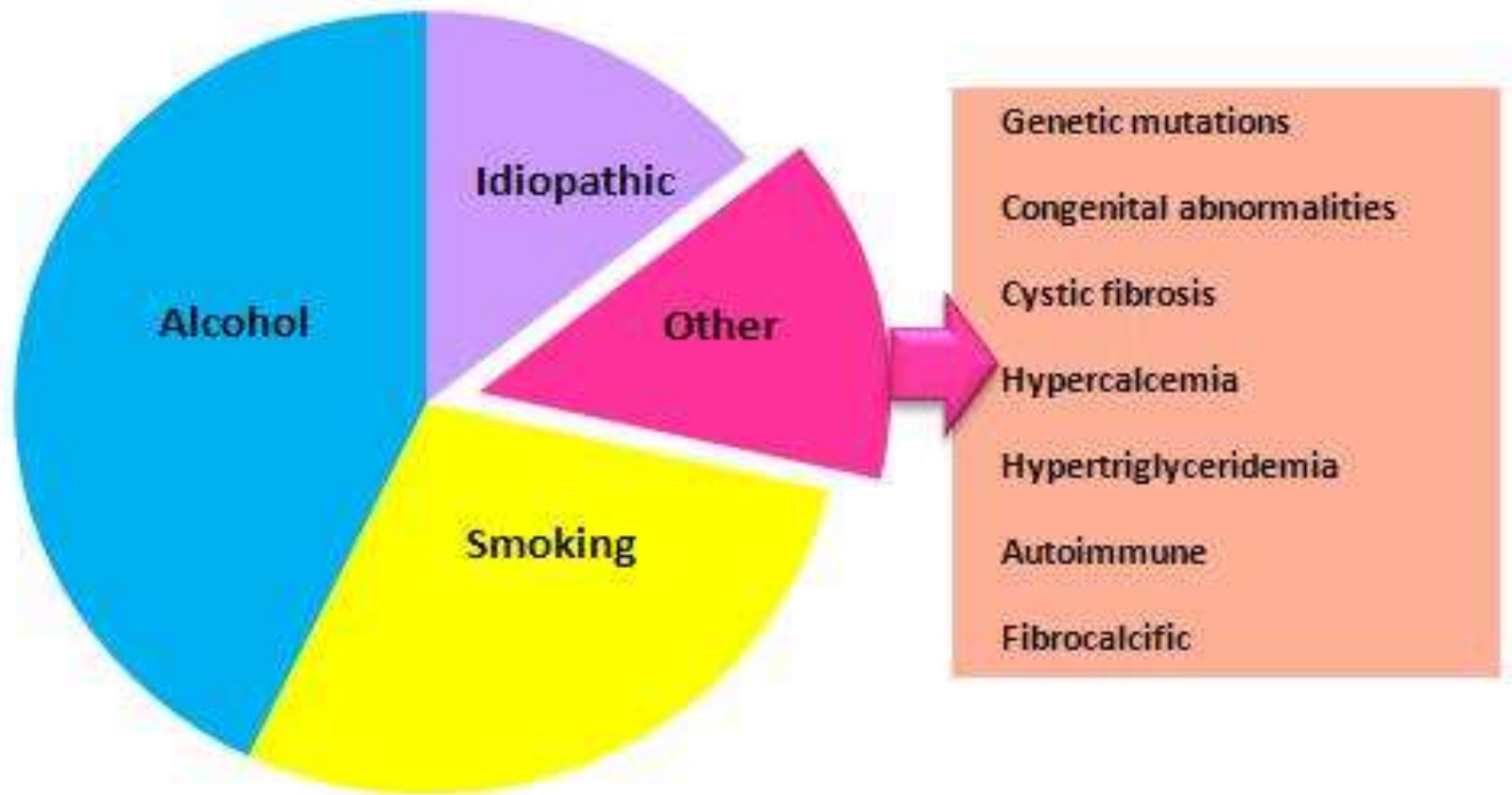
- Some genes and various gene polymorphisms are able to increase susceptibility to develop CP in alcoholics through an increase of pancreatic progressive damage
- Most patients have multiple risk factors and the overall risk is a product of all risk factors in additive or multiplicative fashion.



# Risk Factors & Etiology



# Risk Factors & Etiology



Causes of chronic pancreatitis.

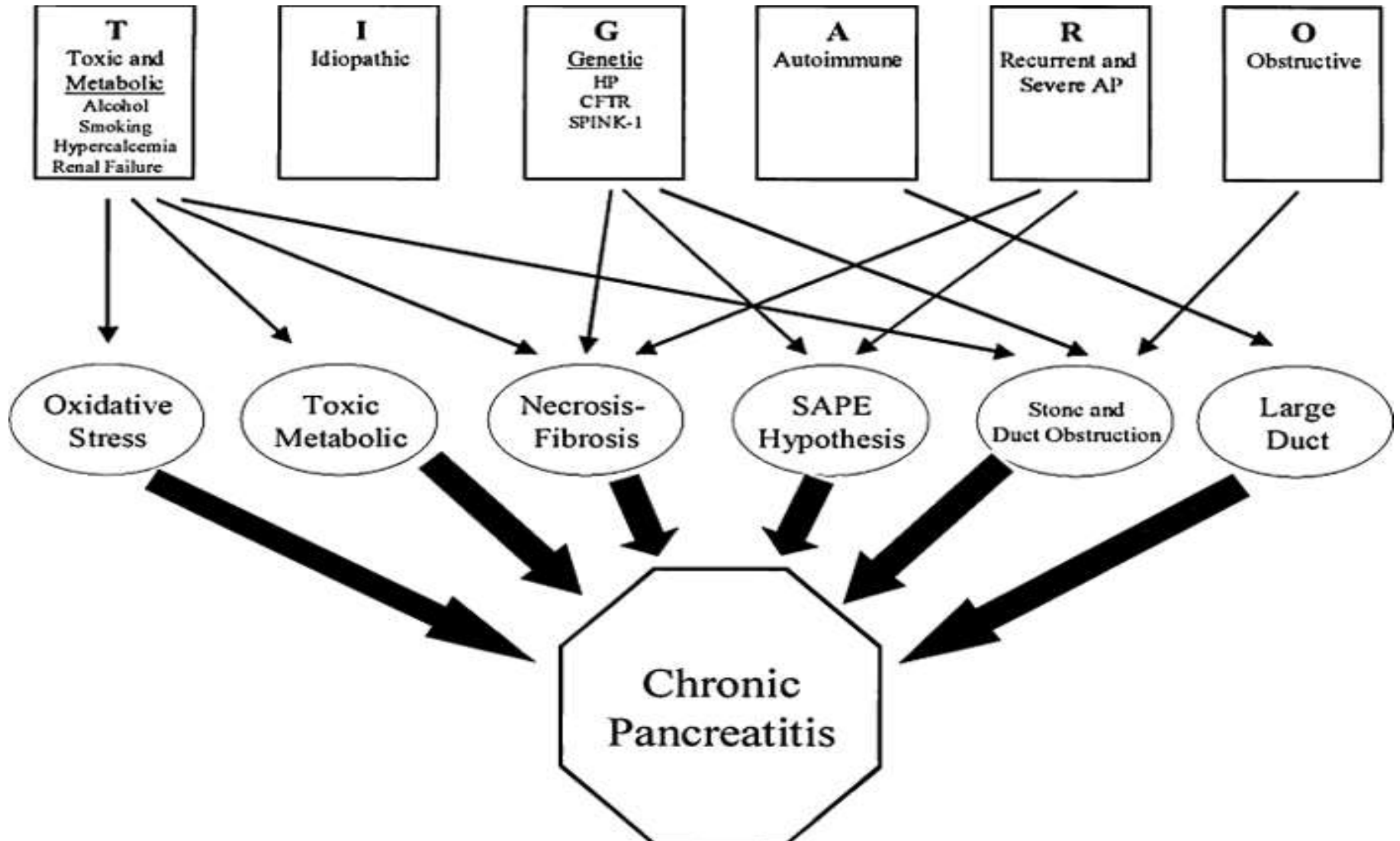
# Mechanism 1

- Most studies of the pathophysiology of CP are performed with patients who drink alcohol
- Disease characteristics include inflammation, glandular atrophy, ductal changes, and fibrosis
- When a person at risk is exposed to toxins and oxidative stress, acute pancreatitis occurs, and if the exposure continues, early- and late-phase inflammatory responses result in production of profibrotic cells, including the stellate cells; this can lead to chronic pancreatitis

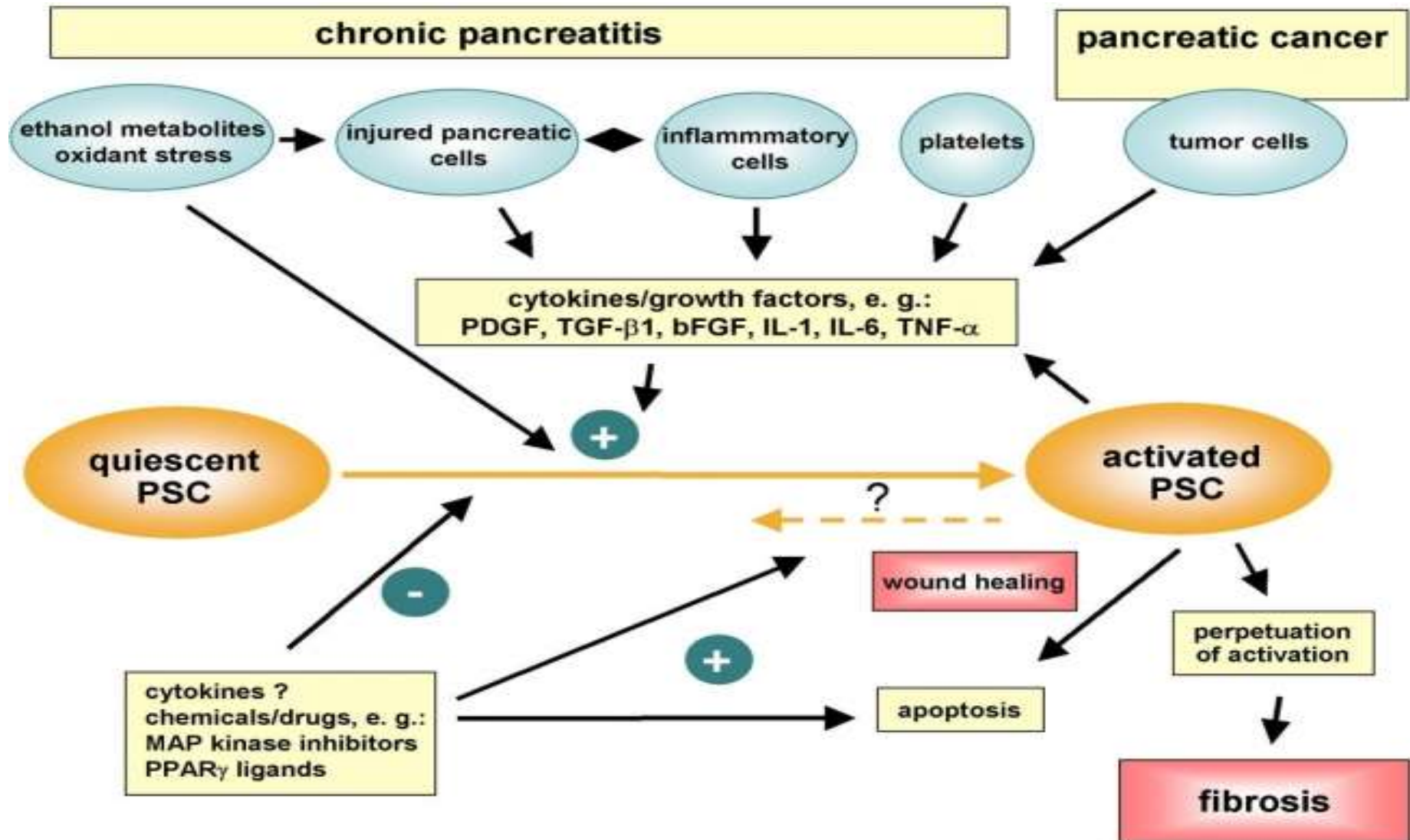
# Mechanism 2

- In addition, several genetic mutations have been associated with idiopathic CP
- Autoimmune pancreatitis accounts for 5 to 6 percent of CP and is characterized by autoimmune inflammation, lymphocytic infiltration, fibrosis, and pancreatic dysfunction.

# Mechanism



# Mechanism



# Classification

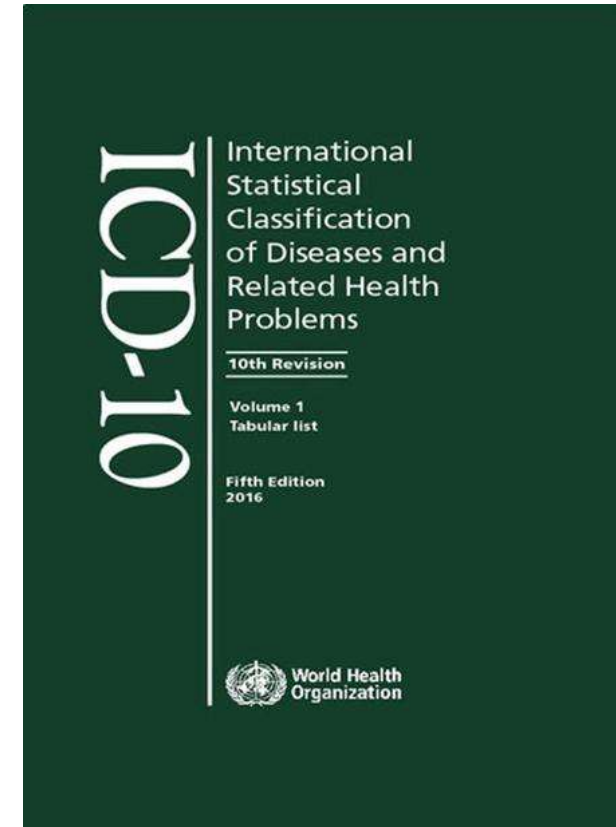
## International Classification of Diseases

XI Diseases of the digestive

K86 Other diseases of  
pancreas

K86.0 Alcohol-induced  
chronic pancreatitis

K86.1 Other chronic  
pancreatitis



# Classification

## Morphology

- A large-duct type
  - With calcification
  - Without calcification
- A small-duct type with or without calcification
  - With calcification
  - Without calcification



# Cronic Pancreatitis

## BMJ best practice

A 41-year-old alcoholic man has a 6-year history of recurrent attacks of pancreatitis characterised by epigastric pain radiating to the back. The initial attack required hospitalization for severe pain, and clinical chemistry showed a >15-fold elevation in serum amylase and lipase. Subsequent attacks were less severe, managed primarily as an outpatient, and lasted less than 10 days, with long symptom-free intervals. After detoxification 6 months ago he had no further attacks, but has recently developed evidence of diabetes and steatorrhoea. CT imaging shows pancreatic calcifications but no cystic or mass lesions.

# Signs and Symptoms 1

- For most patients with CP, abdominal pain is the presenting symptom.
- The patient experiences intermittent attacks of severe pain, often in the mid-abdomen or left upper abdomen and occasionally radiating in a bandlike fashion or localized to the midback .

# Signs and Symptoms 2

- The pain may occur either after meals or independently of meals, but it is not fleeting or transient and tends to last at least several hours
- Other symptoms associated with chronic pancreatitis include diarrhea and weight loss.

# History 1

- For most patients, abdominal pain is the presenting symptom
- Clinically, the patient experiences intermittent attacks of severe pain, often in the midabdomen or left upper abdomen and occasionally radiating in a bandlike fashion or localized to the midback

# History 2

- The pain may occur either after meals or independently of meals, but it is not fleeting or transient and tends to last at least several hours  
Patients often are symptomatic for years before the diagnosis is established
- Diarrhea and weight loss may be due either to fear of eating (e.g., postprandial exacerbation of pain) or due to pancreatic exocrine insufficiency and steatorrhea.

# Physical Exam 1

- In most instances, the standard physical examination does not help to establish a diagnosis of CP; however, a few points are noteworthy
- During an attack, patients may assume a characteristic position in an attempt to relieve their abdominal pain (e.g., lying on the left side, flexing the spine and drawing the knees up toward the chest)

# Physical Exam 2

- Occasionally, a tender fullness or mass may be palpated in the epigastrium, suggesting the presence of a pseudocyst or an inflammatory mass in the abdomen
- Patients with advanced disease (i.e., patients with steatorrhea) exhibit decreased subcutaneous fat, temporal wasting, sunken supraclavicular fossa, and other physical signs of malnutrition.

# Complications

- Pseudocysts
- Biliary Obstruction
- Gastric Outlet Obstruction
- Pancreatic Adenocarcinoma
- Pancreatic Ascites
- Pleural effusion
- Splenic vein thrombosis



# Cronic Pancreatitis

## BMJ best practice

We described a 45-year-old previously healthy man presenting with progressively worsening breathlessness for 10 days. Physical examination was suggestive of a left-sided pleural effusion. A chest X-ray was confirmatory. Analysis of aspirated fluid showed a lymphocytic exudate with grossly elevated amylase and lipase levels. CT revealed chronic calcific pancreatitis as the underlying cause of effusion. Retrospective questioning failed to identify classical symptoms of chronic pancreatitis including abdominal pain and steatorrhoea. The patient was managed with intercostal drainage and supportive care. Although unusual, chronic pancreatitis should be kept as a differential diagnosis in patients with unilateral exudative pleural effusion. Elevated fluid levels of amylase and lipase are useful clues to this uncommon diagnosis.

# Diagnosis 1

- The definitive diagnosis of CP is sometimes difficult, especially if the disease is not considered by the physicians treating the patient

## Diagnosis 2

- CP is suspected, based on signs, symptoms, and laboratory results, including history taking, physical examination, determination methods for pancreatic enzymes in the blood and urine, significance of various imaging methods [radiography, ultrasonography, computed tomography (CT), magnetic resonance imaging (MRI), endoscopic ultrasound, and pancreatography], exocrine pancreatic function testing, pathological diagnosis, differential diagnosis from pancreatic cancer and intraductal papillary mucinous neoplasm (IPMN), and genetic testing.

# Diagnosis

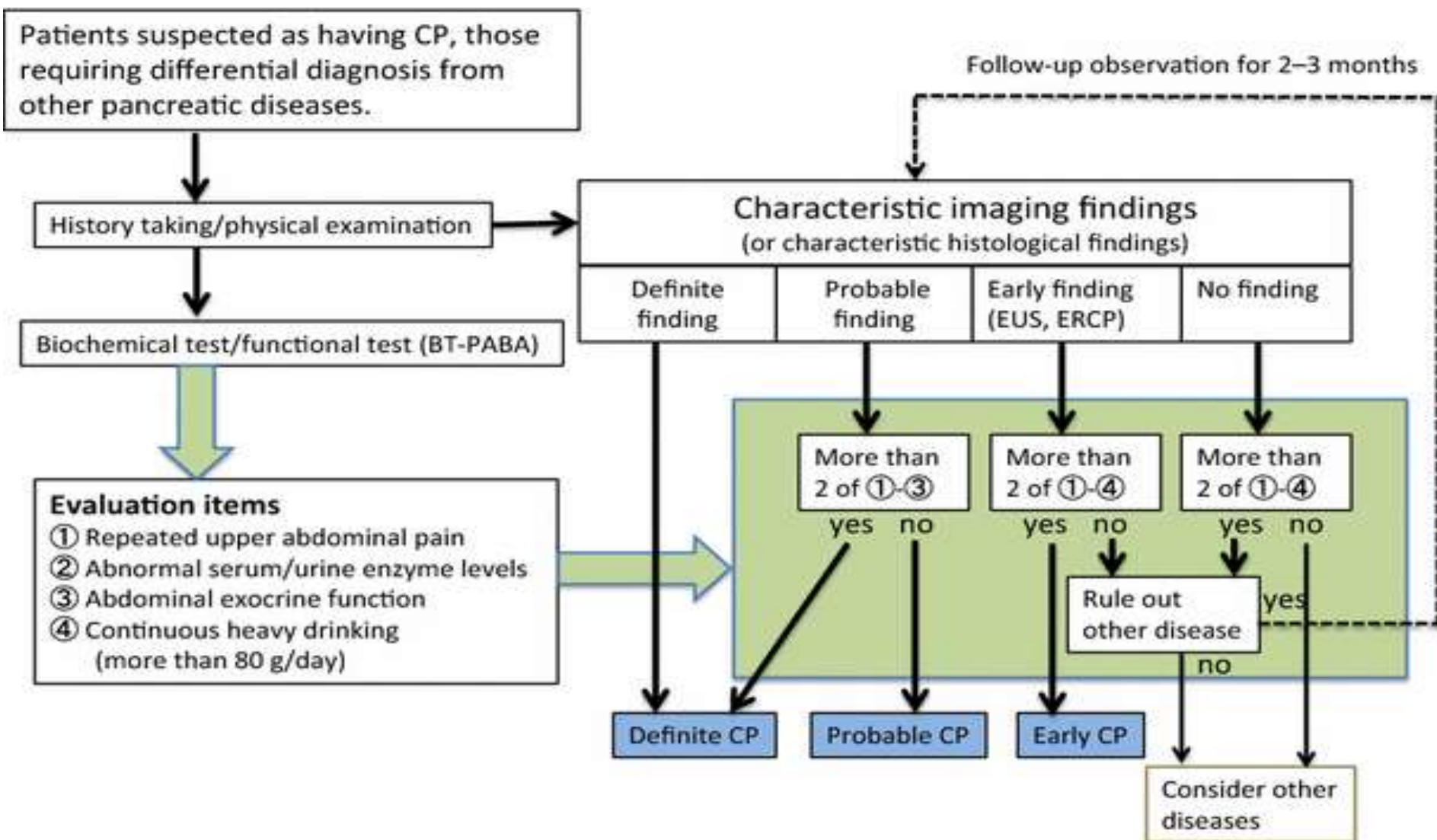
## Laboratory Tests

Tests	Comments
Complete blood count	Elevated with infection, abscess
Serum amylase and lipase	Nonspecific for chronic pancreatitis <sup>1,2,16,18</sup>
Total bilirubin, alkaline phosphatase, and hepatic transaminase	Elevated in biliary pancreatitis and ductal obstruction by strictures or mass <sup>16</sup>
Fasting serum glucose	Elevation suggests pancreatic diabetes <sup>2</sup>
Pancreatic function tests	Sometimes useful in early chronic pancreatitis with normal computed tomography or magnetic resonance imaging <sup>1,2,5,19,20</sup>
Fecal fat estimation	> 7 g fat per day is abnormal; quantitative; requires 72 hours; should be on a diet of 100 g fat per day <sup>1,2,5</sup>
Fecal elastase	< 200 mcg per g (0.20 g per kg) of stool is abnormal; noninvasive; exogenous pancreatic supplementation will not alter results; requires only 20 g of stool <sup>2,5,19</sup>
Secretin stimulation	Peak bicarbonate concentration < 80 mEq per L (80 mmol per L) in duodenal secretion; best test for diagnosing pancreatic exocrine insufficiency <sup>1,2,5,20</sup>
Serum trypsinogen	< 20 ng per mL (0.83 nmol per L) is abnormal <sup>2,5</sup>
Lipid panel	Significantly elevated triglycerides are a rare cause of chronic pancreatitis <sup>2</sup>
Calcium	Hyperparathyroidism is a rare cause of chronic pancreatitis <sup>2</sup>
Immunoglobulin G4 serum antibody, antinuclear antibody, rheumatoid factor, erythrocyte sedimentation rate	Abnormality may indicate autoimmune pancreatitis <sup>10</sup>

*note: The tests are listed in order from most to least commonly performed.  
Information from references 1, 2, 5, 10, 16, and 18 through 20.*

# Diagnosis

## Diagnostic Path



# Diagnosis

## Chronic Pancreatitis: Endoscopic Ultrasound Diagnosis based on Rosemont Classification

I. Consistent with chronic pancreatitis	1 major A feature plus 3 or more minor features 1 major A feature plus 1 major B feature 2 major A features
II. Suggestive of CP	1 major A feature plus 3 minor features 1 major B feature with or without plus 3 minor features 5 or more minor features (any)
III. Indeterminate for CP	3 to 4 minor features, no major features Major B feature alone or with < 3 minor features
IV. Normal	Less than 2 minor features, no major features

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

# Diagnosis 1

## Staging

- CP generally first presents with repeated upper abdominal and back pain, and endocrine and exocrine pancreatic function gradually deteriorates
- In Japan, the disease is classified into three phases: compensated, transitional, and uncompensated, depending on the stage; however, an early chronic pancreatitis category has been added before the compensated phase in this revision



# Diagnosis 2

## Staging

- Exocrine pancreatic disorder (that includes digestive and absorptive disorders) and abnormal glucose tolerance (pancreatic diabetes) occur as chronic pancreatitis progresses; therefore, to improve prognosis, pharmacological and nutritional therapies should be given in accordance with the stage of the disease
- In this regard, staging of chronic pancreatitis is important.



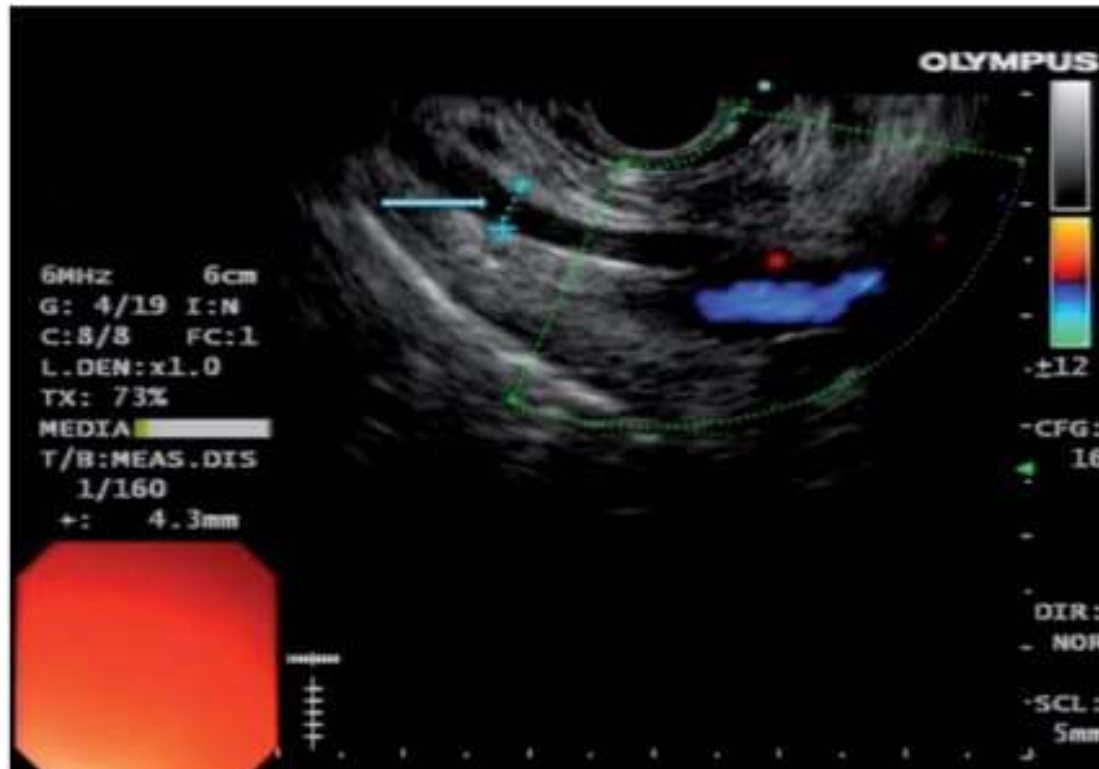
# Diagnosis

## Pancreatic Parenchymal Calcifications



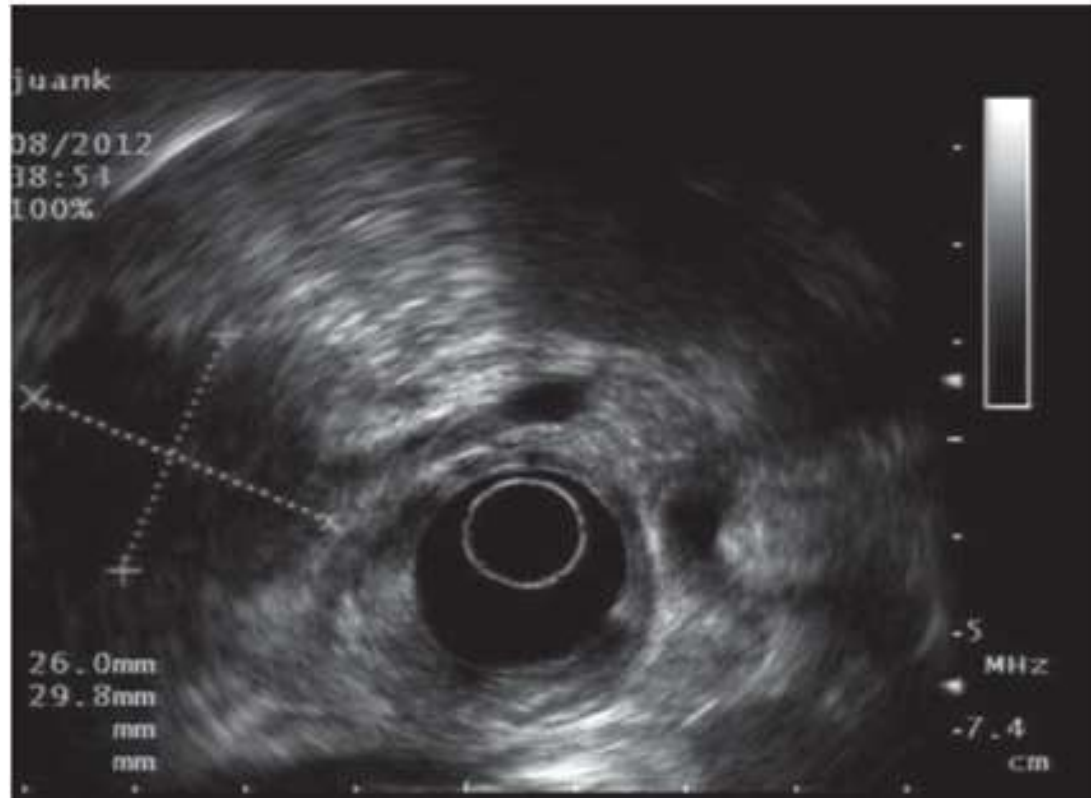
# Diagnosis

## Wirsung Duct Dilatation



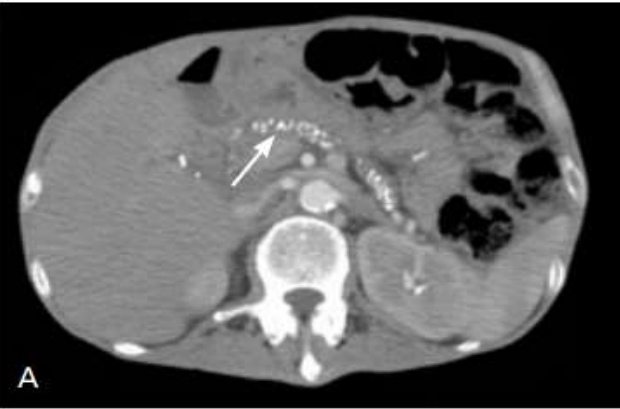
# Diagnosis

## Pseudotumoral CP



# Diagnosis

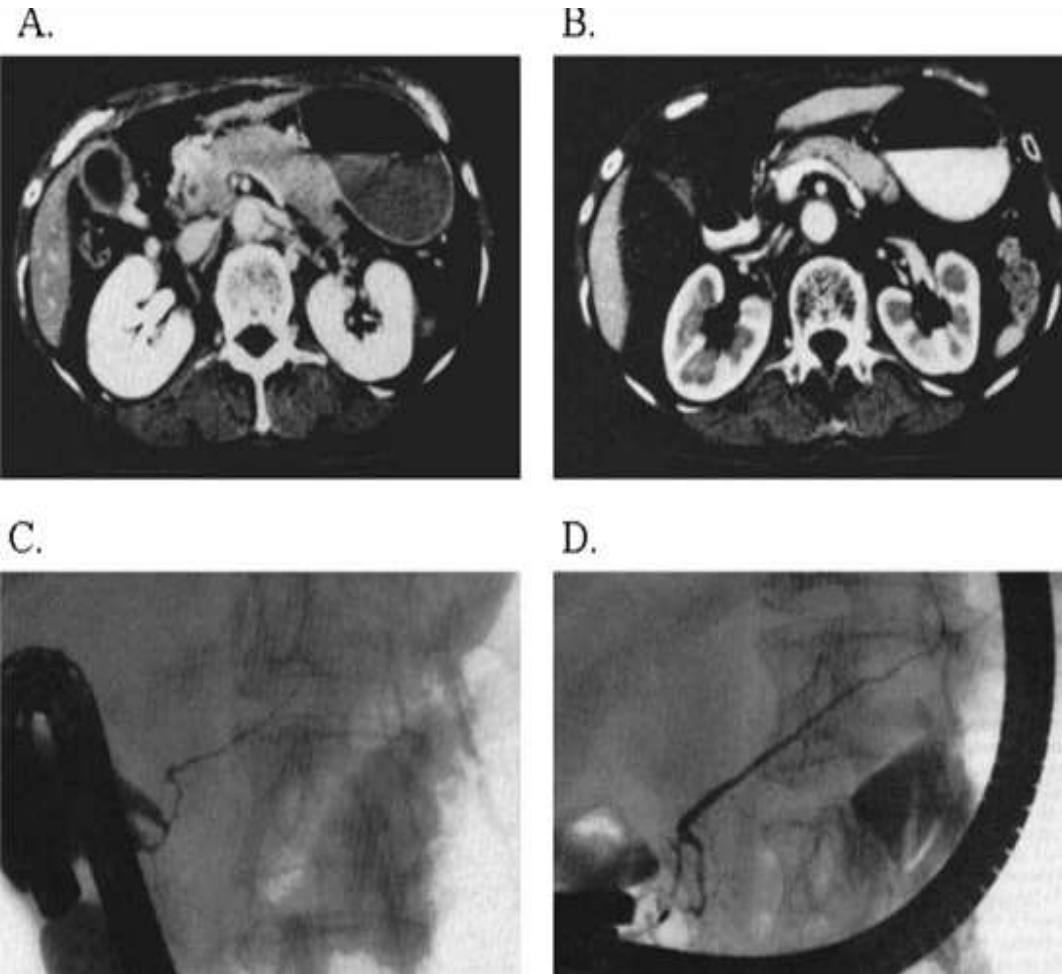
## Pancreatic Calcifications



Contrast-enhanced computed tomography of the upper abdomen showing (A) pancreatic calcifications (arrow) with fluid and edema around the pancreas; and (B) pancreatic calcifications (arrow) with fluid and edema around the head of the pancreas.

# Diagnosis

## Autoimmune Pancreatitis



Computer  
Tomography  
of  
Autoimmune  
Pancreatitis  
Before and  
After  
Treatment.

# Diagnosis

## Differentiation

- Ampullary carcinoma, cholangitis, cholecystitis
- Chronic gastritis
- Community-acquired pneumonia (CAP)
- Crohn disease
- Intestinal perforation
- Mesenteric artery ischemia
- Myocardial infarction
- Pancreatic cancer
- Peptic ulcer disease

# Management 1

The goals of medical treatment are as follows:

- Modify behaviors that may exacerbate the natural history of the disease (cessation of alcohol consumption and tobacco smoking are important)
- Control of pain (determine the cause of abdominal pain and alleviate it)

# Management 2

The goals of medical treatment are as follows:

- Improvement of maldigestion (enable the pancreas to heal itself, detect pancreatic exocrine insufficiency and restore digestion and absorption to normal, diagnose and treat endocrine insufficiency)
- Management of complications.



# Management

## Therapeutic Control of Pain 1

- Medical options for pain relief include abstinence from alcohol and smoking, analgesics, and pancreatic enzymes
- Non-narcotic analgesics (e.g., nonsteroidal anti-inflammatory drugs, acetaminophen, tramadol) are the next step in managing painful CP
- If pain persists, low doses of mild narcotics may be added

# Management

## Therapeutic Control of Pain 2

- Uncoated pancreatic enzymes may be worth trying in all patients because of their safety and minimal side effects
- Antidepressants, anticonvulsants (gabapentin), topical therapy, psychiatric counseling, and opioid rehabilitation may be of use for patients with nonvisceral pain.

# Management

## Improvement of Maldigestion 1

- Pancreatic enzymes are used for the treatment of maldigestion in CP
- Exogenous pancreatic enzymes are safe, are well tolerated, and produce few side effects
- Pancreatic enzyme preparations differ based on enzyme content, the use of microspheres versus microtablets, and the presence of a coating for delayed release

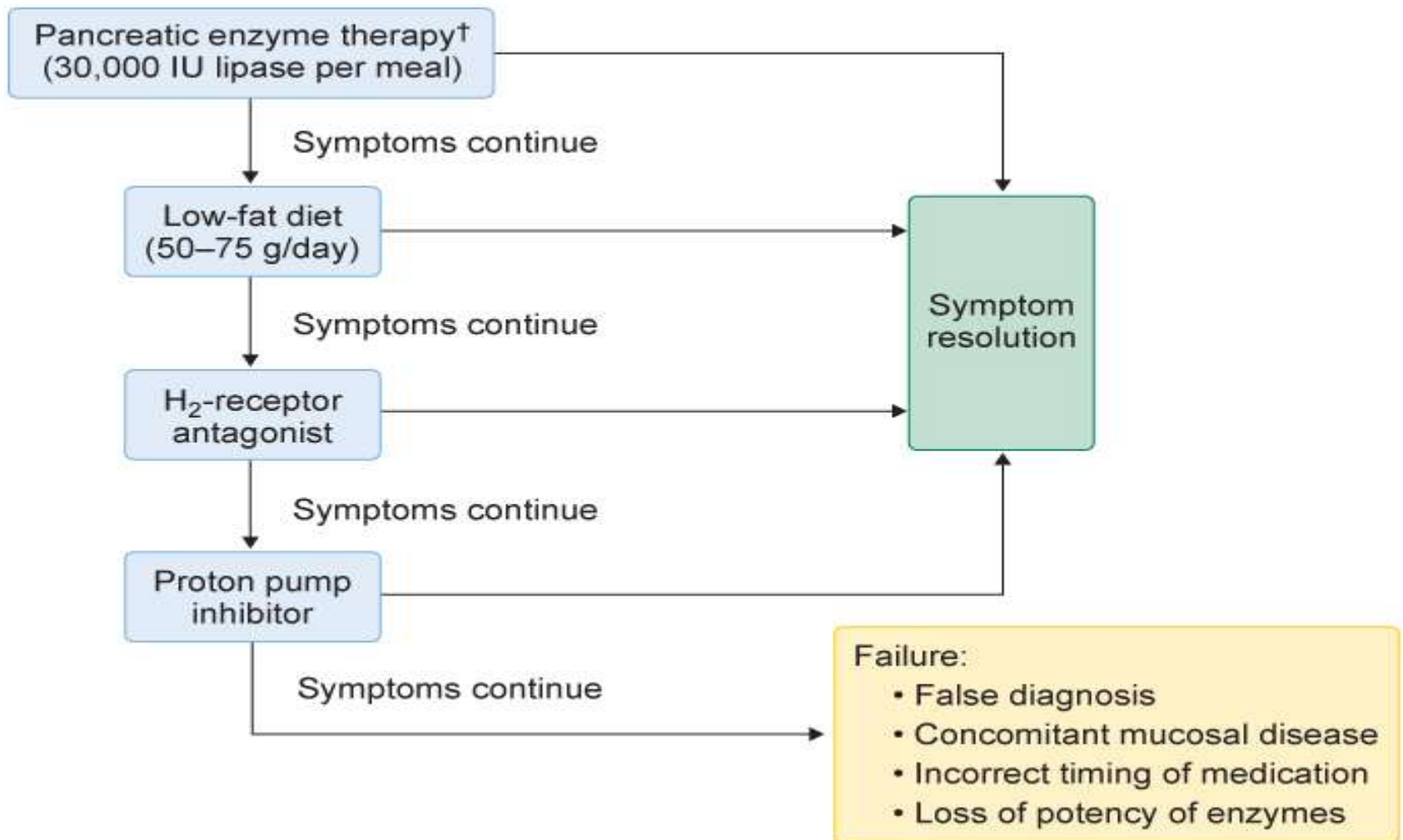
# Management

## Improvement of Maldigestion 2

- Because uncoated preparations are more easily denatured by gastric acid, acid suppression with a proton pump inhibitor or histamine-receptor antagonist is required
- Response to enzyme therapy may be monitored through an assessment of symptoms or, more objectively, through 72-hour stool fat quantification.

# Management

## Chronic Pancreatitis: Management of Maldigestion



# Management

## Minimally Invasive Interventions 1

- A differential nerve blockade is helpful in determining whether there is a central or somatosensory component to the pain syndrome
- Celiac or splanchnic nerve blockade may be used in select patients with visceral pancreatic pain
- Endoscopic techniques include biliary or pancreatic sphincterotomy (or both), removal of pancreatic duct stones, and placement of pancreatic stents

# Management

## Minimally Invasive Interventions 2

- Extracorporeal shockwave lithotripsy (ESWL) is also an effective ancillary treatment for patients with pancreatic ductal stones either alone or in combination of endoscopic therapy.

# Management

## Surgery 1

- In patients with a dilated main pancreatic duct, a side-to-side pancreatojejunostomy (Puestow procedure) may be performed
- The Whipple procedure and distal pancreatectomy have been used in the past to treat patients with small-duct CP



# Cronic Pancreatitis

## BMJ best practice

We report a case of a female patient suffering from severe malnutrition and anorexia with repeated attacks of pancreatic pain and an enlarging cystic lesion in the pancreatic head. Due to a progressively enlarging lesion on CT, a pancreaticoduodenectomy was performed. Histology demonstrated chronic pancreatitis.



**Figure 1.** CT scan at presentation showing cyst in head of pancreas.



**Figure 2.** CT scan after observation showing enlargement of cyst in head of pancreas.



**Figure 3.** ERCP showing pancreatic duct.

# Management

## Surgery 2

- Pancreatic resection is reserved for patients with disease of the small duct and pain unresponsive to medical therapy
- Total pancreatectomy with auto–islet cell transplantation (TP/AIT) has been performed at several centers in the United States.

# Management

## Management of Complications 1

- Large or symptomatic pseudocysts may be drained endoscopically through transmural or transpapillary approaches
- Large pseudocysts may also be drained surgically through cyst gastrostomy
- Biliary and gastric outlet obstructions are best managed through surgical decompression

# Management

## Management of Complications 2

- The initial management of the complications of pancreatic duct disruption or fistulas (pancreatic ascites or pleural effusions) includes prolonged pancreatic rest (parenteral nutrition), octreotide, and endoscopic placement of pancreatic duct stents
- In some cases, surgical resection may be necessary.

# Prognosis 1

- Generally, CP is a progressive inflammatory disease
- Staging and determination of severity are necessary during follow-up observation
- Observation and evaluation of clinical symptoms, such as abdominal pain, changes of pancreatic enzyme levels over time, morphology of the pancreas, and endocrine and exocrine pancreatic functions, are useful

# Prognosis 2

- Patients with CP constitute a high-risk group for ordinary-type pancreatic cancer
- Although clear evidence for testing is lacking, many patients with CP lead a lifestyle associated with carcinogenic risks (alcohol drinking and/or smoking), and it is useful to perform cancer screening.

# Prophylaxis

## Chronic Pancreatitis

- Limit alcohol consumption
- Eat a low-fat diet
- Exercise regularly and lose excess weight
- Skip crash diets
- Don't smoke.

# Abbreviations

CP - chronic pancreatitis

IPMN - intraductal papillary mucinous neoplasm



# Diagnostic and treatment guidelines

[Chronic Pancreatitis Treatment & Management](#)

[American Pancreatic Association Practice Guidelines in Chronic Pancreatitis: evidence-based report on diagnostic guidelines](#)

[Practice Guidelines in Chronic Pancreatitis](#)

[Evidence-based clinical practice guidelines for chronic pancreatitis 2015](#)

[American Pancreatic Association Practice Guidelines in Chronic Pancreatitis: Evidence-Based Report on Diagnostic Guidelines](#)

[Chronic Pancreatitis](#)

[Guidelines: diagnosis and therapy for chronic pancreatitis](#)