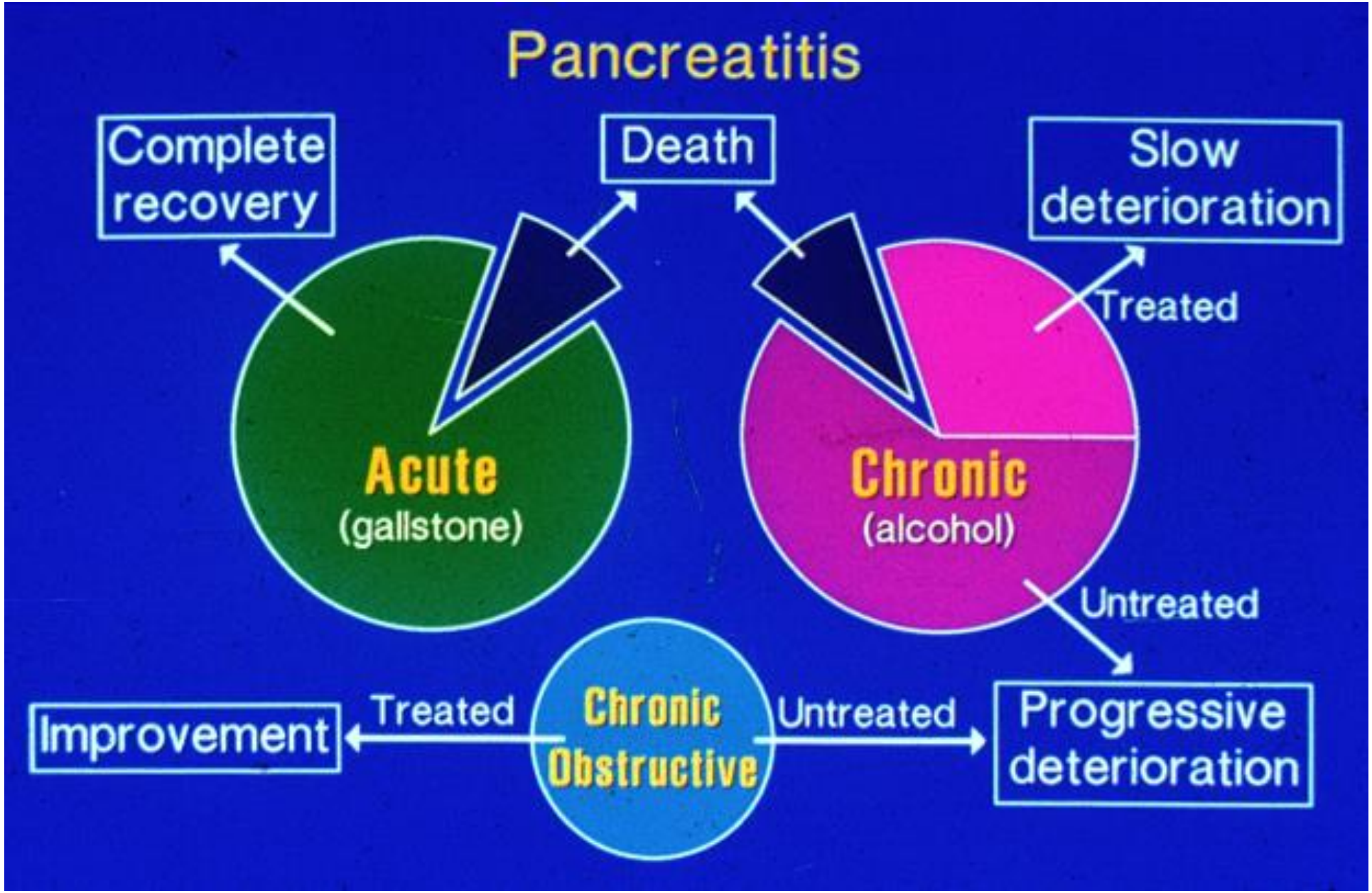
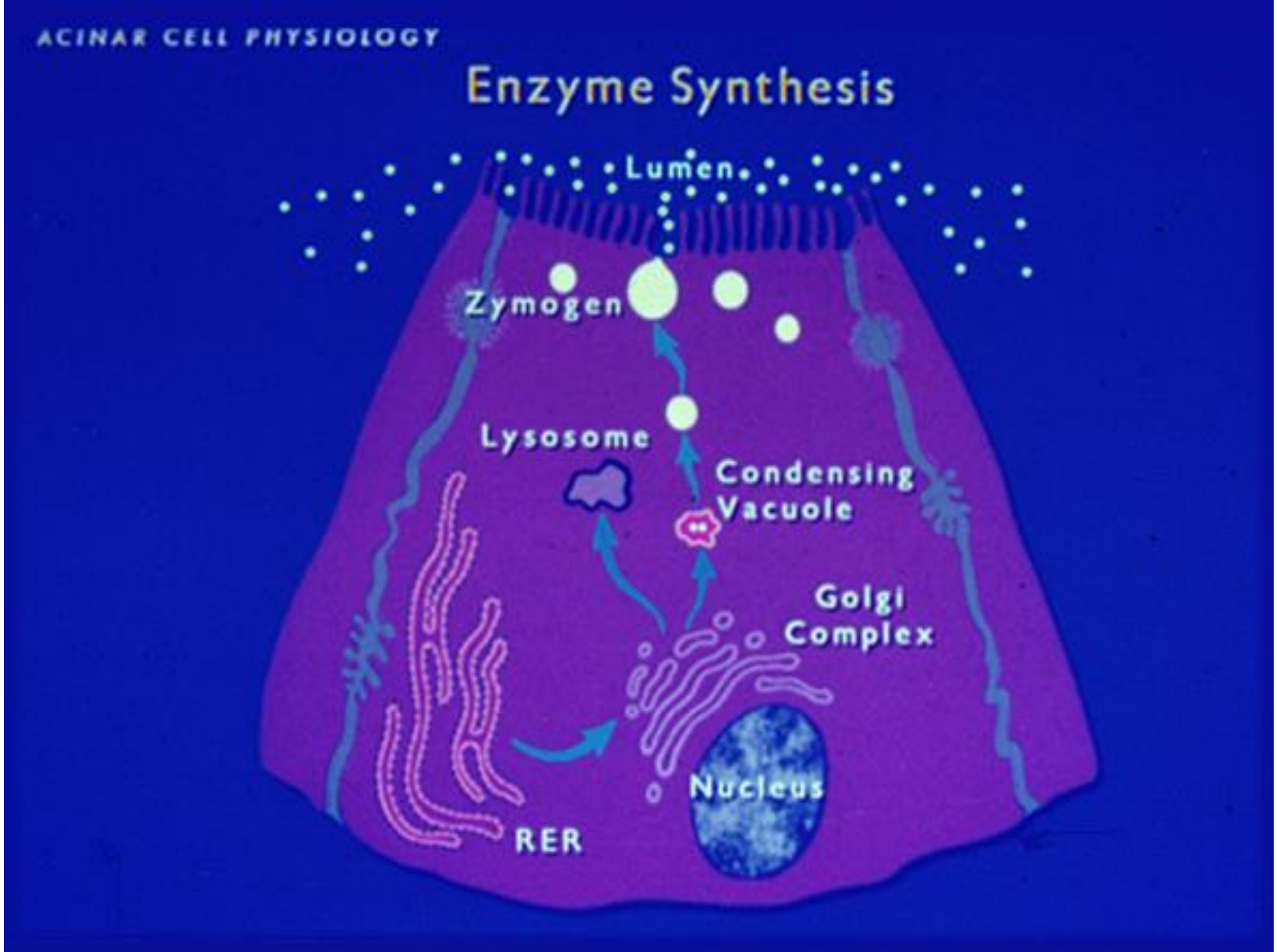
# Diseases of the Pancreas

Jack Bragg DO, MACOI

# I have no disclosures

I work for the Curators of the University of Missouri

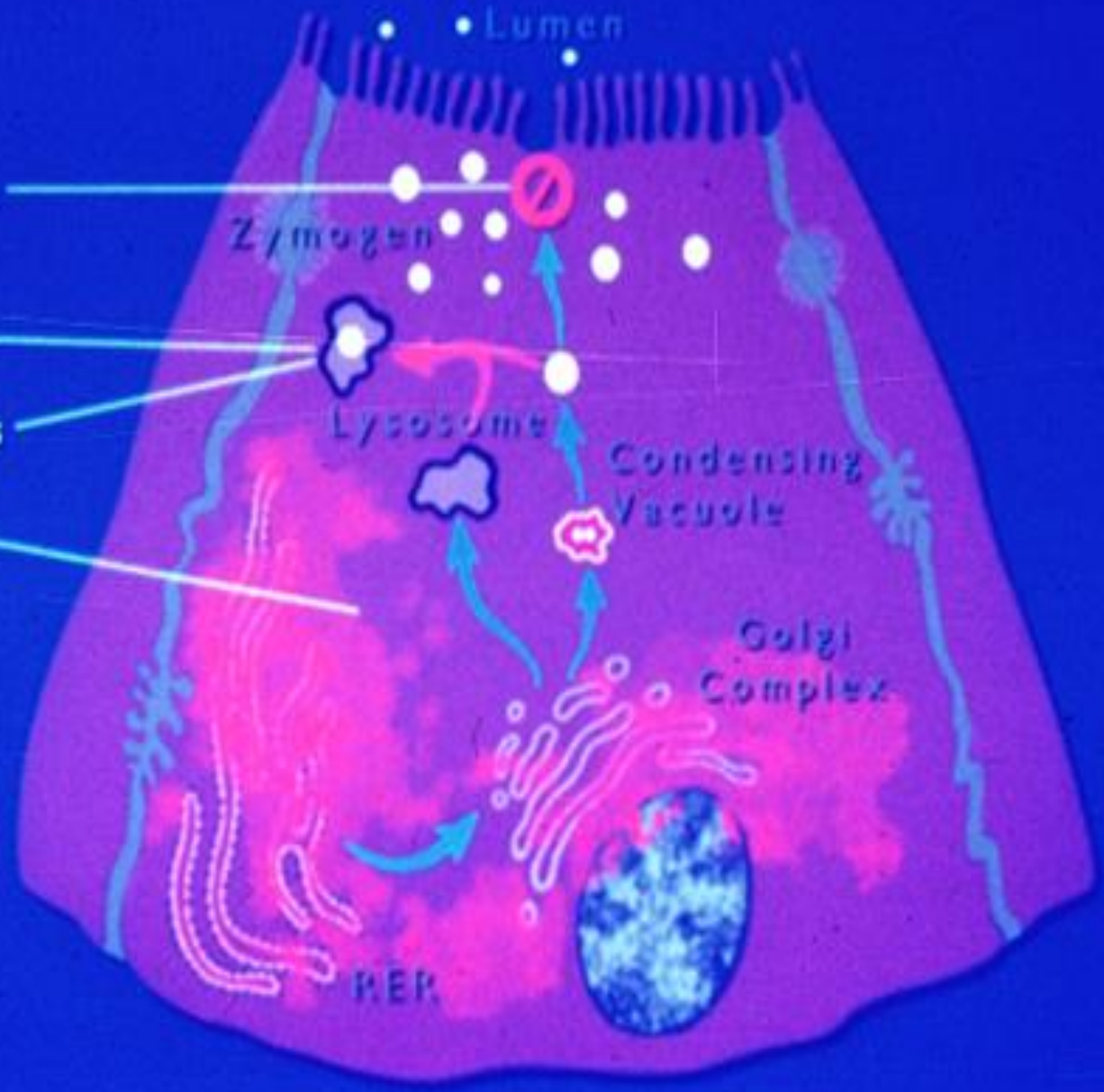

Pancreatitis
Complete recovery
Death
Slow deterioration
Treated
Acute
(gallstone)
Chronic
(alcohol)
Untreated
Improvement
Treated
Chronic Obstructive
Untreated
Progressive deterioration


ACINAR CELL PHYSIOLOGY
Enzyme Synthesis
Lumen
Zymogen
Lysosome
Condensing Vacuole
Golgi Complex
Nucleus
RER

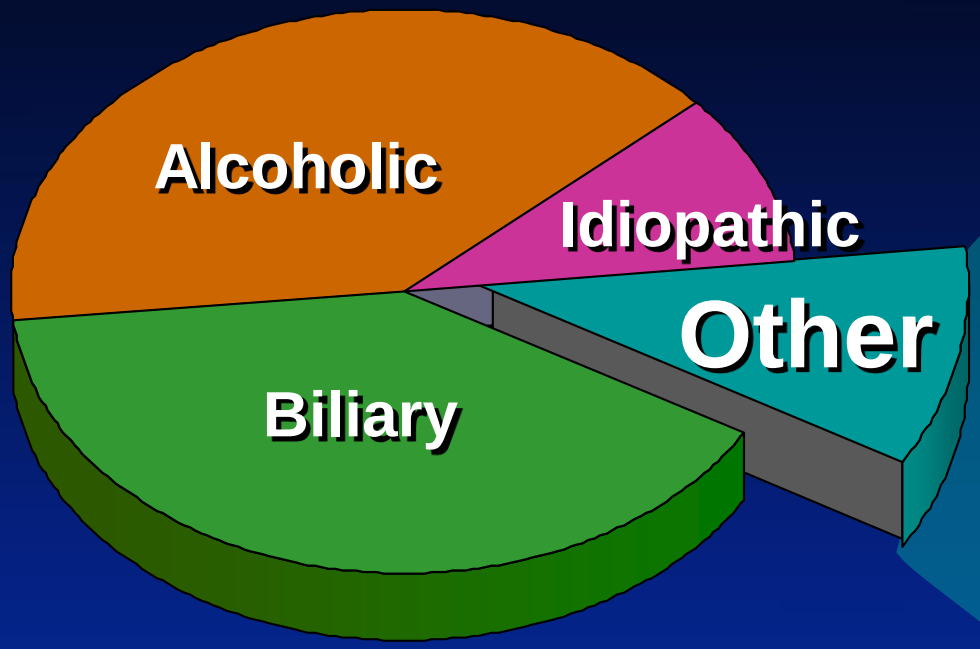
ACUTE PANCREATITIS

# Intracellular Injury

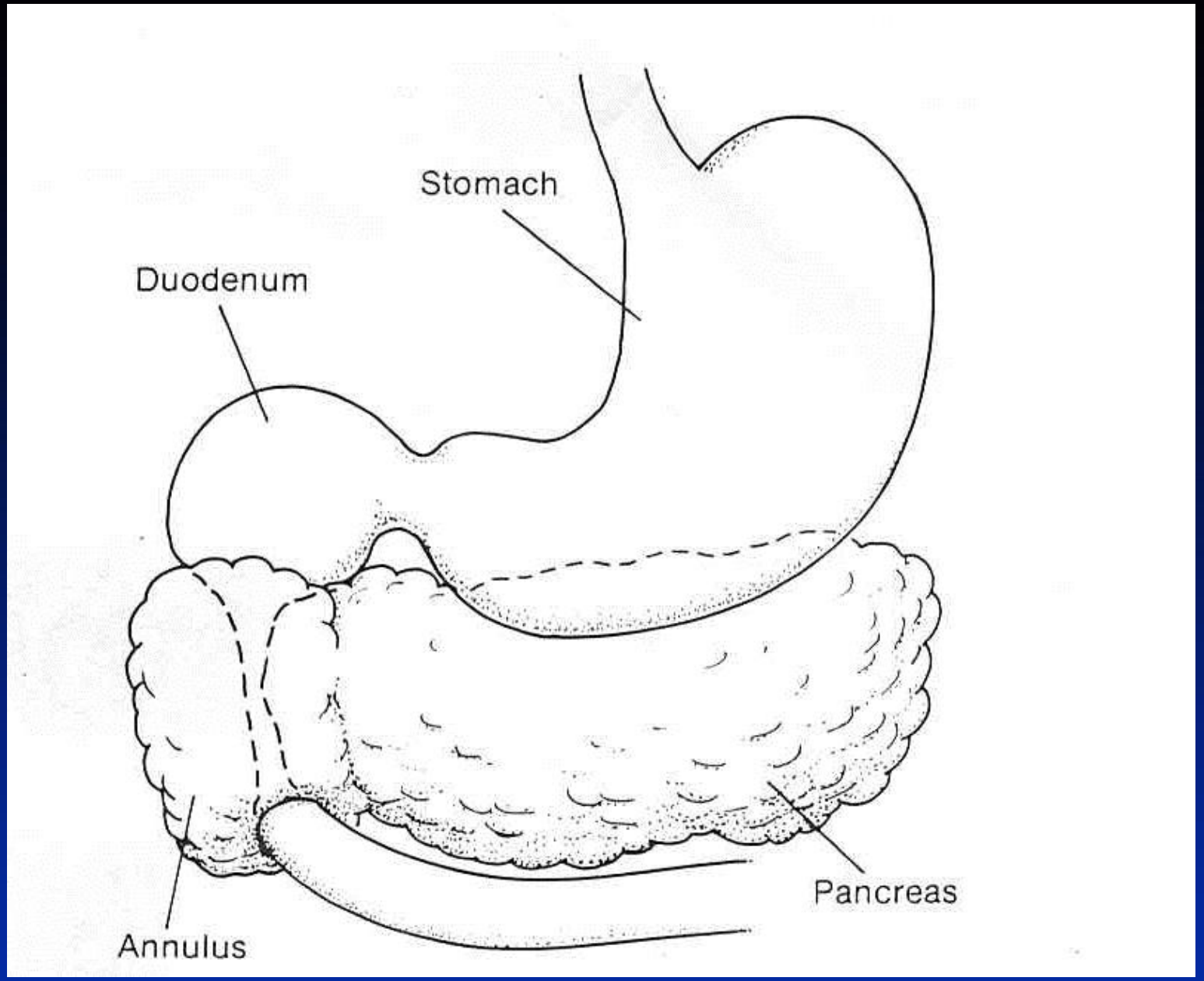
- Blockage of secretion
- Fusion of lysosomes and zymogens
- Activation of enzymes
- Intracellular injury



# Etiologies




- Autoimmune
- Drug-induced
- Iatrogenic
- IBD-related
- Infectious
- Inherited
- Metabolic
- Neoplastic
- Structural
- Toxic
- Traumatic
- Vascular


Stomach
Duodenum
Pancreas
Annulus

# Modified Biliary Classification

A = Elevated liver tests on 1 or more occasions

B = Dilated Common Bile Duct

**Biliary Type I – A+B**

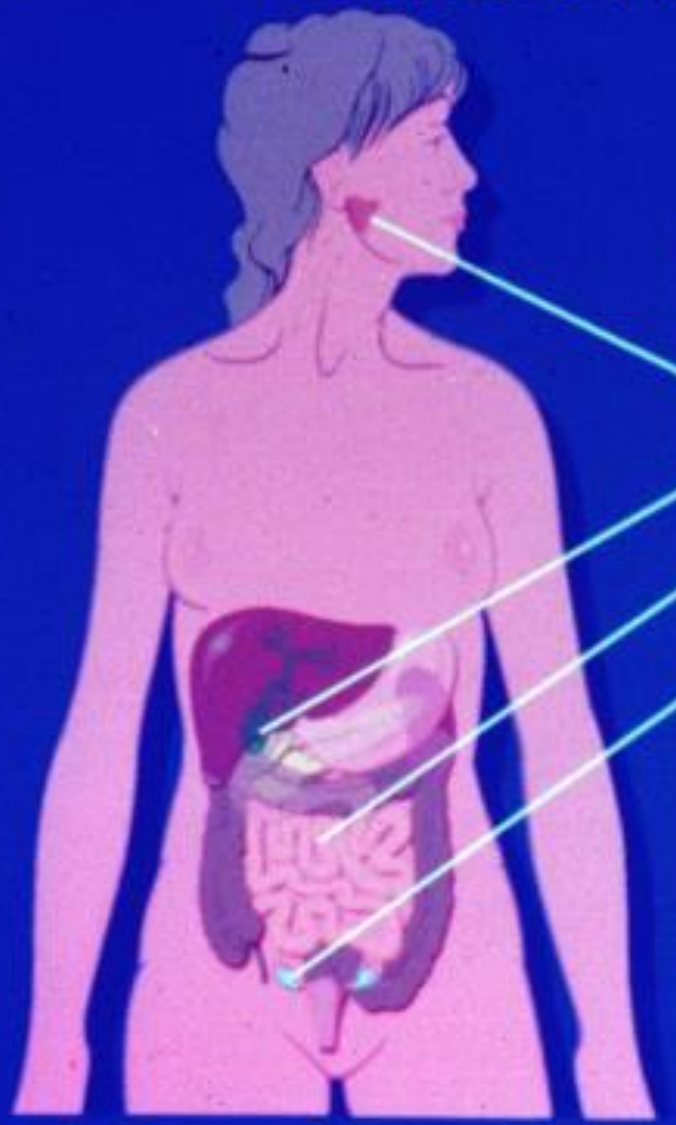
**Biliary Type II – A or B**

**Biliary Type III – Pain only**

# Drug Induced Pancreatitis Sorted by Incidence

| Common | Uncommon | Rare |
|---|---|---|
| asparaginase | ACE inhibitors | carbamazepine |
| azathioprine | acetaminophen | corticosteroids |
| 6-mercaptopurine | 5-amino ASA | estrogens |
| didanosine (DDI) | furosemide | minocycline |
| pentamidine | sulfasalazine | nitrofurantoin |
| valproate | thiazides | tetracycline |

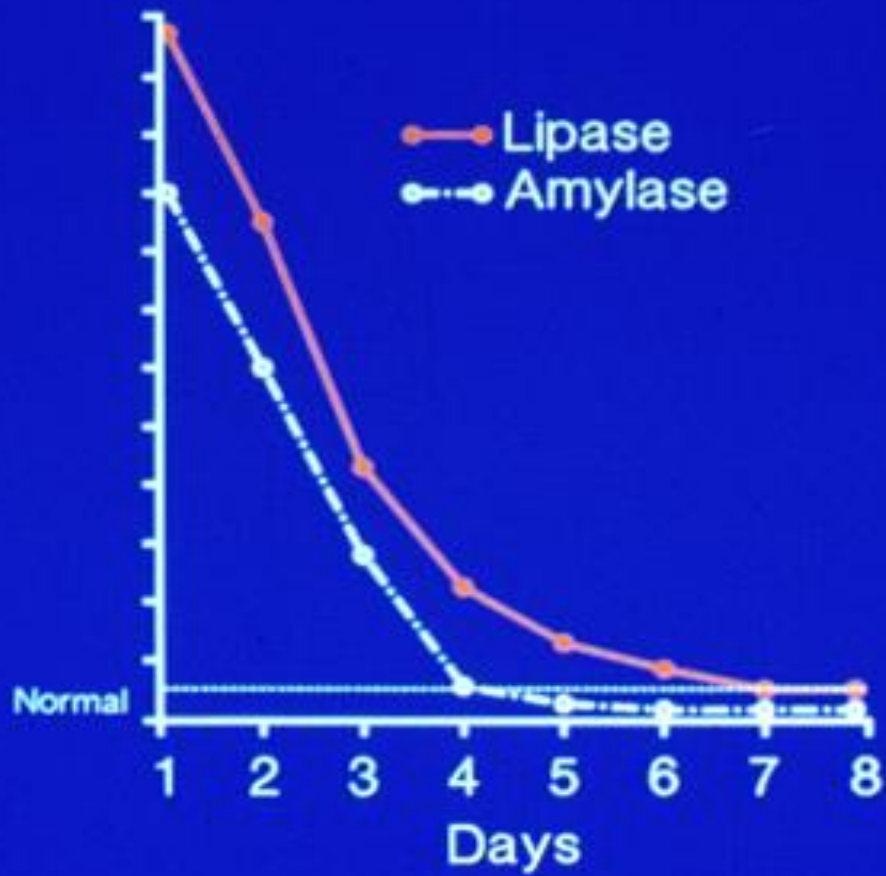
# Causes of Increased Serum Enzymes



| | Amylase | Lipase |
|---|---|---|
| Pancreatitis | ↑ | ↑ |
| Parotitis | ↑ | Normal |
| Biliary stone | ↑ | ↑ |
| Intestinal injury | ↑ | ↑ |
| Tubo-ovarian disease | ↑ | Normal |
| Renal failure | ↑ | ↑ |
| Macroamylasemia | ↑ | Normal |

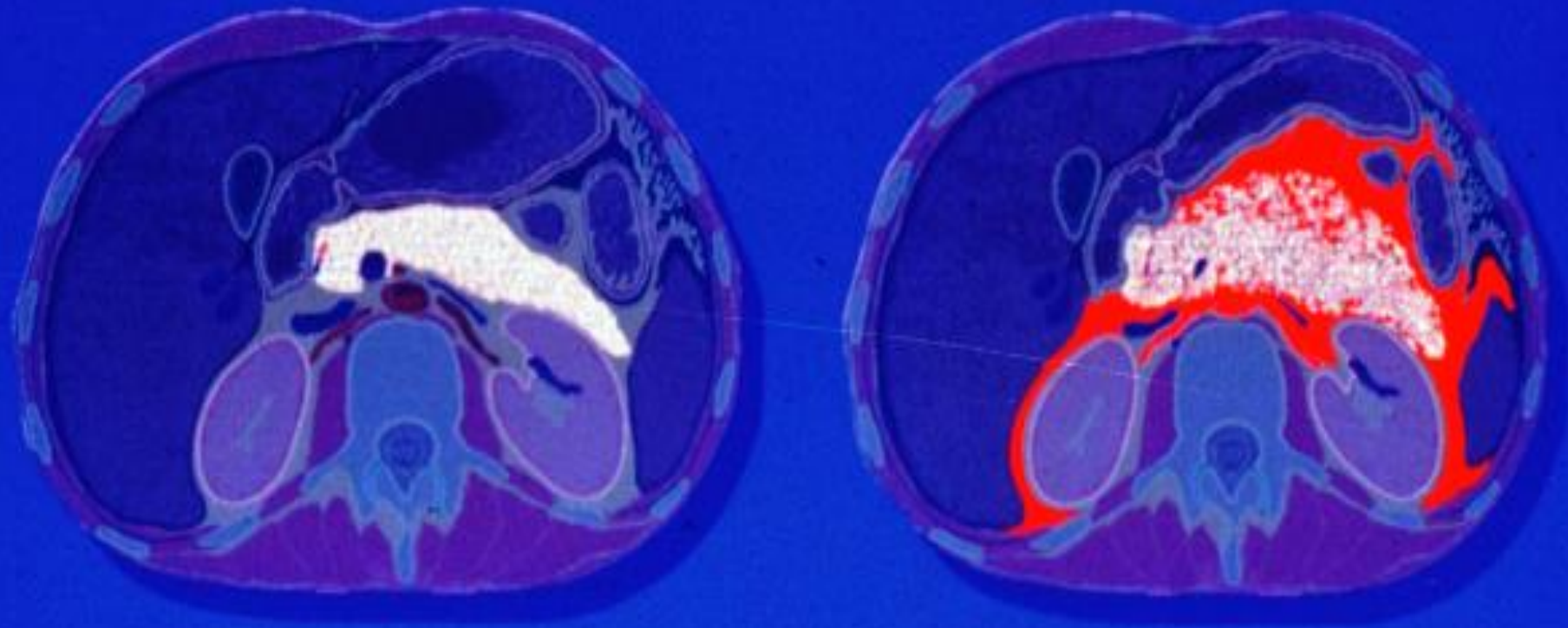
**ACUTE PANCREATITIS**

# Time Course of Serum Enzymes



ACUTE PANCREATITIS

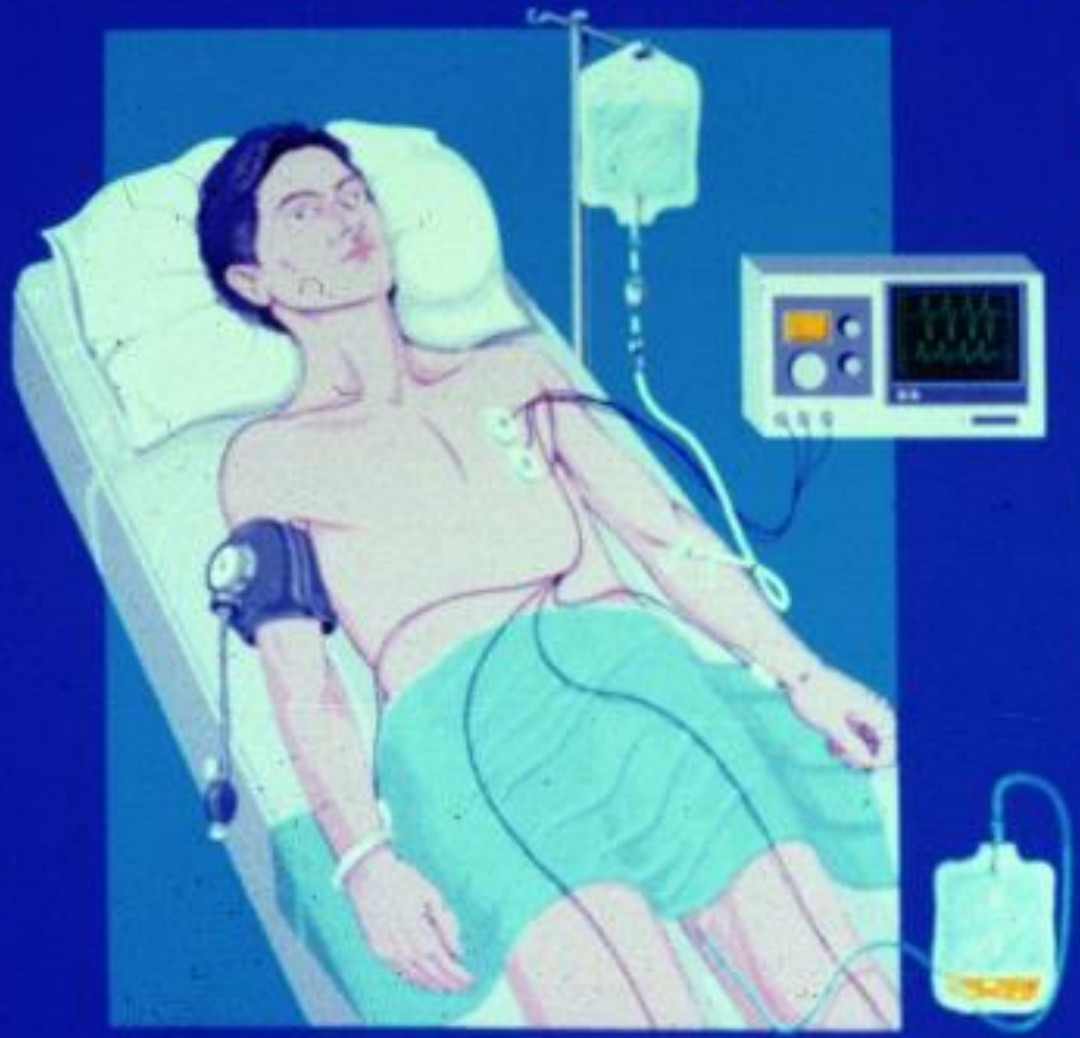
# Local Effects of Enzymes



- Inflammation
- Third space losses
- Fat necrosis
- Pancreatic and peripancreatic necrosis

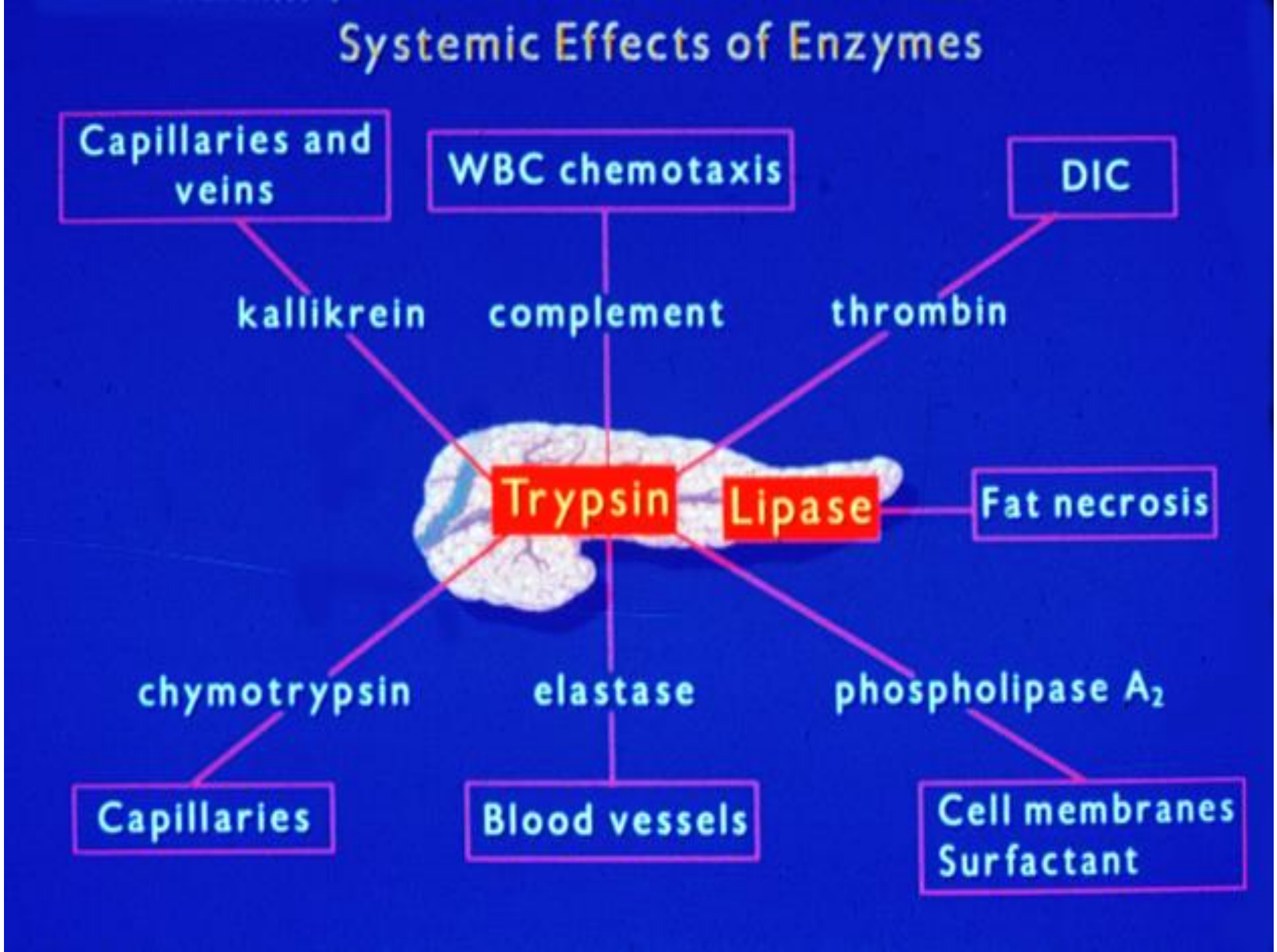
ACUTE PANCREATITIS

# Danger Signals: First Few Hours



- Encephalopathy
- Hypoxemia
- Tachycardia >130/min
- Hypotension <90 mmHg
- Hct >50
- Oliguria <50 ml/hr
- Azotemia

# Systemic Effects of Enzymes



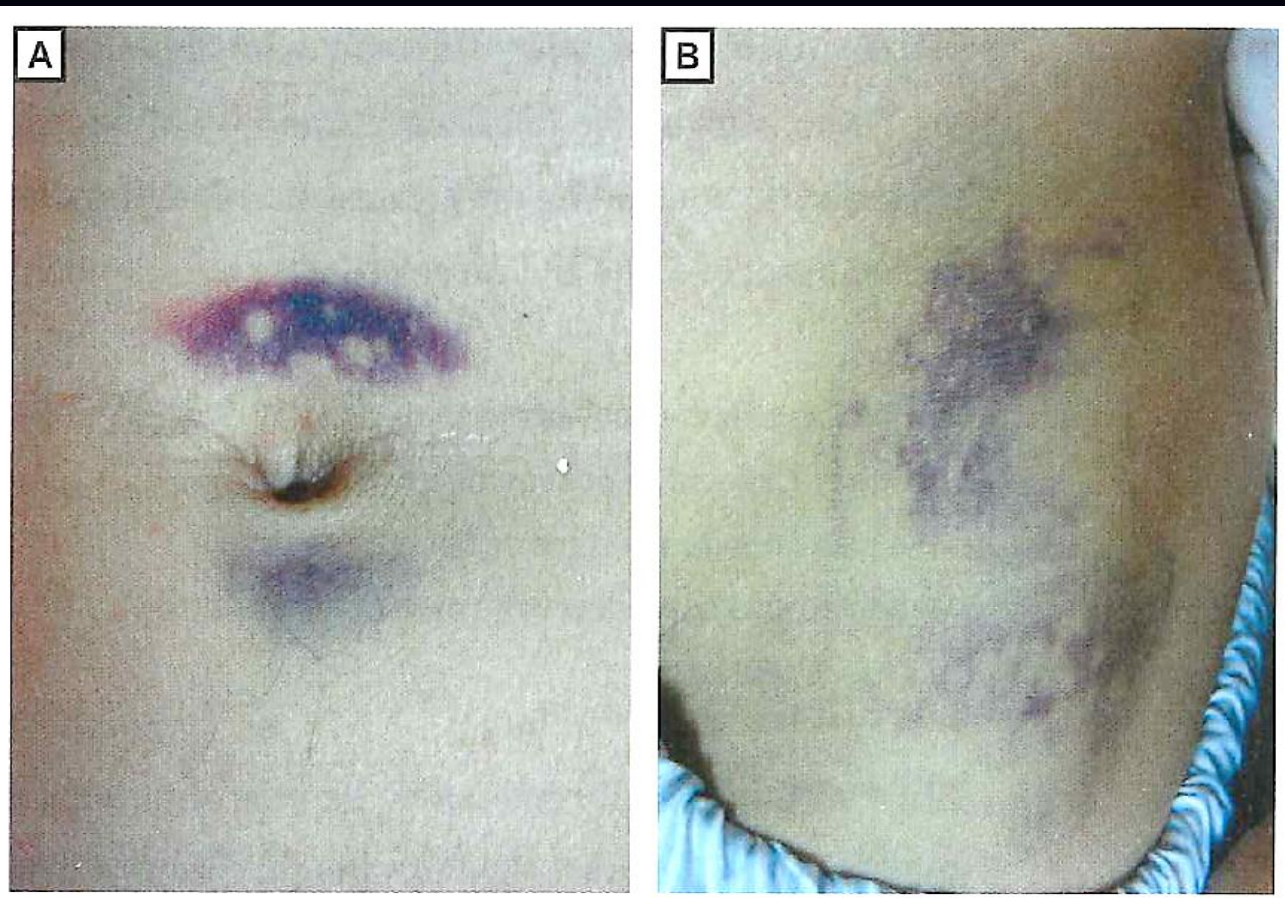
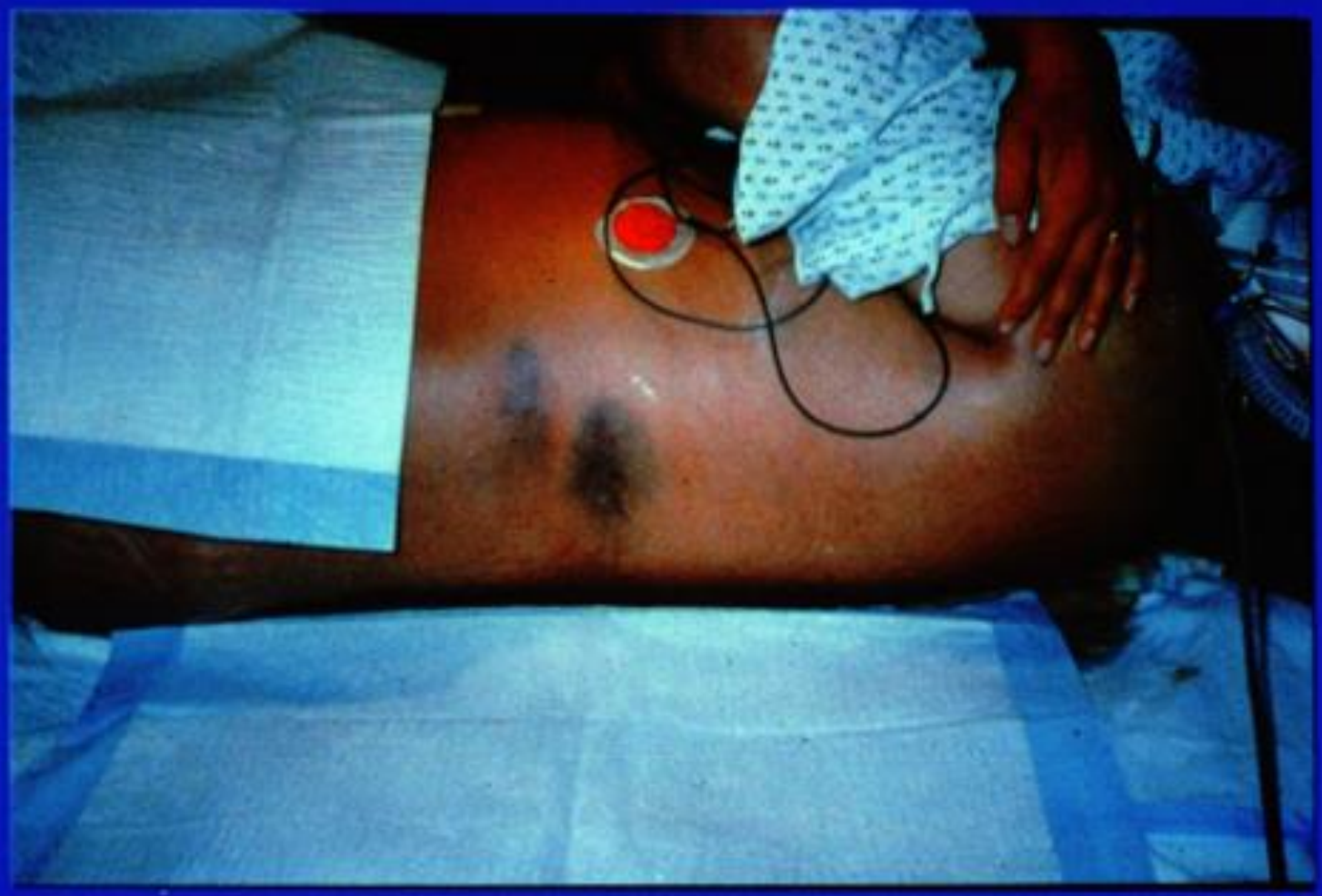



**Figure 1.**

(A) Periumbilical ecchymosis (Cullen sign) and (B) flank ecchymosis (Grey Turner sign). Published with permission from Chung and Chuang.[1]

ACUTE PANCREATITIS

# Grey-Turner Sign



# Ranson's Criteria of Severity

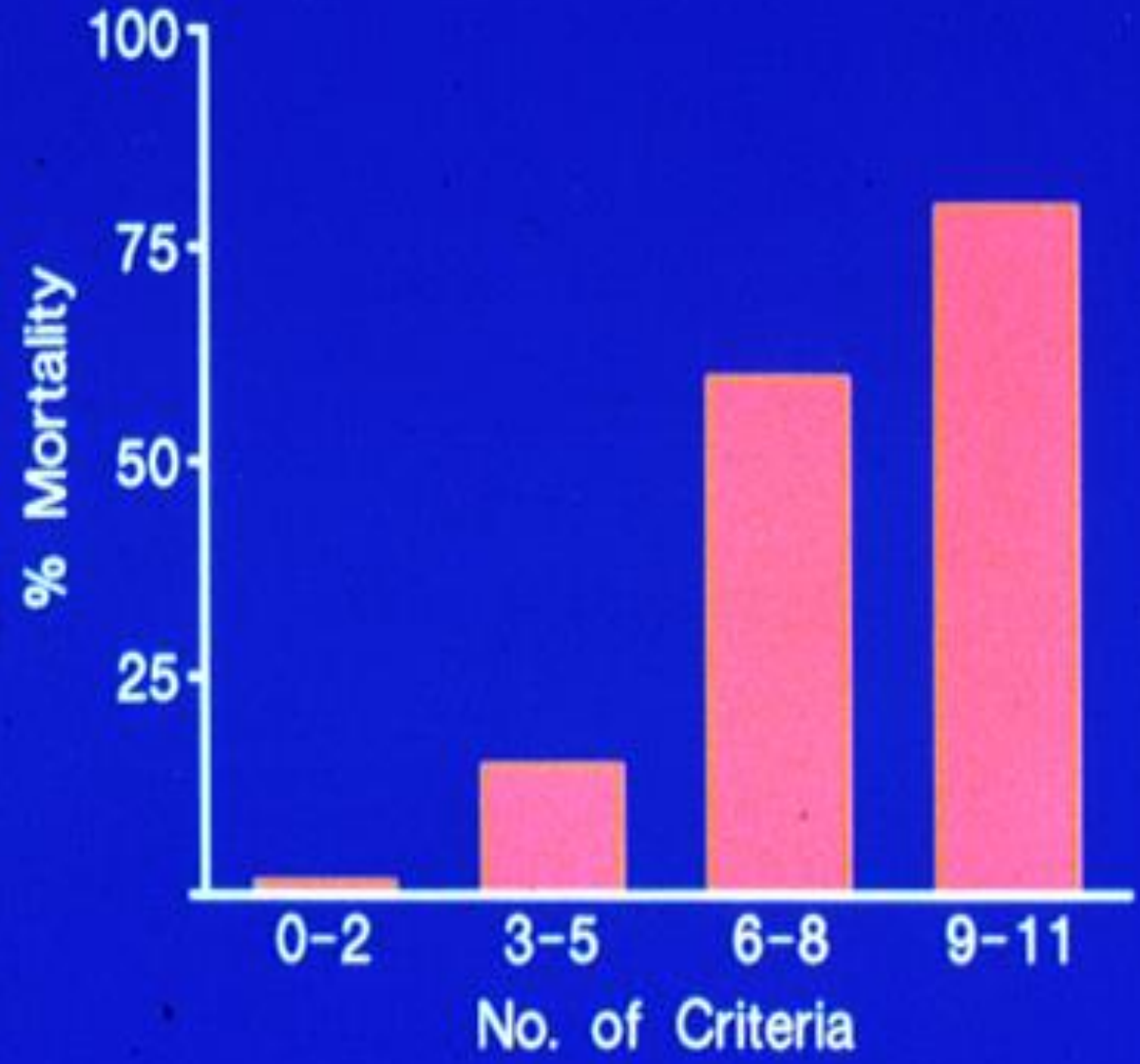
## At admission

- Age >55 years
- WBC >16,000/mm³
- Glucose >200 mg/dl
- LDH >350 IU/L
- AST >250 U/L

## During initial 48 hours

- Hct decrease of >10
- BUN increase of >5 mg/dl
- $Ca^{++}$ <8 mg/dl
- $PaO_2$ <60 mm Hg
- Base deficit >4 mEq/L
- Fluid sequestration >6 L

# Mortality Related to Ranson's Criteria



# Treatment

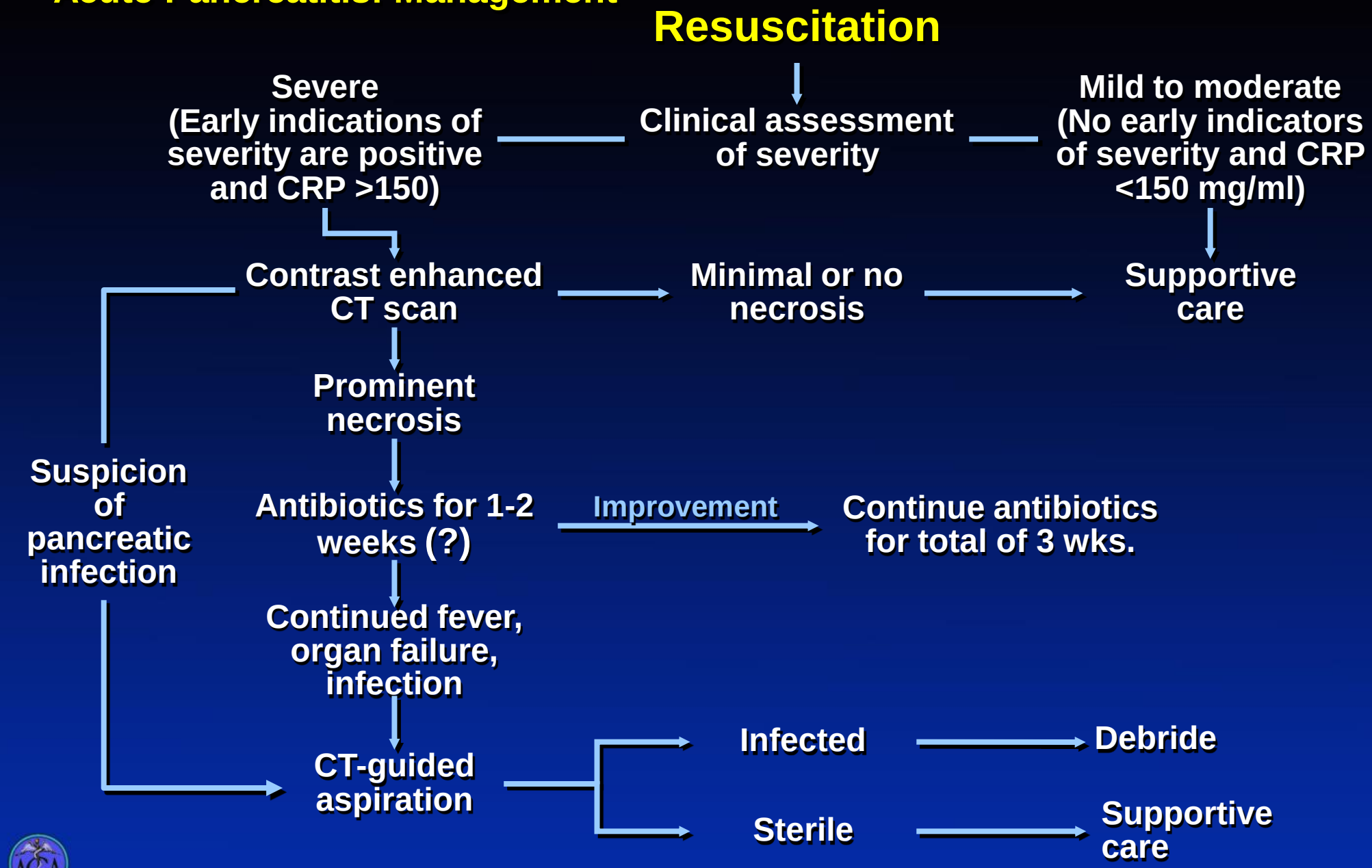
## Supportive care

- Aggressive fluid and electrolyte replacement
- Monitoring
  - Vital signs
  - Urine output
  - $O_2$ saturation
  - Pain
- Analgesia, anti-emetics

## Other treatments

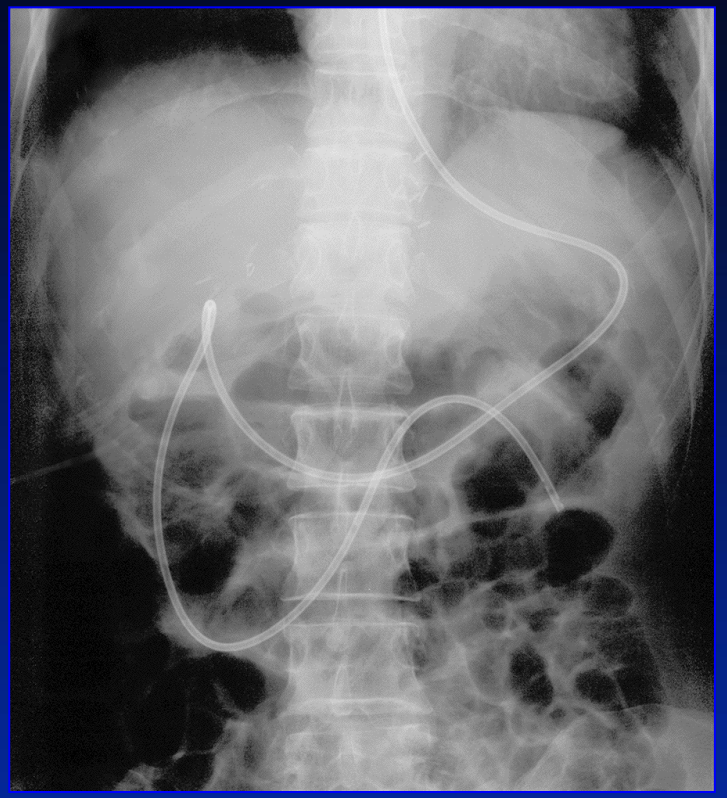
- Acid suppression
- Antibiotics
- NG tube
- Nutritional support
- Urgent ERCP

# Acute Pancreatitis: Management



# Nutritional Support

- Consider when protracted course is likely
- Enteral vs parenteral
  - Safety
  - ? Effect on outcome
- Monitor calcium and triglycerides



# Major Complications

## Local

- Fluid collections
- Necrosis
- Infection
- Ascites
- Erosion into adjacent structures
- GI obstruction
- Hemorrhage

## Systemic

- Pulmonary
- Renal
- CNS
- Multiorgan failure

## Metabolic

- Hypocalcemia
- Hyperglycemia

# Causes of mortality

## Acute Pancreatitis

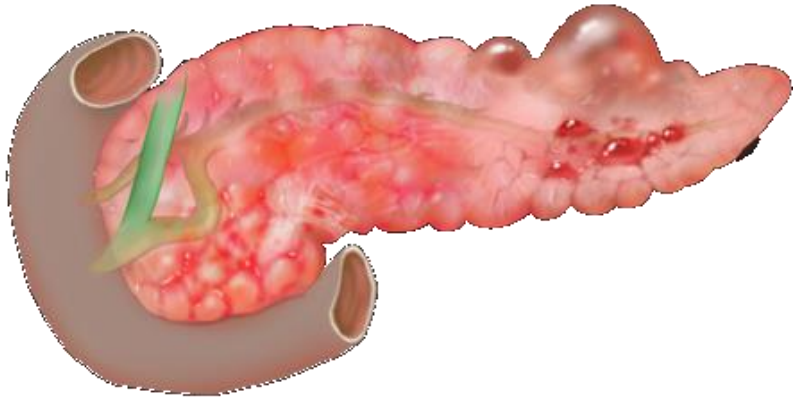
**DEATH**

### Early (< one week)

- Systemic inflammatory response syndrome (SIRS)
- Multiorgan failure

### Late (> one week)

- Multiorgan failure
- Pancreatic infections/sepsis

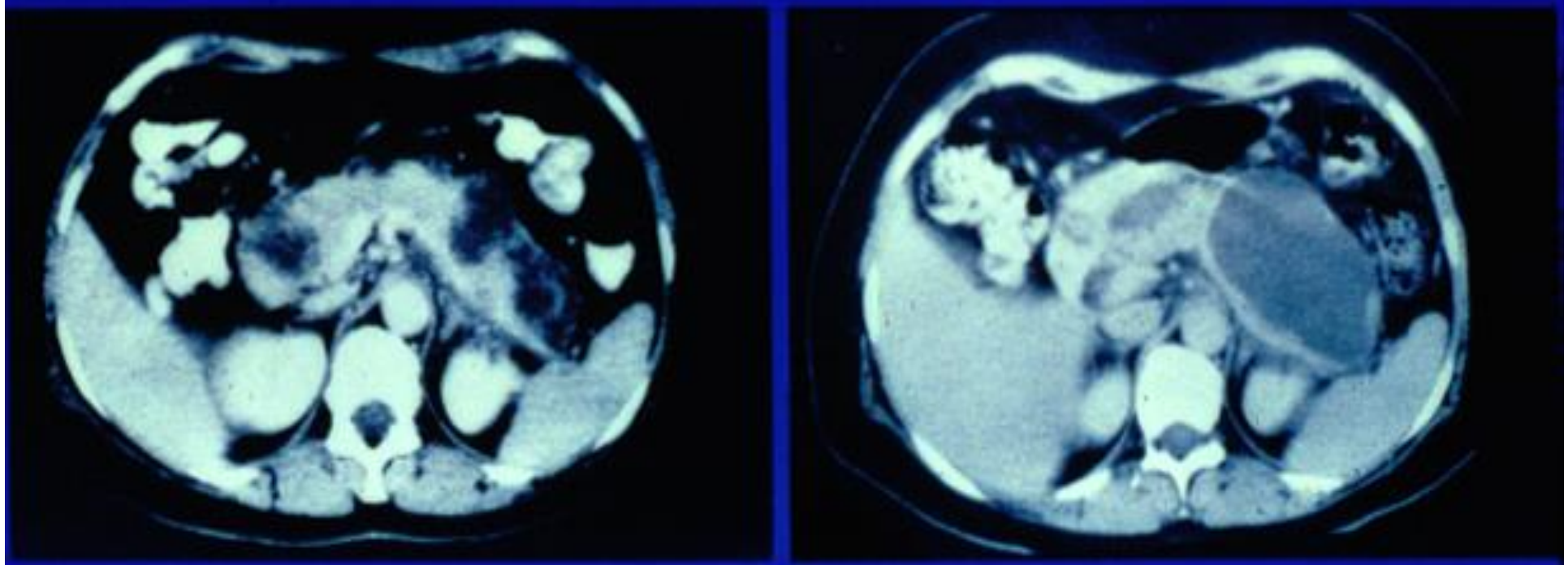


# Reduction of Inflammation: Proposed Methods

- Remove impacted gallstones (papillotomy)
- Remove ascites (peritoneal lavage)
- Remove circulating proteases
  - protease inhibitors
  - fresh frozen plasma
  - plasmapheresis
  - stimulation of monocyte-macrophage system
- Remove $O_2$-derived free radicals

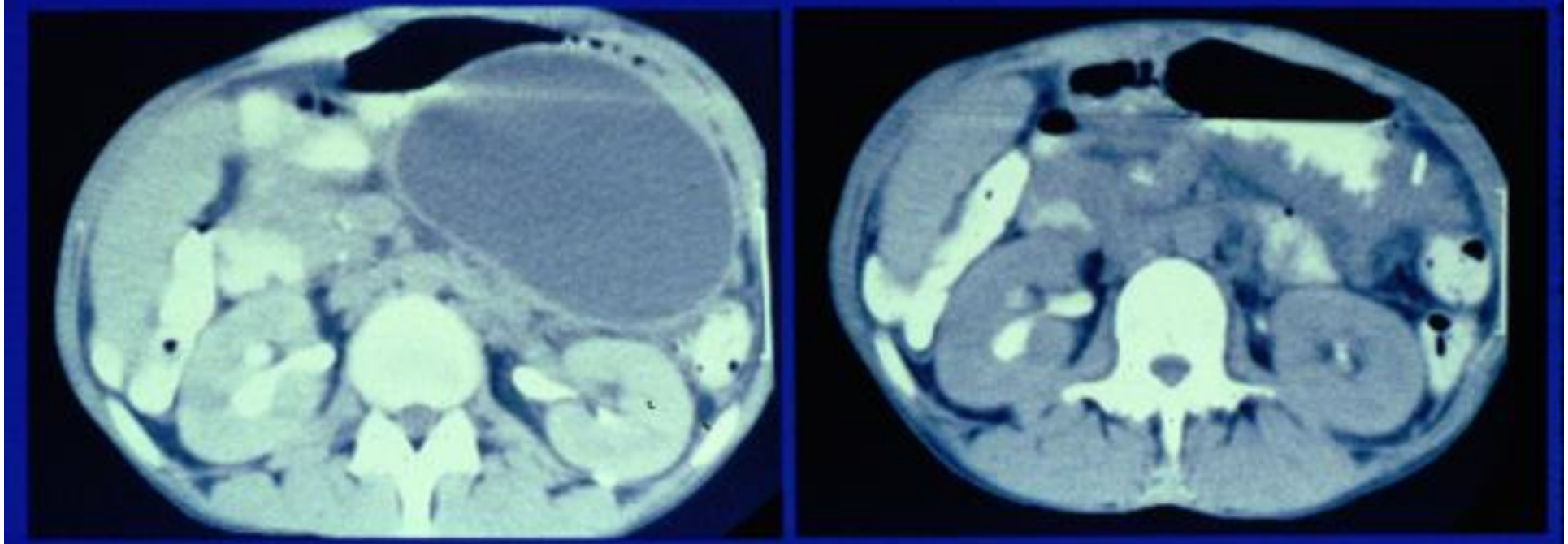
ACUTE PANCREATITIS

# Progression to Pseudocyst



PSEUDOCYST

# Needle Aspiration

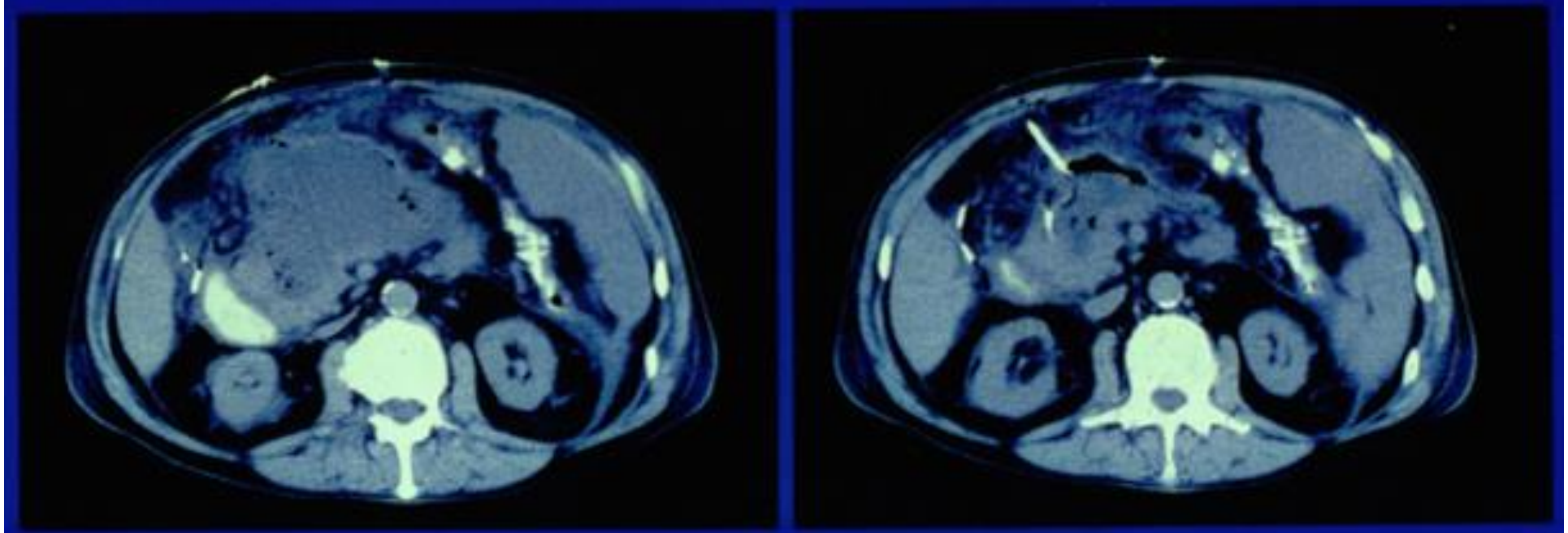


# Complications

- Severe pain
- Obstruction (CBD, duodenum)
- Dissection
- Bleeding
- Infection
- Leakage (ascites, pleural effusion)
- Rupture

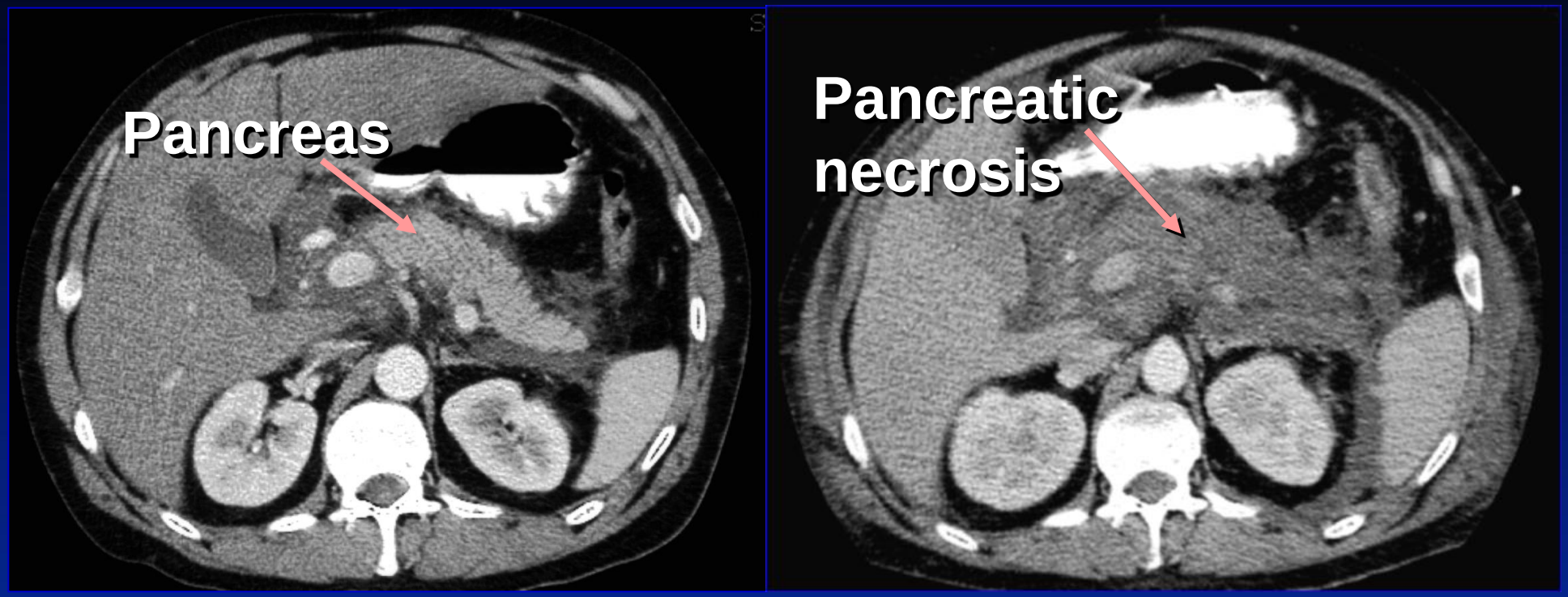
**ACUTE PANCREATITIS: COMPLICATIONS**

# Abscess Drainage



## Acute Pancreatitis: Necrosis

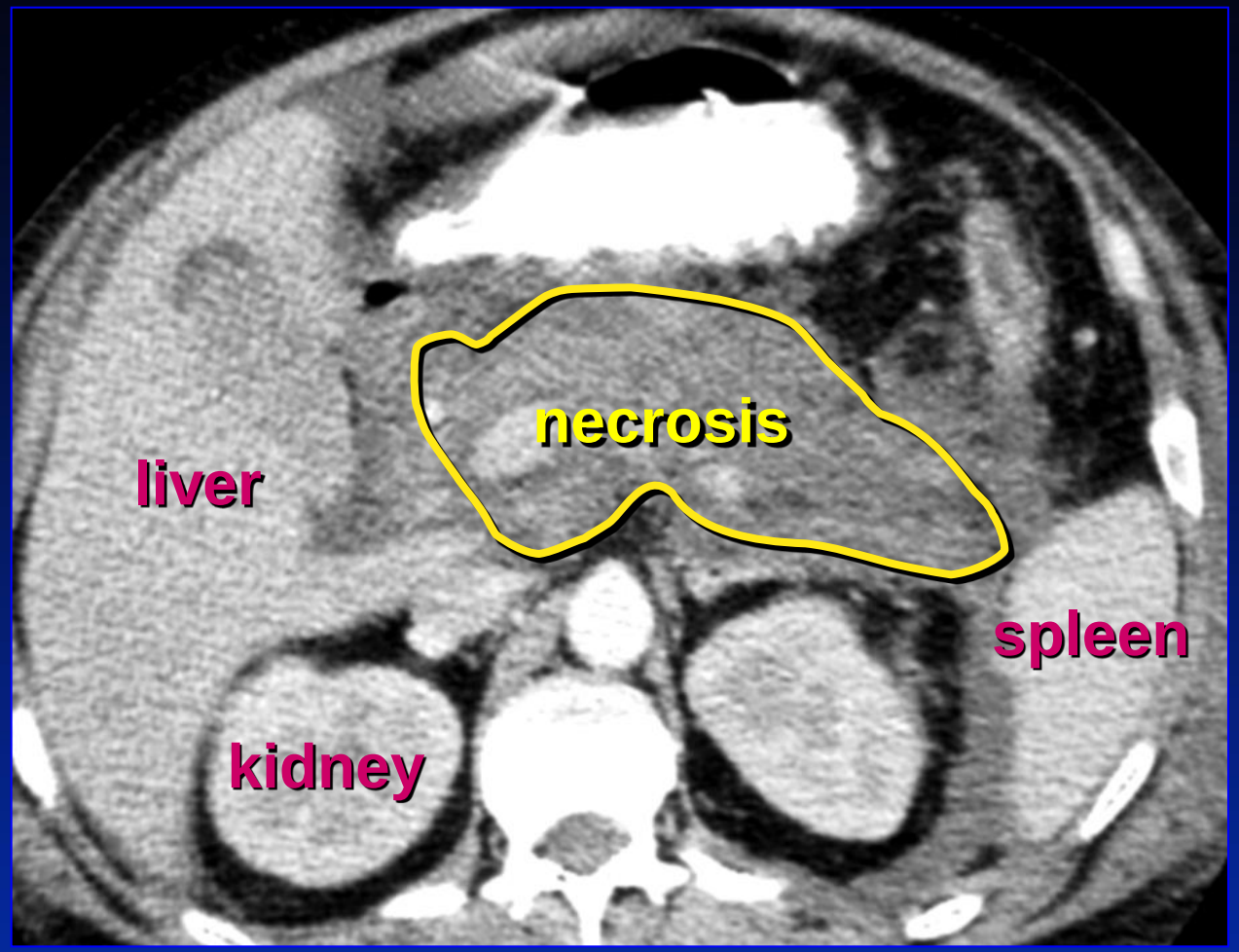
# Progression




Day 1

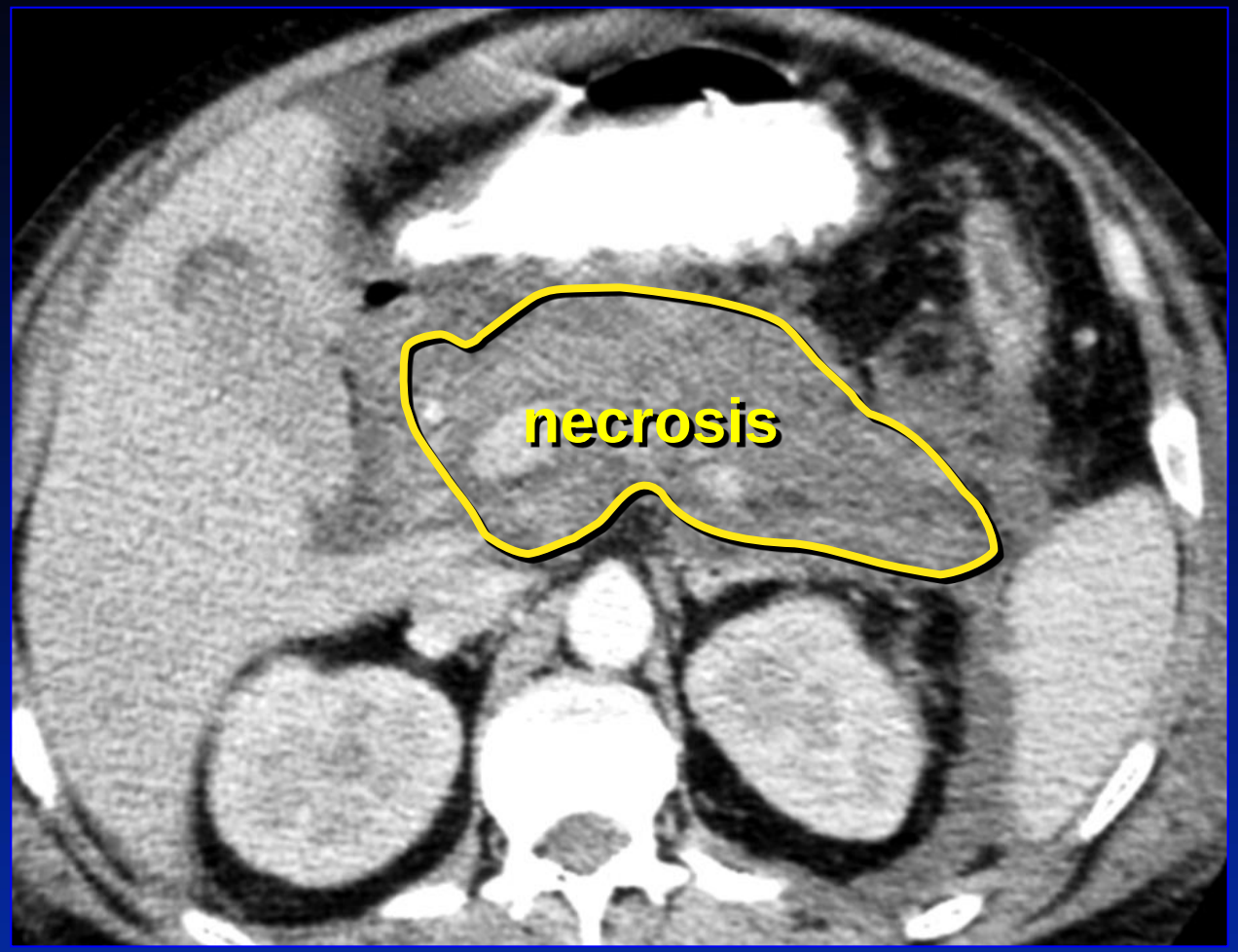
Day 3

## Pancreatic Necrosis




- Non-perfusion
- Systemic complications
- Local complications
  - Hemorrhage
  - Infection

## Pancreatic Necrosis




Debridement

vs

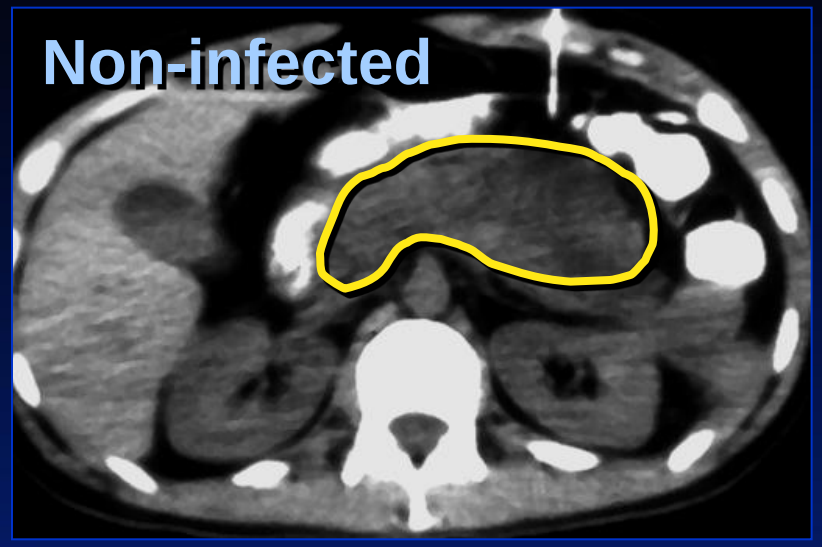
Observation

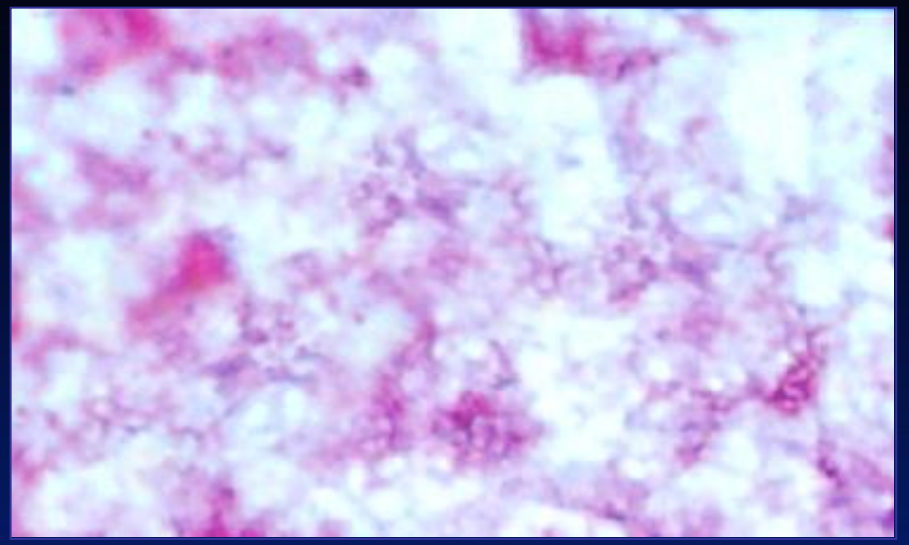
# Signs of Infected Pancreatic Necrosis

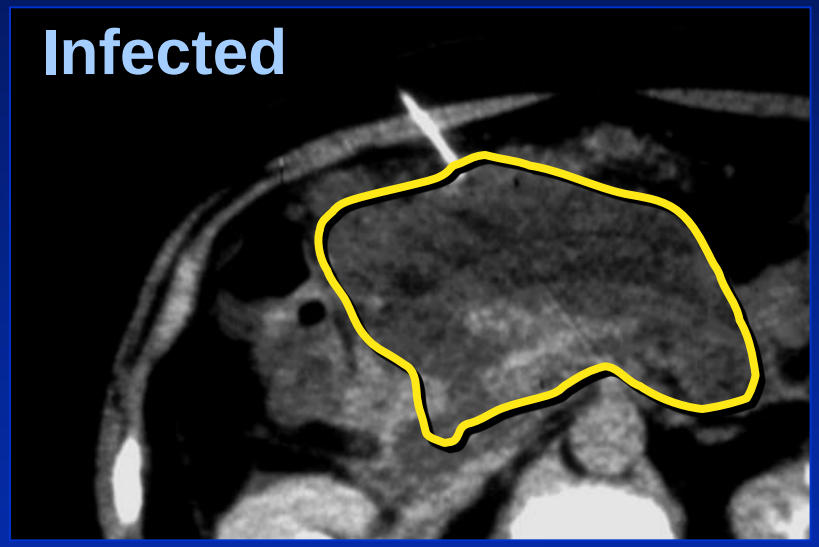
- Increasing markers of inflammation
  (serum CRP, white blood cell count)
- Newly developed fever without extra pancreatic infection
- Signs of infection on CT
  (gas collection within areas of necrosis)

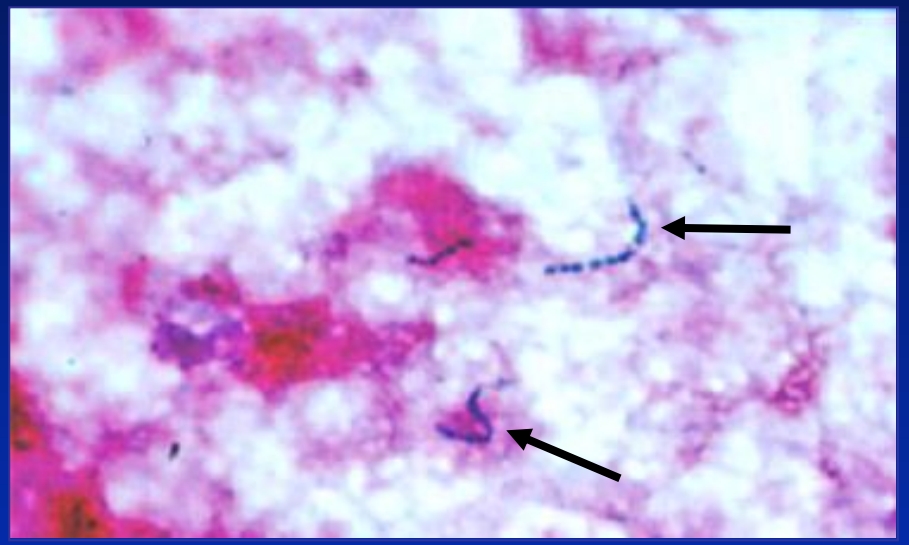
## Acute Pancreatitis

# Necrosis





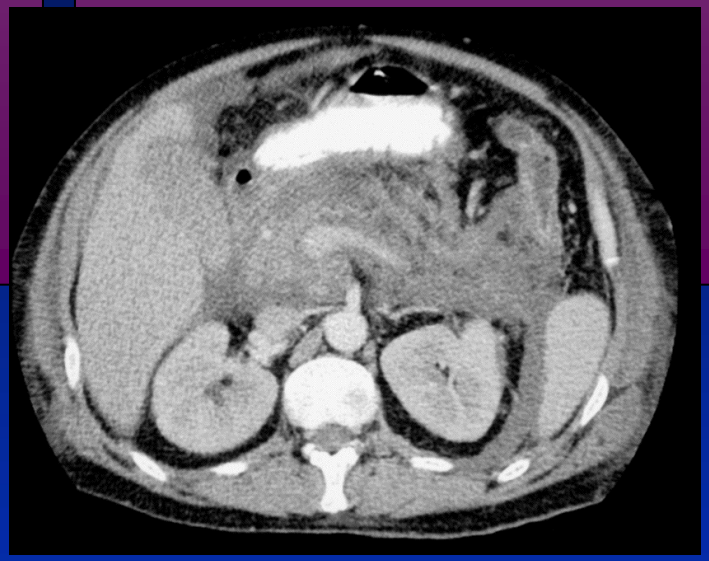
# Treatment Strategies

## Sterile

- Medical therapy
- Debridement for persistent organ failure?

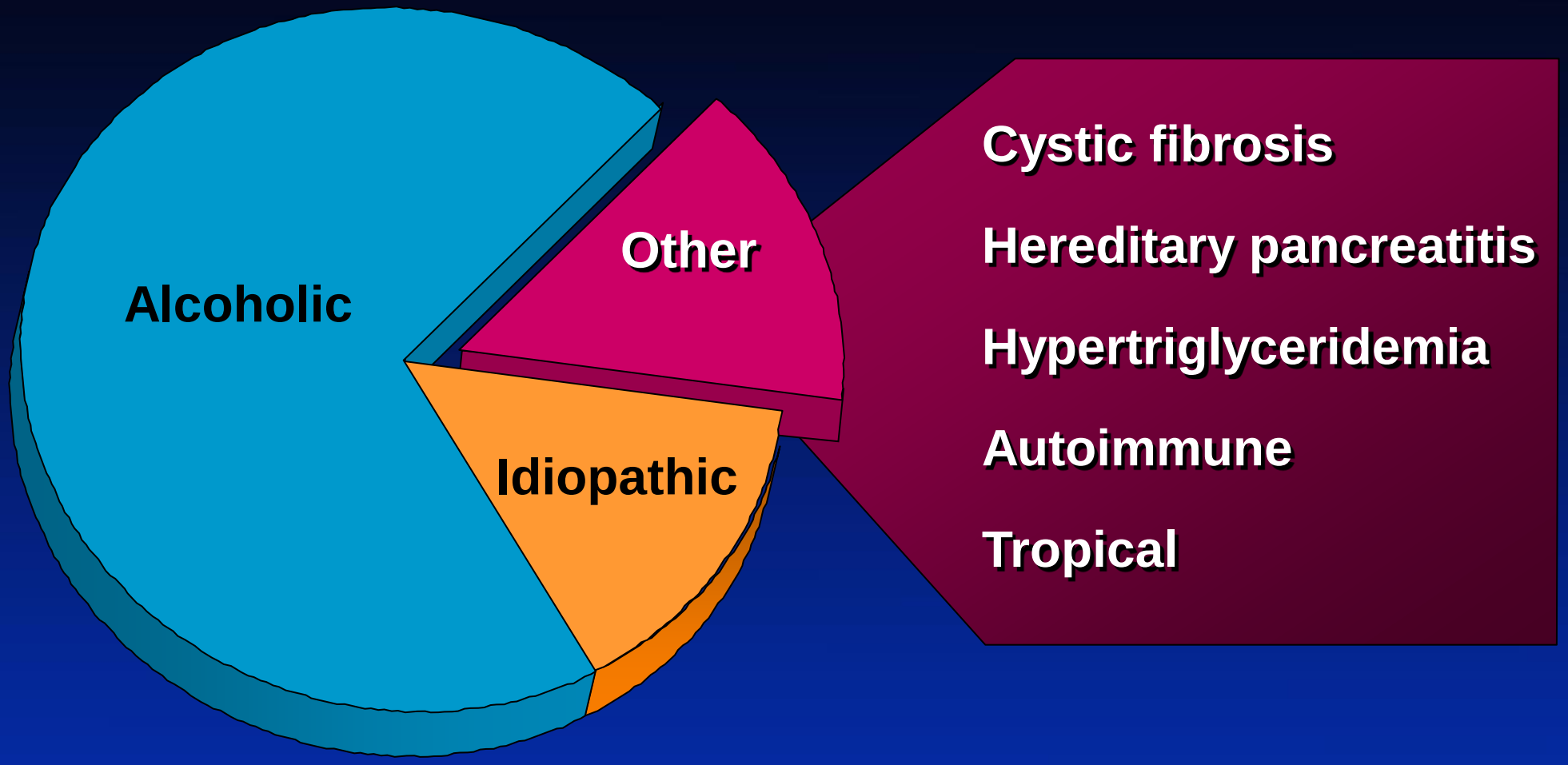
## Infected

- Antibiotics
- Debridement

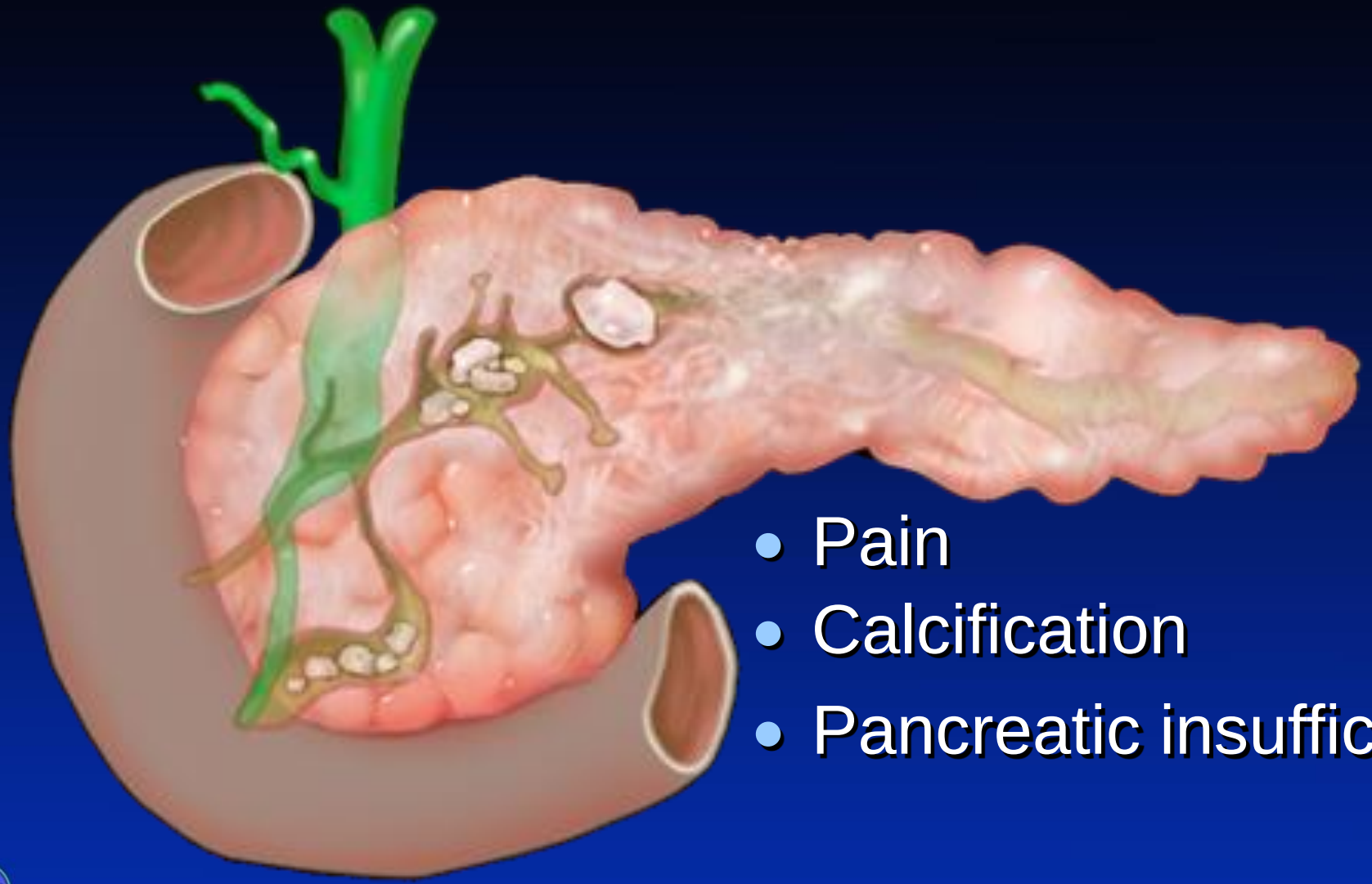


## Chronic Pancreatitis

# Etiologies

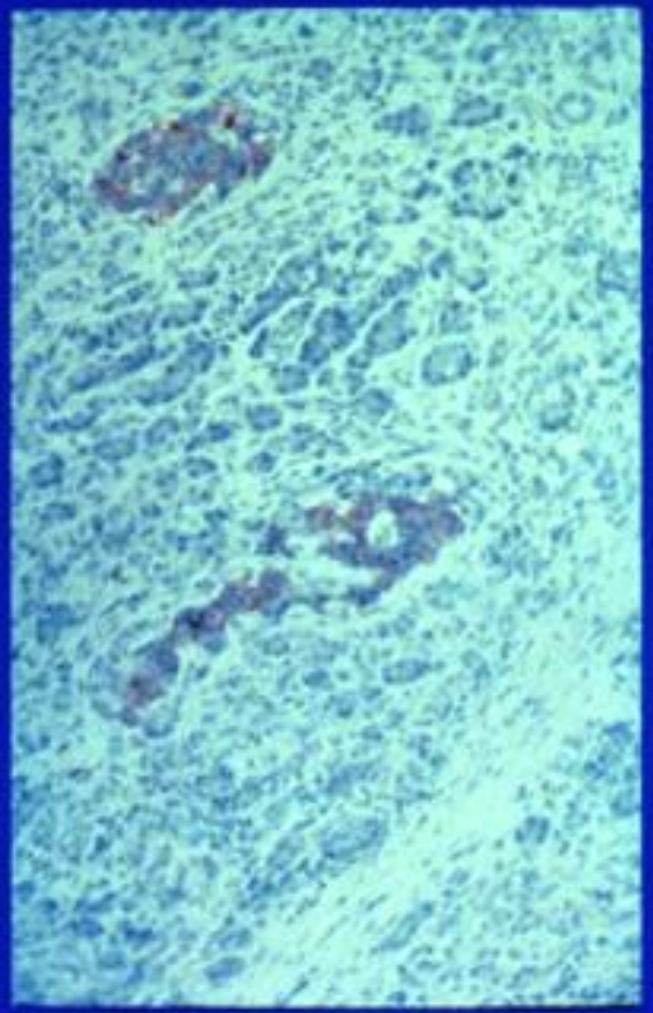


# Chronic Pancreatitis



- Pain
- Calcification
- Pancreatic insufficiency

## CHRONIC PANCREATITIS



## Diabetes

- Loss of insulin and glucagon
- Only in severe disease
- Brittle
- Insulin requirement low
- Ketoacidosis rare

CHRONIC PANCREATITIS

# Diagnostic Tests

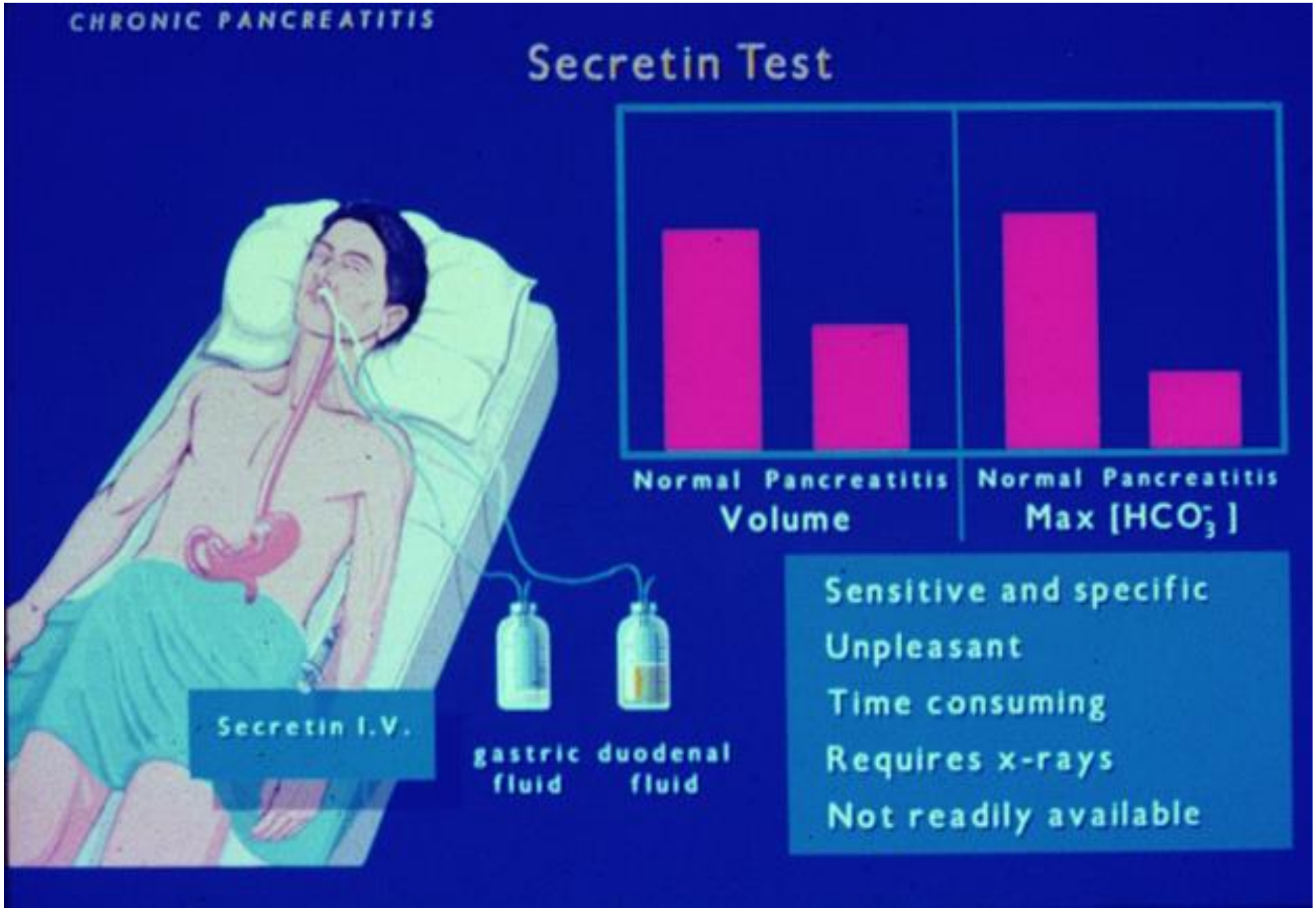
| Structure | | Function |
|---|---|---|
| ERCP | Most sensitive | Secretin test |
| CT scan<br>Ultrasonogram | Less sensitive | Bentiromide (PABA)<br>Serum trypsinogen<br>Fecal chymotrypsin |
| Abdominal x-ray | Least sensitive | Fecal fat<br>Blood glucose |

# Clinical Assessment

| Presentation | Order of evaluation |
| --- | --- |
| Pain | Imaging |
| Malabsorption | Imaging<br>Trial of pancreatic enzymes<br>Tests of pancreatic insufficiency |

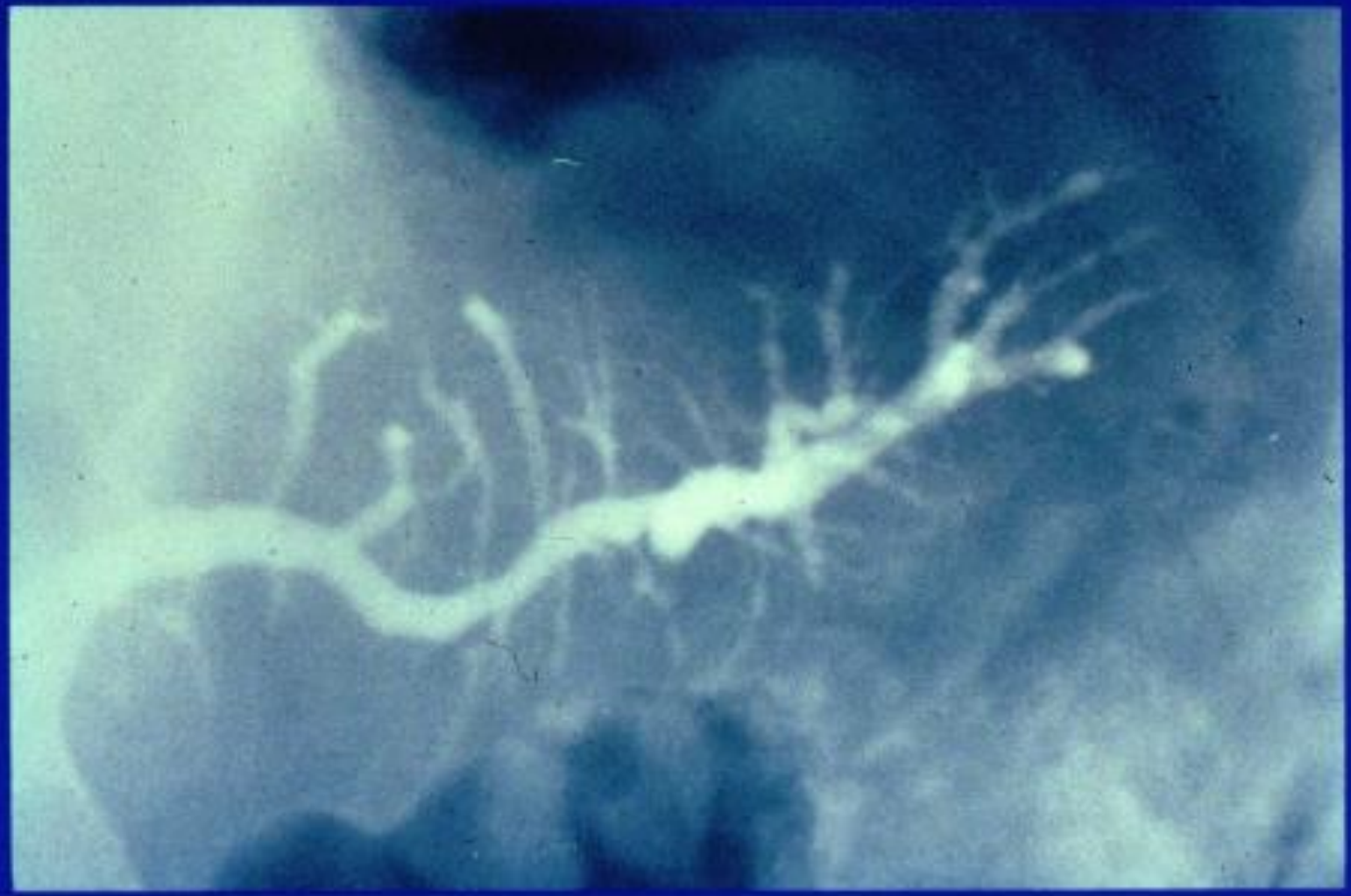
CHRONIC PANCREATITIS

# Secretin Test

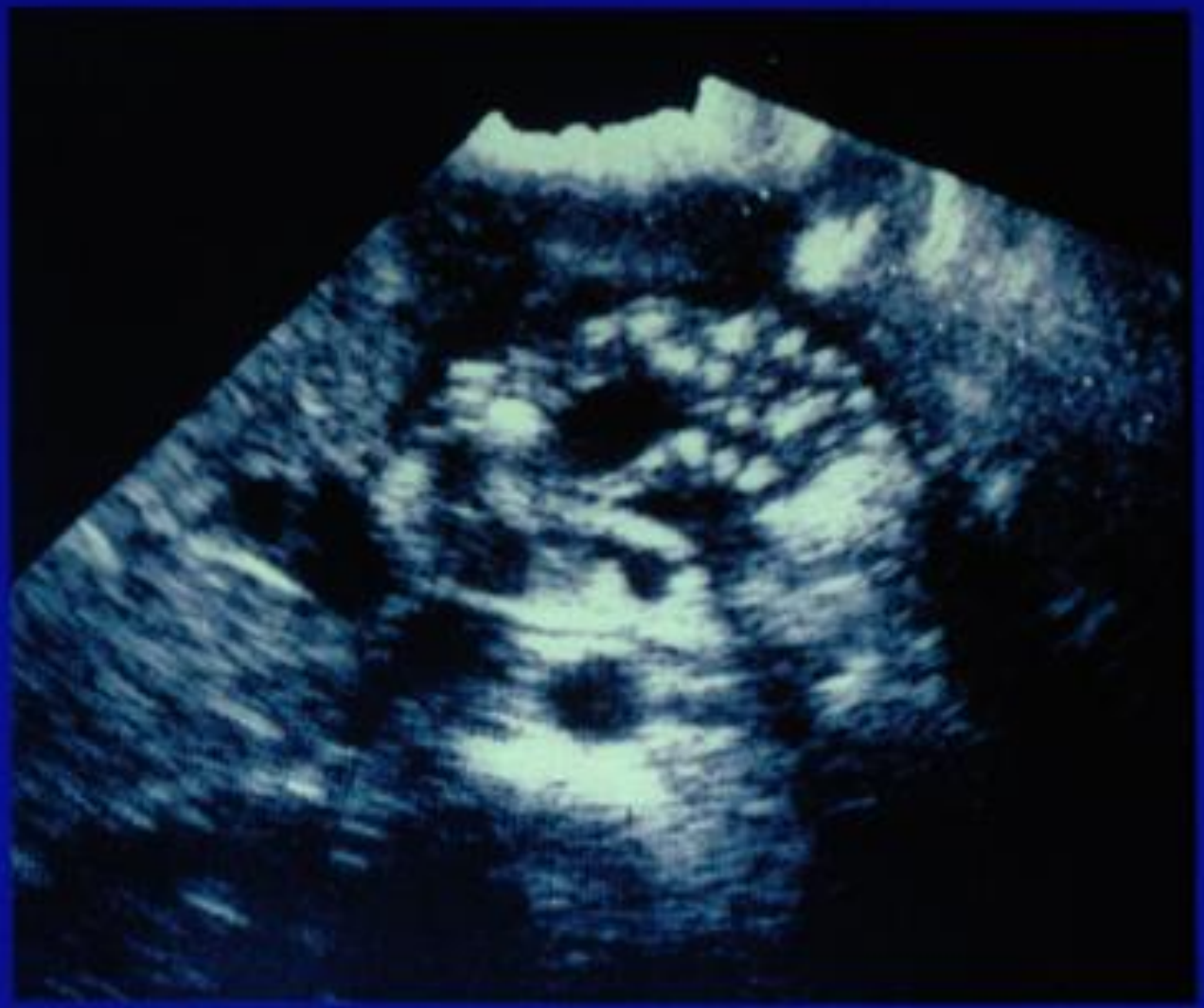



- Sensitive and specific
- Unpleasant
- Time consuming
- Requires x-rays
- Not readily available

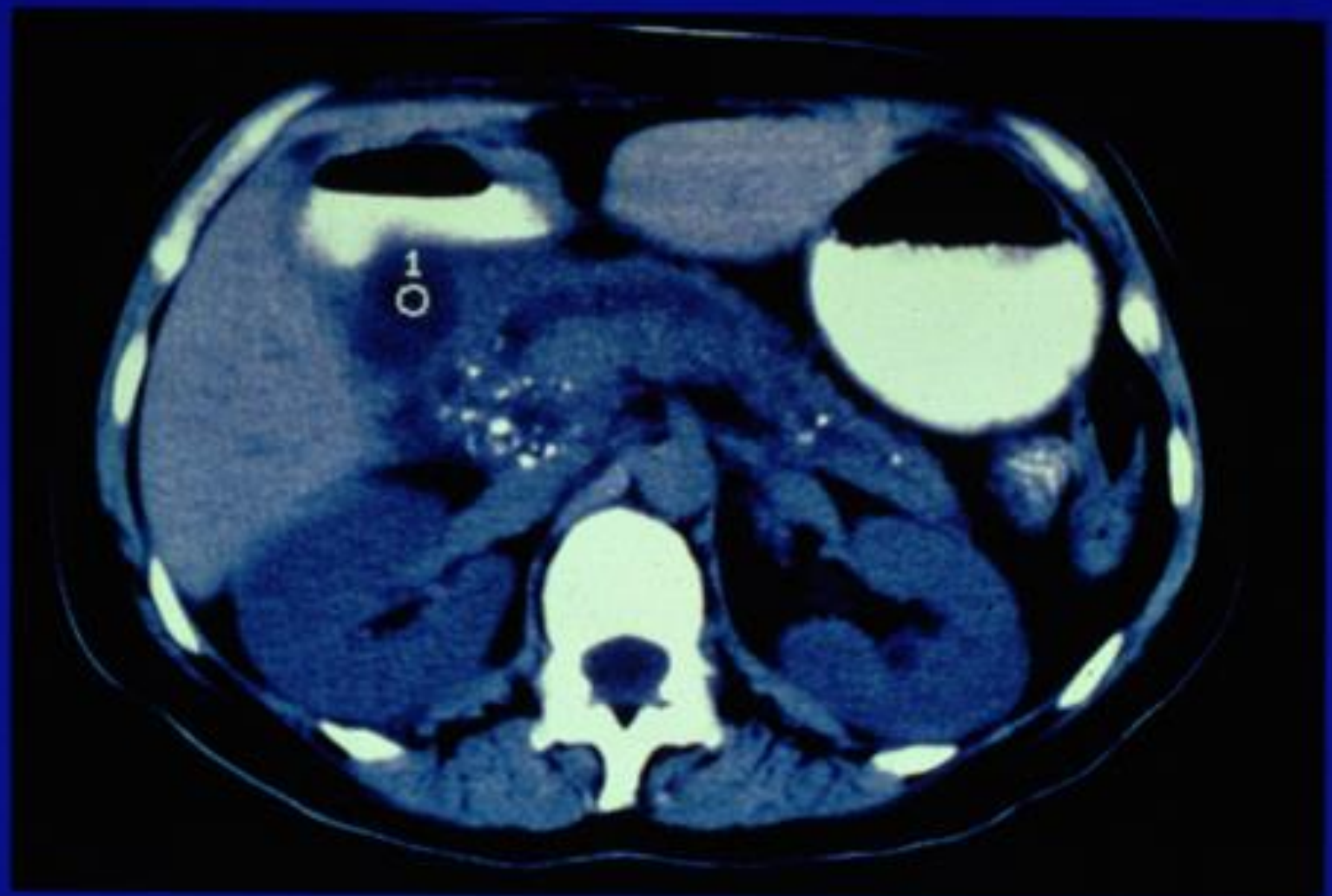
CHRONIC PANCREATITIS



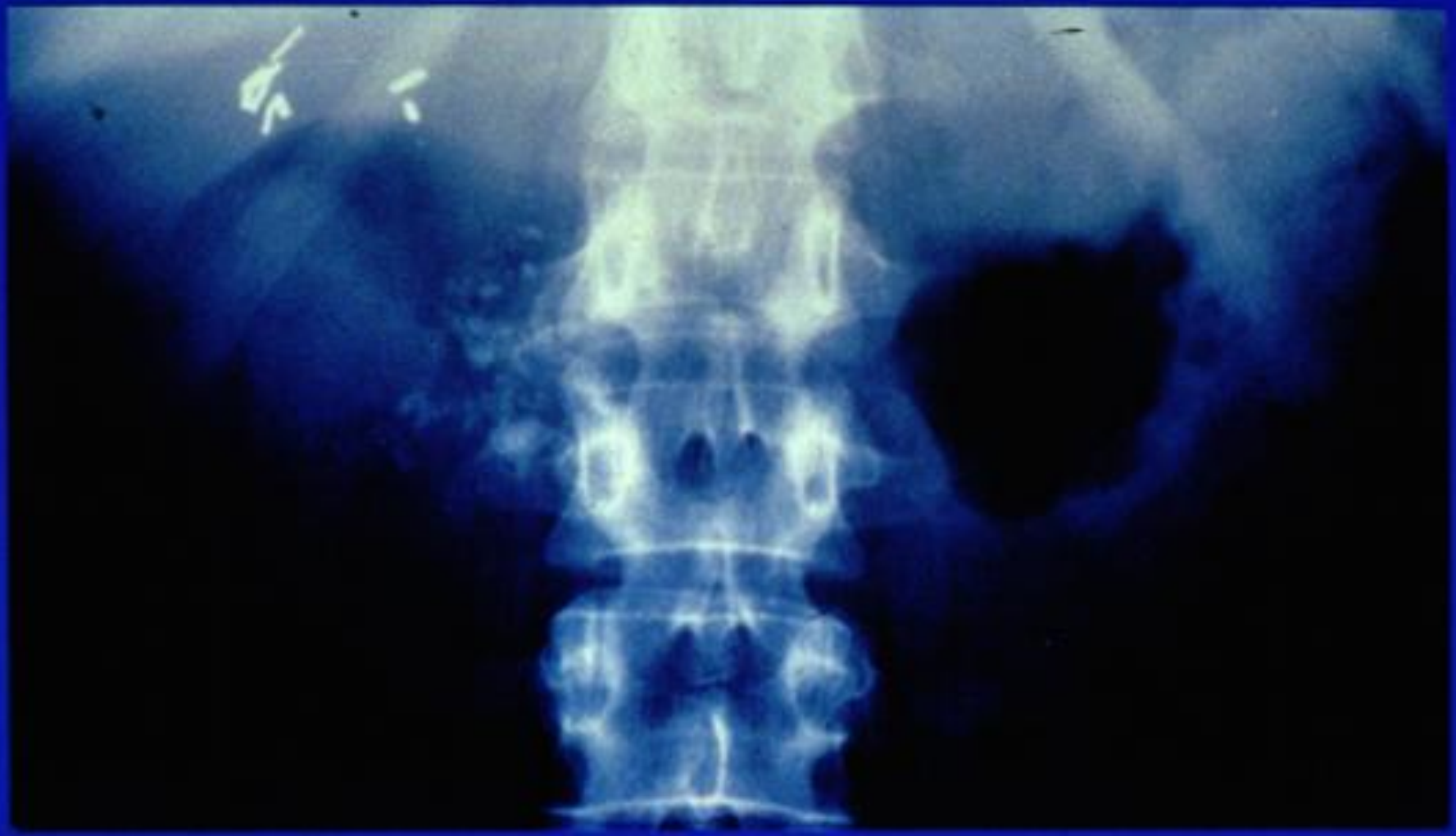
CHRONIC PANCREATITIS



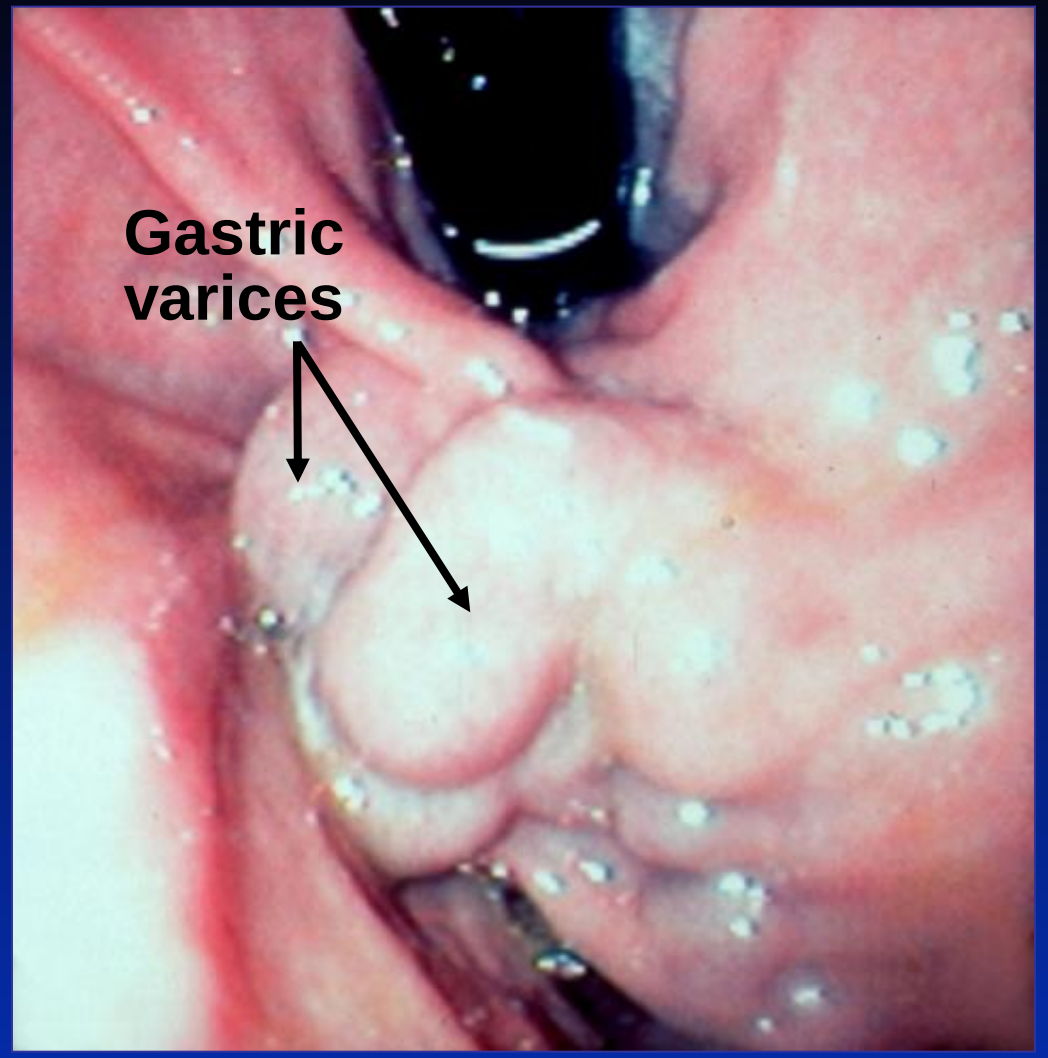
# CHRONIC PANCREATITIS



# CHRONIC PANCREATITIS

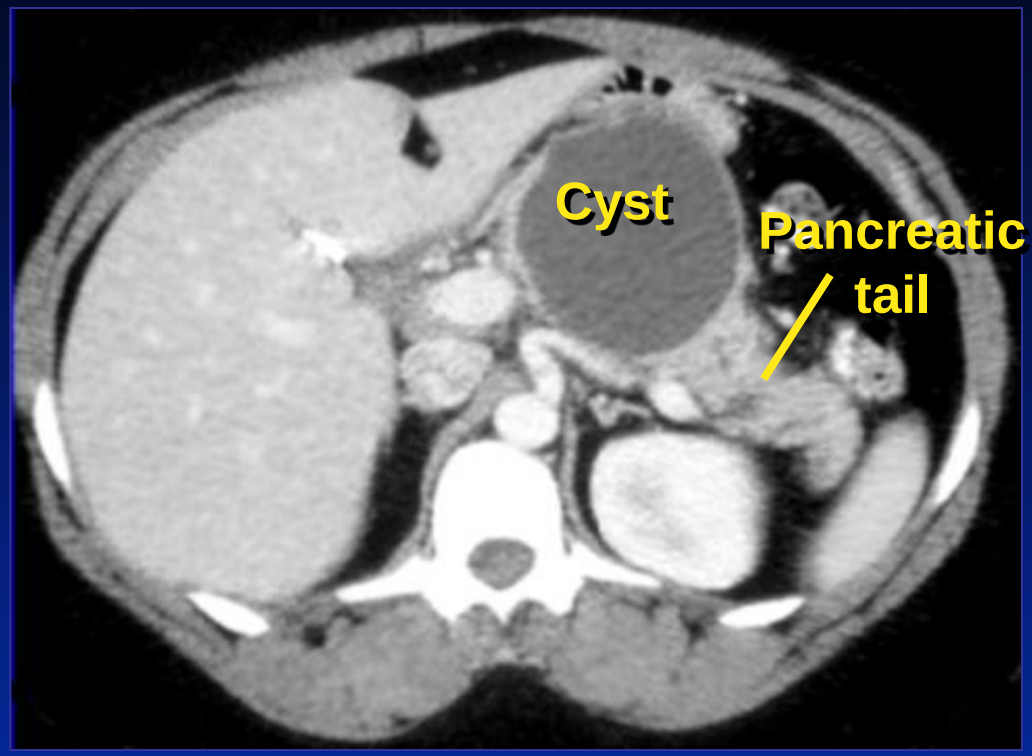


# Splenic Vein Thrombosis




- Associated with chronic disease
- Splenomegaly
- Large gastric varices without esophageal varices
- Splenectomy for bleeding

# Cystic Neoplasm




## Clinical clues

- No prior pancreatitis
- Unexplained pancreatitis
- Cyst present on 1st CT

## Diagnosis

- Fluid analysis
- EUS, ERCP
- Resection

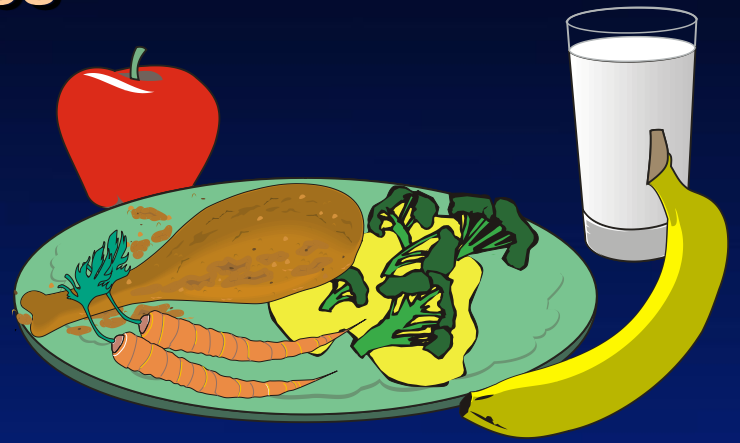
## Cystic Pancreatic Lesions

| Type | Features | Cancer risk |
|---|---|---|
| Pseudocyst | Macrocystic<br>Thick wall | None |
| Serous cystadenoma | Micro- or macrocystic | Low |
| Mucinous cystadenoma | Macrocystic | High |
| Mucinous cystadenocarcinoma | Macrocystic<br>Thick wall<br>Intracystic mass | Cancer present |

# Nutritional Management of Exocrine Insufficiency

## Diet and exogenous enzymes

- Modify fat intake
- Medium chain triglycerides
- Enzyme replacement
  - Coated vs uncoated
  - Acid suppression



## Vitamins, supplements

- Fat soluble
- Calcium
- Cyanocobalamin ($B_{12}$)

# Pain Management

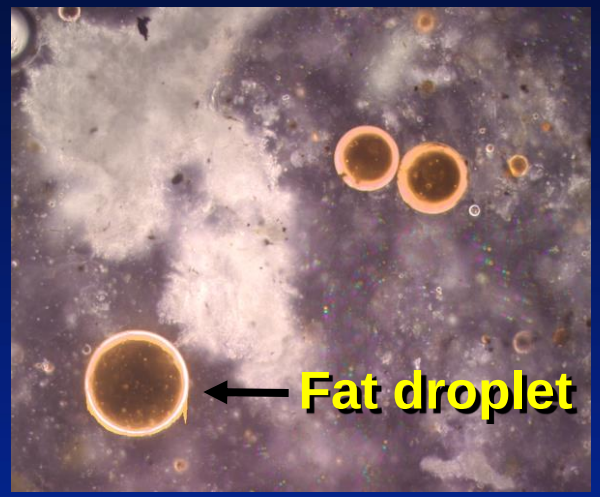
| Treatment | Effectiveness |
|---|---|
| No alcohol | Low to moderate |
| Analgesia | Moderate |
| Enzyme replacement | Low |
| Neurolytic therapy | Moderate short term |
| Pseudocyst drainage | High |
| Duct decompression | Moderate |
| Stone removal | Moderate |

# Use of Exogenous Enzymes for Pain

| Study | Preparation | Response |
|---|---|---|
| Isaksson (1983) | uncoated | yes |
| Slaff (1984) | uncoated | yes |
| Halgreen (1986) | coated | no |
| Mossner (1992) | coated | no |
| Malesci (1995) | coated | no |

# Steatorrhea

Stool with excessive fat



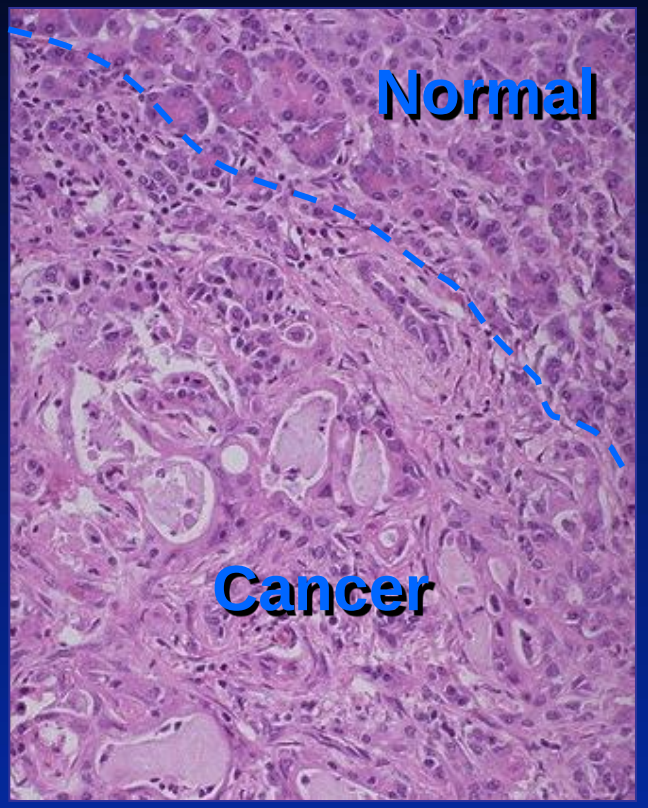

Sudan stain

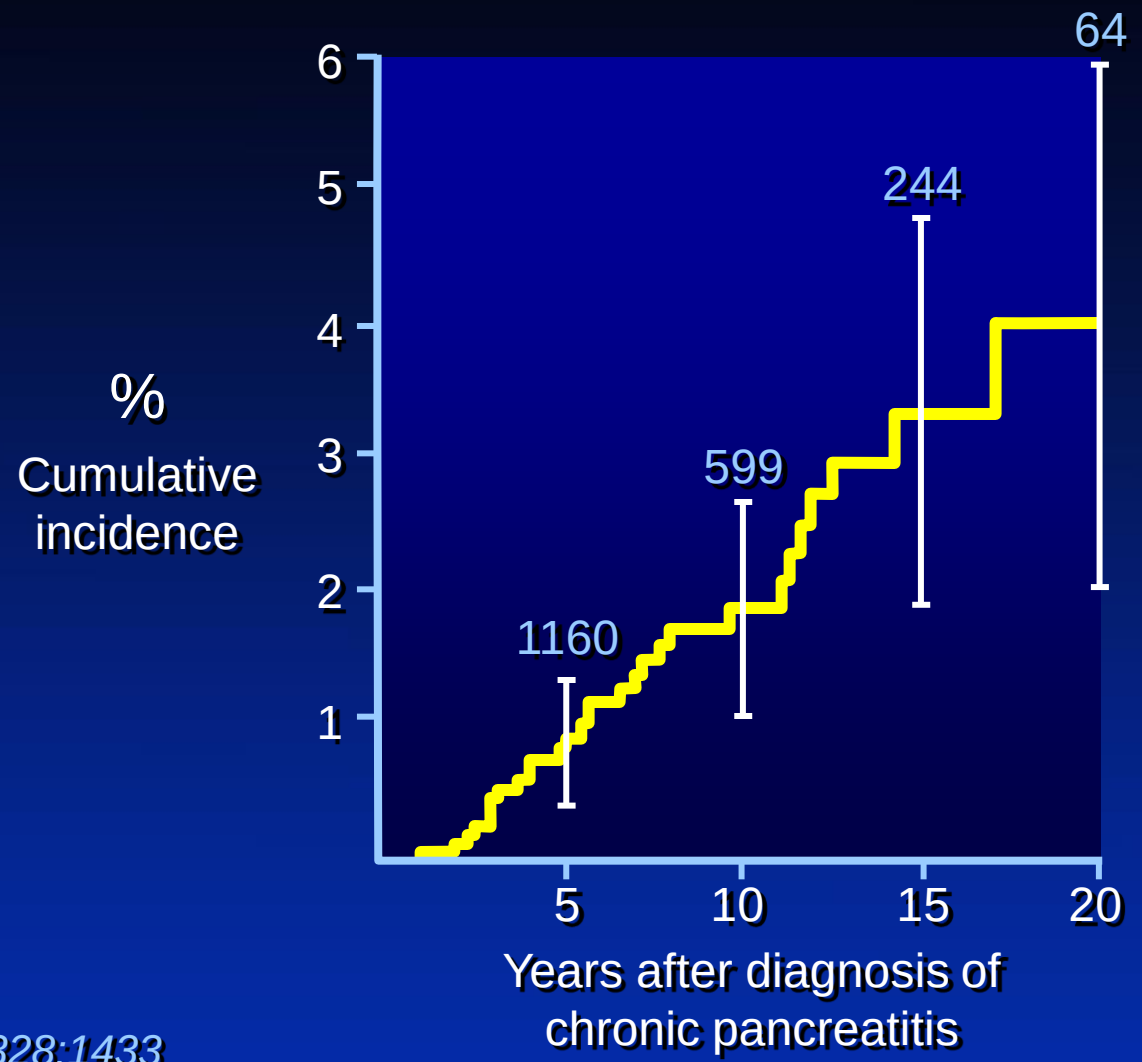
## Mechanisms

- Decreased concentration of lipase and colipase
- ↓ Duodenal pH
  - Inactivation of pancreatic lipase pH<4.5
  - Precipitation of bile salts

# Pancreatic Cancer Risk

3-15 fold increase



# Pancreatic Insufficiency Without Pancreatitis

## Non-pancreatic

- Mucosal disease
  - ↓ CCK release
  - Enterokinase deficiency *
- Gastrinoma
- Bilroth II reconstruction

## Pancreatic

- Cystic fibrosis *
- Pancreatic tumors
- Shwachman-Diamond syndrome *
- Childhood pancreatic atrophy *
- Johanson-Blizzard syndrome*
- Adult lipomatosis or atrophy
- Protein-calorie malnutrition

*** inherited**

# Diagnostic Criteria: I

**Imaging**

- Diffuse pancreatic duct narrowing
- Diffuse pancreatic enlargement

**Immunity**

- Autoantibodies
- Elevated gammaglobulins or IgG4

**Histology**

- Periductular lymphoblastic infiltrate
- Phlebitis
- Fibrosis

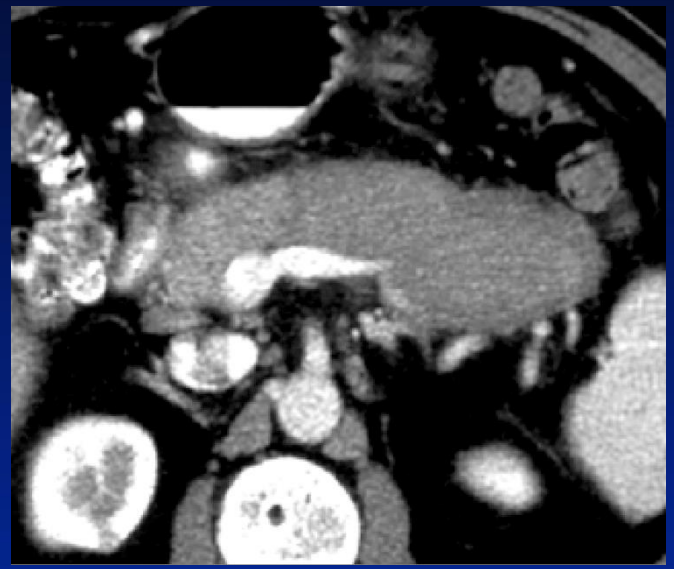
# Presentation

## Symptoms

- Asymptomatic or mild pain
- Acute pancreatitis, rare
- Obstructive jaundice

## Imaging

- Incidental pancreatic mass



# Diagnostic Criteria: II

Other organ involvement

- Biliary
- Liver
- Kidney
- Lung

Response to steroids

# Patient Characteristics

## Gender

- Male > female

## Age

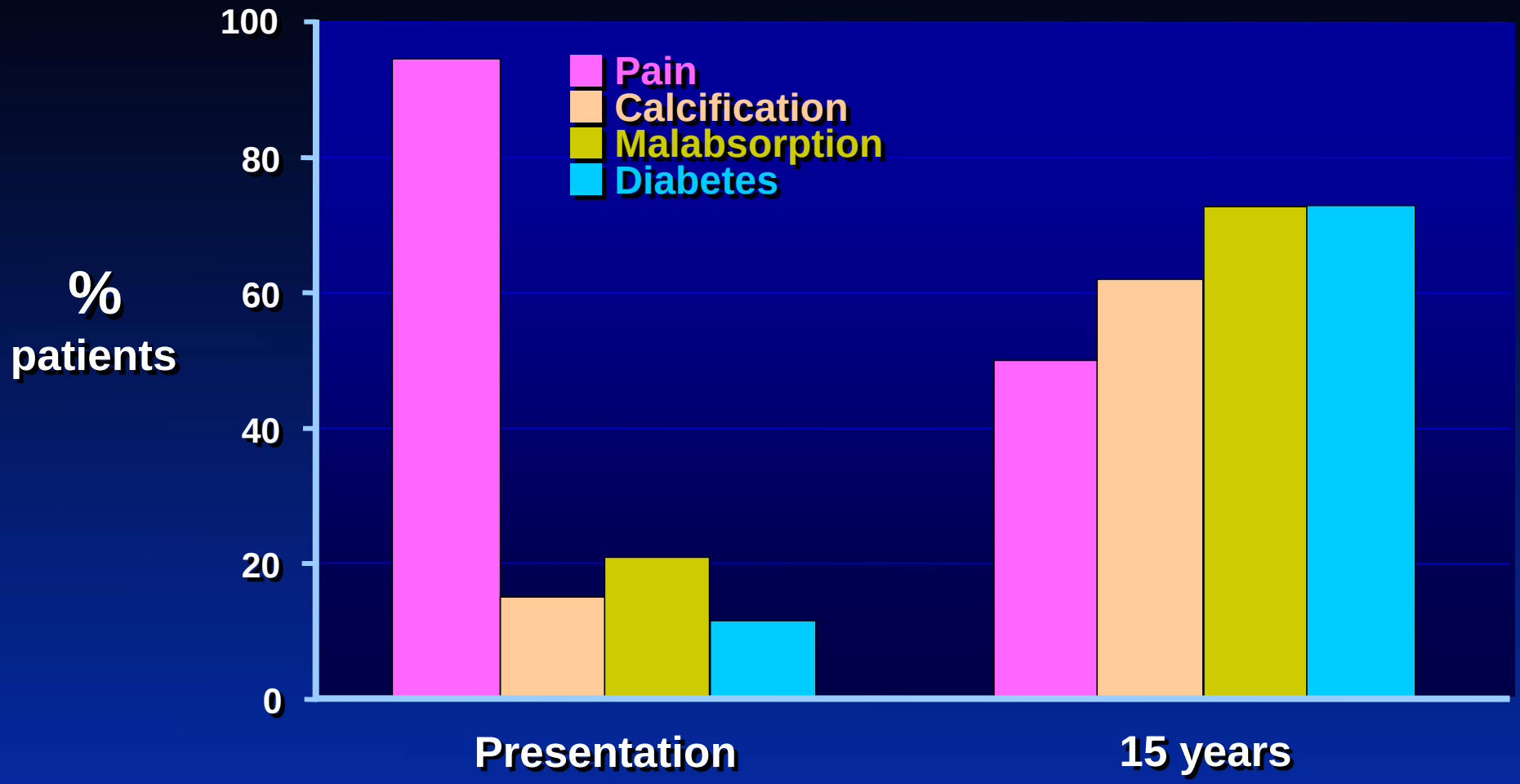
- Wide range (20-80 years), most > 50 years

## Comorbidity

- Autoimmune diseases

## Chronic Pancreatitis

# Course




*Tsiotos, 2002*
*Lankisch PG, Pancreatology 2001; 1:3*