

# ACUTE PANCREATITIS

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•Acute pancreatitis is best defined clinically by a patient presenting with two of the following criteria:

(1) symptoms, such as epigastric pain, consistent with the disease;

(2) a serum amylase or lipase greater than three times the upper limit of normal; or

(3) radiologic imaging consistent with the diagnosis, usually using computed tomography (CT) or magnetic resonance imaging (MRI).

# Etiology

# Causes of Acute Pancreatitis

## **Common Causes**

Gallstones (including microlithiasis)

Alcohol (acute and chronic alcoholism)

Hypertriglyceridemia

Endoscopic retrograde cholangiopancreatography (ERCP), especially after biliary manometry

Trauma (especially blunt abdominal trauma)

Postoperative (abdominal and nonabdominal operations)

Drugs (azathioprine, 6-mercaptopurine, sulfonamides, estrogens, tetracycline, valproic acid, anti-HIV medications)

Sphincter of Oddi dysfunction

## **Uncommon Causes**

Vascular causes and vasculitis (ischemic-hypoperfusion states after cardiac surgery)

Connective tissue disorders and thrombotic thrombocytopenic purpura (TTP)

Cancer of the pancreas

Hypercalcemia

Periampullary diverticulum

Pancreas divisum

Hereditary pancreatitis

Cystic fibrosis

Renal failure

## **Rare Causes**

Infections (mumps, coxsackievirus, cytomegalovirus, echovirus, parasites)

Autoimmune (e.g., Sjögren's syndrome)

## **Causes to Consider in Patients with Recurrent Bouts of Acute Pancreatitis without an Obvious Etiology**

Occult disease of the biliary tree or pancreatic ducts, especially microlithiasis, sludge

Drugs

Hypertriglyceridemia

Pancreas divisum

Pancreatic cancer

Sphincter of Oddi dysfunction

Cystic fibrosis

Idiopathic

- Gallstones continue to be the leading cause of acute pancreatitis in most series (30–60%).
- The risk of acute pancreatitis in patients with at least one gallstone <5 mm in diameter is fourfold greater than that in patients with larger stones.



- Alcohol is the second most common cause, responsible for 15–30% of cases.
- The incidence of pancreatitis in alcoholics is surprisingly low (5/100,000), indicating that in addition to the amount of alcohol ingested, unknown factors affect a person's susceptibility to pancreatic injury.

- It occurs in 5–20% of patients following endoscopic retrograde cholangiopancreatography (ERCP).
- Risk factors for post-ERCP pancreatitis include
  1. minor papilla sphincterotomy,
  2. sphincter of Oddi dysfunction,
  3. prior history of post-ERCP pancreatitis,
  4. age <60 years,
  5. >2 contrast injections into the pancreatic duct,
  6. endoscopic trainee involvement.

- Hypertriglyceridemia is the cause of acute pancreatitis in 1-4% of cases; serum triglyceride levels are usually  $>1000$  mg/dL.
- Any factor (e.g., drugs or alcohol) that causes an abrupt increase in serum triglycerides to levels  $>1000$  mg/dL can precipitate a bout of acute pancreatitis.

- Approximately 2–5% of cases of acute pancreatitis are drug related.
- Drugs cause pancreatitis either by a hypersensitivity reaction or by the generation of a toxic metabolite.

# Pathogenesis

- Autodigestion is a currently accepted pathogenic theory; according to it, pancreatitis results when proteolytic enzymes are activated in the pancreas rather than in the intestinal lumen.
- A number of factors (e.g., *endotoxins, exotoxins, viral infections, ischemia, anoxia, lysosomal calcium, and direct trauma*) are believed to facilitate activation of trypsin.
- Activated trypsin, also can activate other enzymes, such as elastase and phospholipase A<sub>2</sub>.
- Spontaneous activation of trypsin also can occur.

- The **initial phase** is characterized by intrapancreatic digestive enzyme activation and acinar cell injury.
- The **second phase** of pancreatitis involves the activation, chemoattraction, and sequestration of leukocytes and macrophages in the pancreas, resulting in an enhanced intrapancreatic inflammatory reaction.
- The **third phase** of pancreatitis is due to the effects of activated proteolytic enzymes and cytokines, released by the inflamed pancreas, on distant organs.

- There is also evidence to support the concept that neutrophil sequestration can activate trypsinogen.
- Thus, intrapancreatic acinar cell activation of trypsinogen could be a two-step process (i.e., an early neutrophil-independent and a later neutrophil-dependent phase).



# Clinical features

- *Abdominal pain* is the major symptom of acute pancreatitis.
- Characteristically, the pain, which is *steady and boring* in character, is located in *the epigastrium* and *periumbilical* region and often radiates to *the back* as well as to the chest, flanks, and lower abdomen.
- The pain is frequently more intense when the patient is supine, and patients may obtain some relief by sitting with the trunk flexed and knees drawn up.

- Nausea, vomiting, and abdominal distention due to gastric and intestinal hypomotility and chemical peritonitis are also frequent complaints.
- Low-grade fever, tachycardia, and hypotension are fairly common.
- Shock may result.

- Jaundice occurs infrequently.
- Erythematous skin nodules due to subcutaneous fat necrosis may occur.
- In 10–20% of patients, there are pulmonary findings, including basilar rales, atelectasis, and left sided pleural effusion.

- A faint blue discoloration around the umbilicus (**Cullen's sign**) may occur as the result of *hemoperitoneum*, and green-brown discoloration of the flanks (**Turner's sign**) reflects *tissue catabolism of hemoglobin* and indicate the presence of a severe necrotizing pancreatitis.



Grey Turner's sign.

- Serum lipase activity increases in parallel with amylase activity.
- A threefold elevated serum lipase value is usually diagnostic of acute pancreatitis;
- These tests are especially helpful in patients with nonpancreatic causes of hyperamylasemia.

## Nonpancreatic Disorders

I. Renal insufficiency

### II. Salivary gland lesions

A. Mumps

B. Calculus

C. Irradiation sialadenitis

D. Maxillofacial surgery

### III. "Tumor" hyperamylasemia

A. Carcinoma of the lung

B. Carcinoma of the esophagus

C. Breast carcinoma, ovarian carcinoma

IV. Macroamylasemia

V. Burns

VI. Diabetic ketoacidosis

VII. Pregnancy

VIII. Renal transplantation

IX. Cerebral trauma

X. Drugs: morphine

## Other Abdominal Disorders

I. Biliary tract disease: cholecystitis, choledocholithiasis

II. Intraabdominal disease

A. Perforated or penetrating peptic ulcer

B. Intestinal obstruction or infarction

C. Ruptured ectopic pregnancy

D. Peritonitis

E. Aortic aneurysm

F. Chronic liver disease

G. Post-op hyperamylasemia



- *Hyperglycemia* is common and is due to multiple factors, including
  - ✓ decreased insulin release,
  - ✓ increased glucagon release, and
  - ✓ an increased output of adrenal glucocorticoids and catecholamines.
- *Hypocalcemia* occurs in 25% of patients, and its pathogenesis is incompletely understood.

- *Hypertriglyceridemia* occurs in 5–10% of patients, and serum amylase levels in these individuals are often spuriously normal.
- Approximately 5–10% of patients have *hypoxemia* (arterial  $P_{O_2}$  60 mmHg), which may herald the onset of ARDS.
- Finally, the ECG is occasionally abnormal in acute pancreatitis with ST-segment and T-wave abnormalities simulating myocardial ischemia.

The *differential diagnosis* should include the following disorders:

- (1) perforated viscus, especially peptic ulcer;
- (2) acute cholecystitis and biliary colic;
- (3) acute intestinal obstruction;
- (4) mesenteric vascular occlusion;
- (5) renal colic;
- (6) myocardial infarction;
- (7) dissecting aortic aneurysm;
- (8) connective tissue disorders with vasculitis;
- (9) pneumonia; and
- (10) diabetic ketoacidosis

- The course of acute pancreatitis is defined by two phases.
- In the **first phase**, which lasts one to two weeks, severity is defined by clinical parameters rather than morphologic findings. The most important clinical parameter is persistent organ failure (i.e., lasting longer than 48 hours), which is the usual cause of death.
- Severity in the **second phase** is defined by both clinical parameters and morphologic criteria. The morphologic criteria of greatest interest is the development of necrotizing pancreatitis.

- Traditional severity indices such as APACHE II and Ranson's criteria have not been clinically useful.
- A recent simplified scoring system for the early prediction of mortality was developed.
- This scoring system, referred to as the *Bedside Index of Severity in Acute Pancreatitis (BISAP)*

## Severe Acute Pancreatitis

### **Risk Factors for Severity**

- Age >60 years
- Obesity, BMI >30
- Comorbid disease

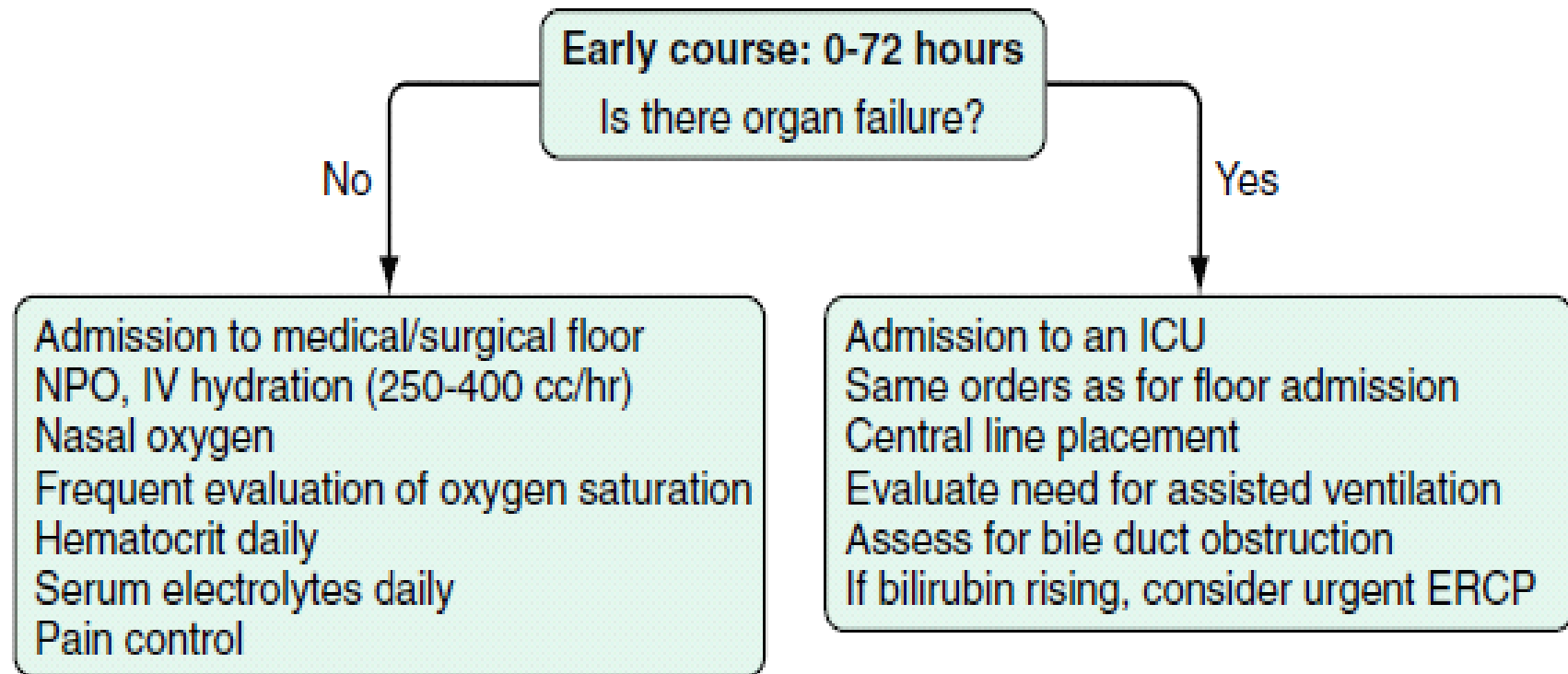
### **Markers of Severity within 24 Hours**

- SIRS [temperature >38° or <36°C (>100.4° or 96.8°F), Pulse >90, Tachypnea >24, WBC >12,000]
- Hemoconcentration (Hct >44%)
- *BISAP*
  - *(B) Blood urea nitrogen (BUN) >22 mg%*
  - *(I) Impaired mental status*
  - *(S) SIRS: 2/4 present*
  - *(A) Age >60 years*
  - *(P) Pleural effusion*
- Organ Failure
  - Cardiovascular: systolic BP <90 mmHg, heartrate >130
  - Pulmonary: Pao<sub>2</sub> <60 mmHg
  - Renal: serum creatinine >2.0 mg%

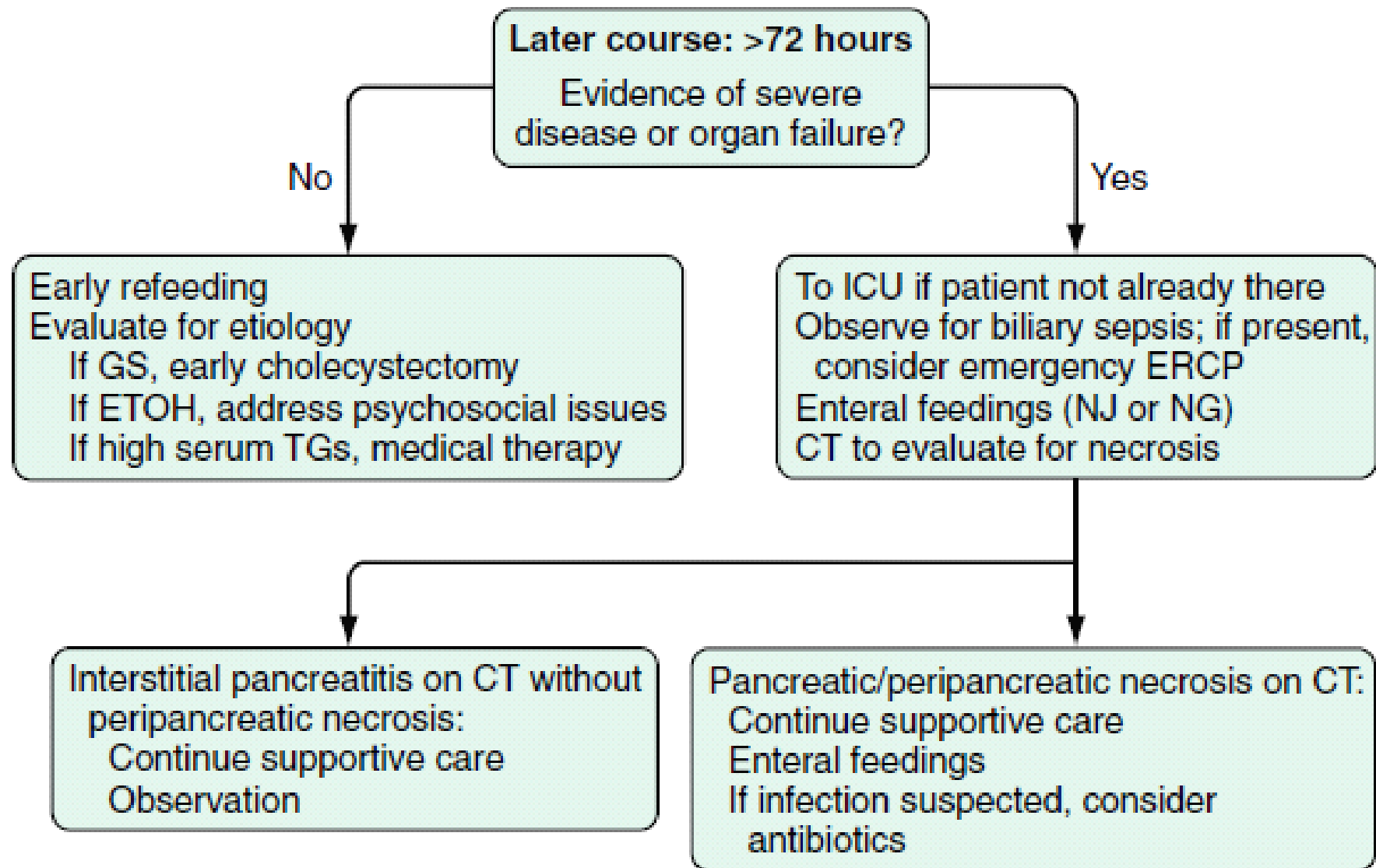
### **Markers of Severity during Hospitalization**

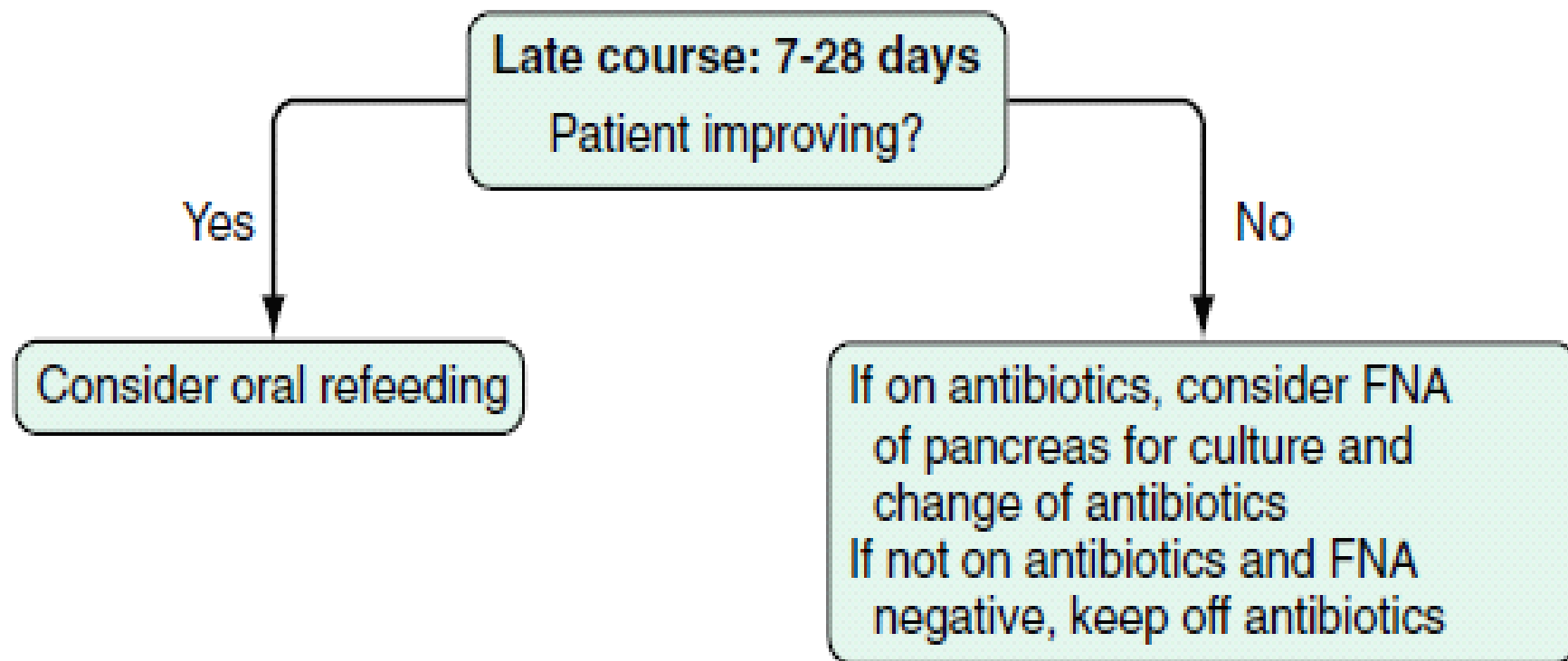
- Persistent organ failure
- Pancreatic necrosis
- Hospital-acquired infection

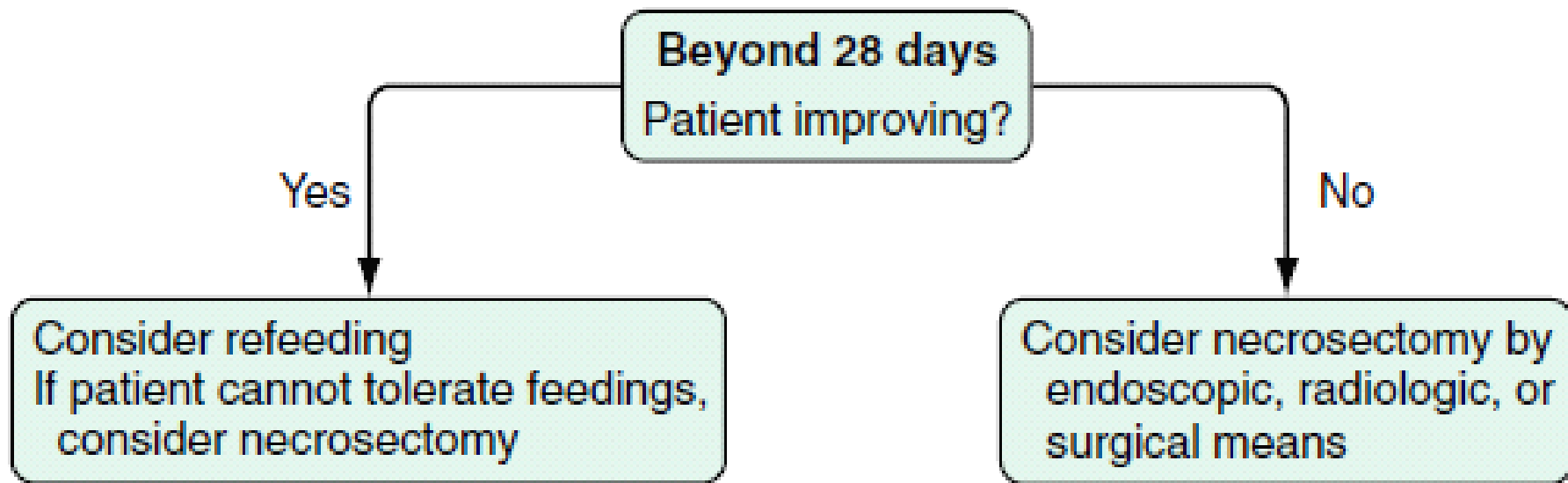
Treatment











The treatment for patients with hypertriglyceridemia-associated pancreatitis includes

- (1) weight loss to ideal weight,
- (2) a lipid-restricted diet,
- (3) exercise,
- (4) avoidance of alcohol and of drugs that can elevate serum triglycerides (i.e., estrogens, vitamin A, thiazides, and propranolol), and
- (5) control of diabetes.

- A recent meta-analysis of somatostatin, octreotide, and the antiprotease gabexate mesylate in the therapy of acute pancreatitis suggested

(1) a reduced **mortality** rate but no change in complications with octreotide and

(2) no effect on the mortality rate but reduced **pancreatic damage** with gabexate.

# Complications

## Local

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Necrosis

    Sterile

    Infected

    Organized

Pancreatic fluid collections

    Pancreatic abscess

    Pancreatic pseudocyst

        Pain

        Rupture

        Hemorrhage

        Infection

        Obstruction of gastrointestinal tract (stomach, duodenum, colon)

Pancreatic ascites

    Disruption of main pancreatic duct

    Leaking pseudocyst

Involvement of contiguous organs by necrotizing pancreatitis

    Massive intraperitoneal hemorrhage

    Thrombosis of blood vessels (splenic vein, portal vein)

    Bowel infarction

Obstructive jaundice

## Systemic

### Pulmonary

- Pleural effusion
- Atelectasis
- Mediastinal abscess
- Pneumonitis
- Adult respiratory distress syndrome

### Cardiovascular

- Hypotension
- Hypovolemia
- Sudden death
- Nonspecific ST-T changes in electrocardiogram simulating myocardial infarction

### Pericardial effusion

### Hematologic

- Disseminated intravascular coagulation

### Gastrointestinal hemorrhage

- Peptic ulcer disease
- Erosive gastritis
- Hemorrhagic pancreatic necrosis with erosion into major blood vessels

- Portal vein thrombosis, variceal hemorrhage

### Renal

- Oliguria
- Azotemia
- Renal artery and/or renal vein thrombosis
- Acute tubular necrosis

### Metabolic

- Hyperglycemia
- Hypertriglyceridemia
- Hypocalcemia
- Encephalopathy
- Sudden blindness (Purtscher's retinopathy)

### Central nervous system

- Psychosis
- Fat emboli

### Fat necrosis

- Subcutaneous tissues (erythematous nodules)

### Bone

- Miscellaneous (mediastinum, pleura, nervous system)



- Approximately one-half of cases of **infected necrosis** can be diagnosed between the 7th and 21st day, the remainder after 21 days.
- The diagnosis can be accomplished by CT-guided needle aspiration with Gram stain and culture.
- The organisms are most frequently gram-negative bacteria of intestinal origin.

- Eventually, after three to six weeks, there is coalescence of the pancreatic necrosis and peripancreatic fat necrosis into a structure that is encapsulated by fibrous tissue refers to as "walled-off necrosis."

- Choices of treatment in infected pancreatic necrosis include
  1. surgical debridement;
  2. endoscopic debridement, if walled-off necrosis that affects the posterior wall of the stomach; and,
  3. on occasion, radiologic catheter drainage with irrigation.

- **Pseudocysts** of the pancreas are extrapancreatic collections of pancreatic fluid containing pancreatic enzymes and a small amount of debris.
- Approximately 85% are located in the body or tail and 15% in the head. Some patients have two or more pseudocysts.
- A palpable, tender mass may be found in the middle or left upper abdomen.

- Sonography, is reliable in detecting pseudocysts.
- Furthermore, serial ultrasound studies will indicate whether a pseudocyst has resolved.
- A significant number of these pseudocysts resolve spontaneously in 6 weeks after their formation.
- Large pseudocyst size is not an absolute indication for interventional therapy.

- A pseudocyst that does not resolve spontaneously can occasionally lead to serious complications, such as
  - (1) pain caused by expansion of the lesion and pressure on other viscera,
  - (2) rupture,
  - (3) hemorrhage, and
  - (4) abscess.
- These patients should be operated on.

- **Pseudoaneurysms** develop in up to 10% of patients.
- *The splenic artery is most frequently* involved, followed by the inferior and superior pancreatic duodenal arteries.
- This diagnosis should be suspected in patients with pancreatitis who develop upper gastrointestinal bleeding without an obvious cause.
- CT angiography can identify the lesion, which can then be treated with angiographic embolization.

- If the pancreatic duct disruption is **posterior**, an internal fistula may develop between the pancreatic duct and the pleural space, producing a pleural effusion (**pancreaticopleural fistula**) that is usually left-sided and often massive.
- If the pancreatic duct disruption is **anterior**, amylase- and lipase-rich peritoneal fluid accumulate (**pancreatic ascites**).
- This diagnosis is suggested when both increased levels of albumin [ $>30$  g/L ( $>3$  g/dL)] and a markedly elevated level of amylase.



- The differential diagnosis of pancreatic ascites should include
  1. intraperitoneal carcinomatosis,
  2. tuberculous peritonitis,
  3. constrictive pericarditis, and
  4. Budd-Chiari syndrome.

- A leaking, disrupted pancreatic duct is best treated by ERCP and “bridging” stent placement.
- If ascites or pleural fluid persists after two to three weeks of medical management, and the disruption is unable to be stented, the patient should be considered for surgical intervention after retrograde pancreatography to define the anatomy of the disrupted duct.

*Thank you*