Acute Pancreatitis

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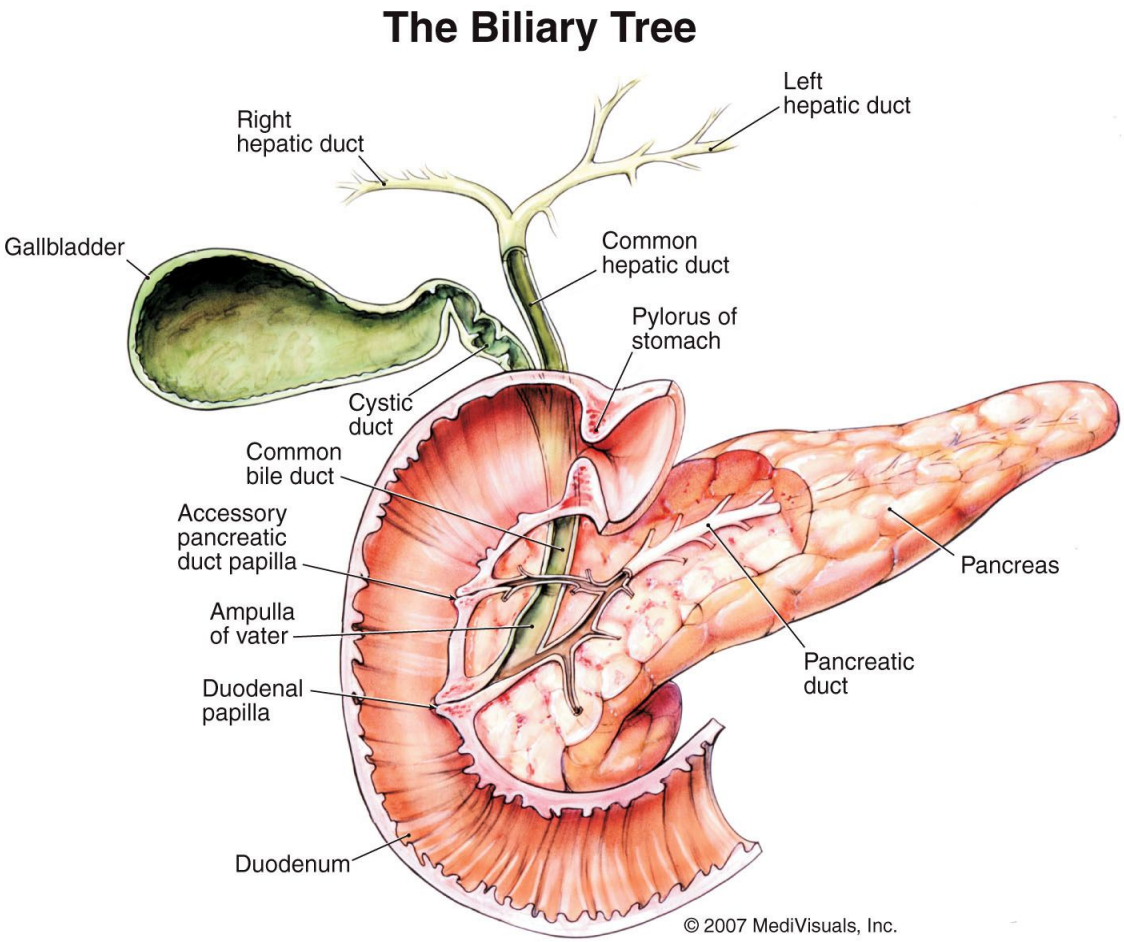
Anatomy


The Biliary Tree
Left hepatic duct
Right hepatic duct
Gallbladder
Common hepatic duct
Pylorus of stomach
Cystic duct
Common bile duct
Accessory pancreatic duct papilla
Ampulla of vater
Duodenal papilla
Duodenum
Pancreas
Pancreatic duct
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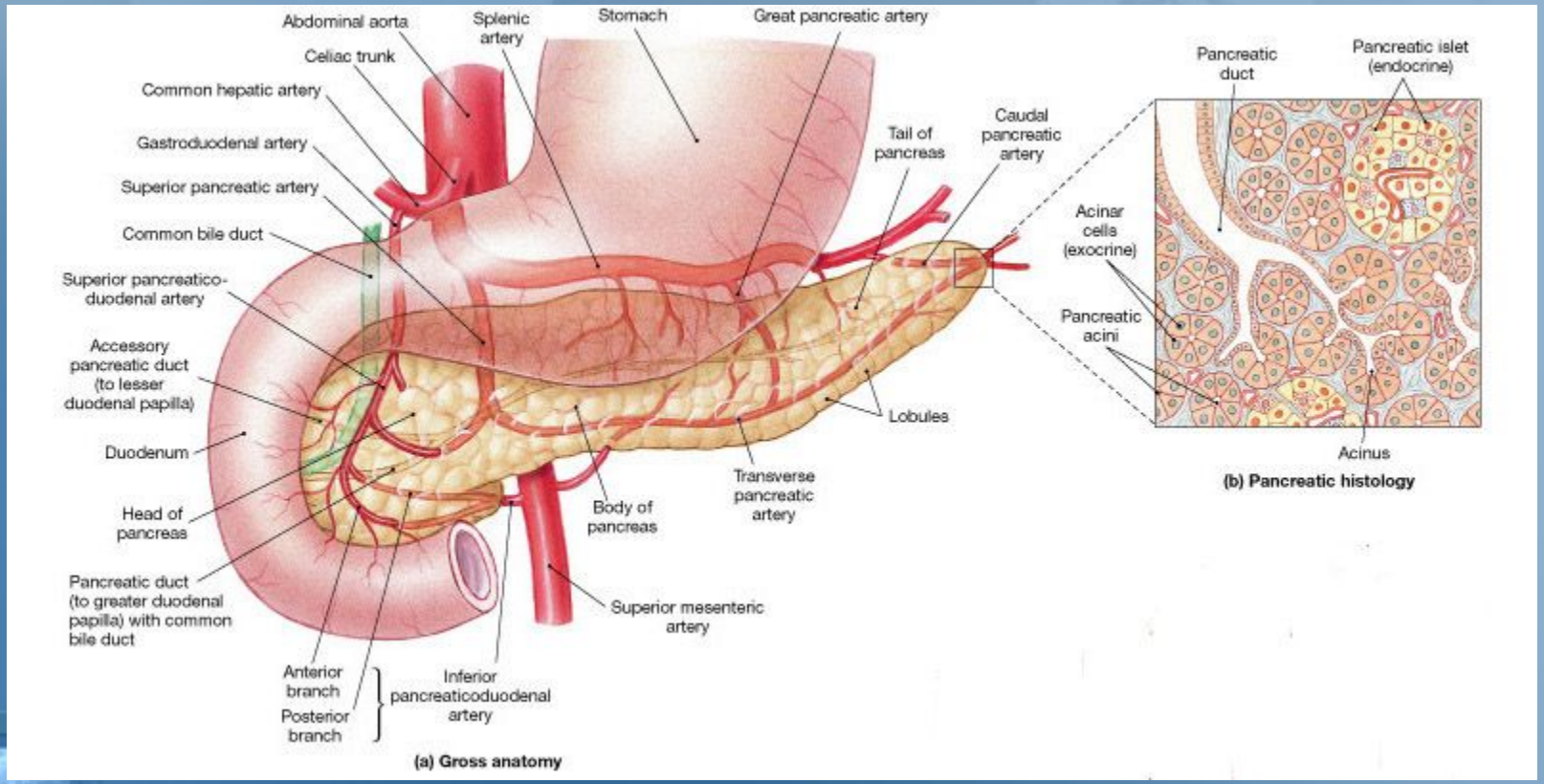

Abdominal aorta
Splenic artery
Stomach
Great pancreatic artery
Celiac trunk
Common hepatic artery
Gastroduodenal artery
Superior pancreatic artery
Common bile duct
Superior pancreatico-duodenal artery
Accessory pancreatic duct (to lesser duodenal papilla)
Duodenum
Head of pancreas
Pancreatic duct (to greater duodenal papilla) with common bile duct
Anterior branch
Posterior branch
Inferior pancreaticoduodenal artery
Superior mesenteric artery
Body of pancreas
Transverse pancreatic artery
Lobules
Tail of pancreas
Caudal pancreatic artery
(a) Gross anatomy
Pancreatic duct
Pancreatic islet (endocrine)
Acinar cells (exocrine)
Pancreatic acini
Acinus
(b) Pancreatic histology

Introduction

- Water & Electrolyte Secretion
  - Bicarbonate – most important
  - Na, K, Cl, Ca, Zn, PO_4, SO_4
- Enzyme Secretion
  - Amylolytic (amylase)
  - Lipolytic (lipase, phospholipase A, cholesterol esterase)
  - Proteolytic (endopeptidase, exopeptidase, elastase)
    - Zymogen or inactive precursors
    - Enterokinase (duodenum) cleaves trypsinogen to trypsin

What are the two most common etiologies for acute pancreatitis in the western civilization?

1. Drugs and alcohol
2. Neoplastic and metabolic
3. Bile stones and alcohol
4. Structural and drugs
5. Toxic and idiopathic

Etiology

Etiologies

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

Gallstone pancreatitis

- Mechanism is not entirely clear
- Common-channel theory

  "Blockage below junction of biliary and pancreatic duct cause bile flow into pancreas"

  BUT…

  – short channel that stone located would block both biliary and pancreatic duct

  –Hydrostatic pressure in biliary<pancreatic duct

Mechanism???

- **Ductal hypertension**
  - Cause rupture of small ducts and leakage of pancreatic juice
  - pH in pancreatic tissue ↓
  - activation of protease
  - “Colocalization”

Alcoholic pancreatitis

- Common in pt. alcohol drinking > 2yr.
- Often much longer up to 10 yr.
- Sphincter spasm
- Decrease pancreatic blood flow

Etiologies

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

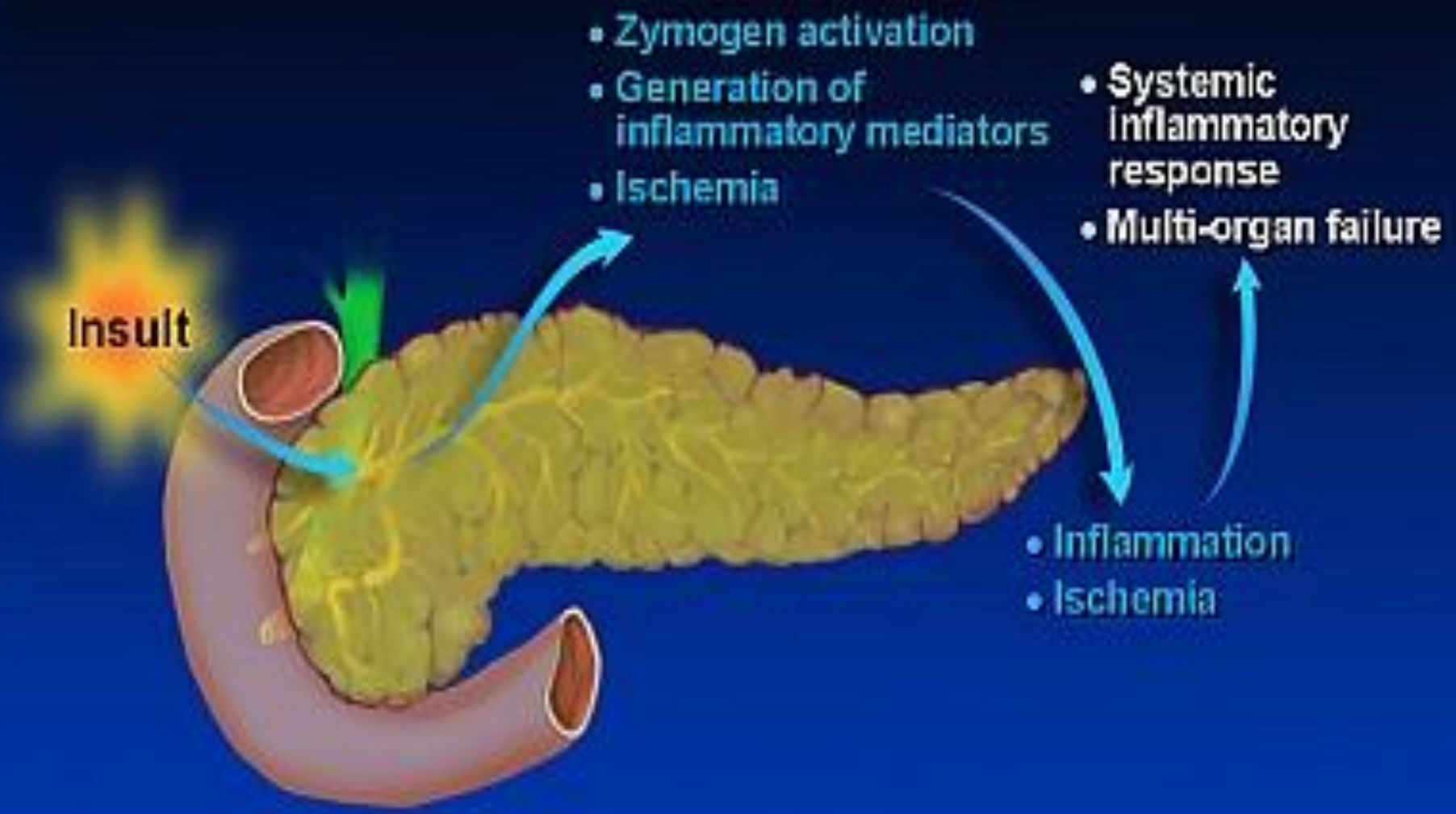
Which of the following drugs is well known for it's ability to induce pancreatitis?

1. Propranolol
2. Erythromycin
3. Azathioprin
4. Codein

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

Acute Pancreatitis: Mechanisms



Diagnosis

Diagnostic criteria

Two of following three features

- Upper abd. pain of acute onset often radiating to back
- Serum amylase or lipase > 3times normal
- Finding on cross sectional abd. imaging

Reference : 2012 revision of Atlanta classification of acute pancreatits

Physical exam

- Grey Turner's Sign
  - ecchymosis in 1 or both flanks
- Cullen's sign
  - ecchymosis in periumbilical area

- Associated with Necrotizing pancreatitis
- poor prognosis occurs in 1% of cases

Grey Turner's Sign

Cullen's Sign

Serum markers

Serum amylase

- Elevates within HOURS and can remain elevated for 3-5 days
- High specificity when level >3x normal
- Many false positives
- Most specific = pancreatic isoamylase (fractionated amylase)

Urine amylase

- urinary levels may be more sensitive than serum levels.
- Urinary amylase levels usually remain elevated for several days after serum levels have returned to normal.

Serum lipase

- The preferred test for diagnosis
- Begins to increase 4-8H after onset of symptoms and peaks at 24H
- Remains elevated for days
- Sensitivity 86-100% and Specificity 60-99%
- >3X normal S&S ~100%

Conditions Associated with Hyperamylasemia and Hyperlipasemia

	Amylase	Lipase
Paroditis	yes	no
Tumors	yes	no
Biliary disease	yes	slight
Pancreatitis	yes	yes
Renal failure	yes	slight
Intestinal obstruction, ulceration, Ischemia	yes	yes
Ectopic pregnancy	yes	no
Macroamylasemia	yes	no
Perforated viscus	yes	yes

Plain Abdominal Radiograph

Plain Abdominal Radiograph

- Bowel ileus
- “Sentinel Loop”
- “Colon cut off sign”
- Loss of psoas shadow

- Helps exclude other causes of abdominal pain: bowel obstruction and perforation

Radiologic Findings

- ***Plain radiographs*** contribute little
- ***Ultrasound*** may show the pancreas in only 25-50%
- ***CT scan*** provides better information
  - Severity and prognosis
  - Exclusion of other diseases
- ***EUS & MRI with MRCP*** – cause of pancreatitis

Assessment of severity

Classification of severity

- *Mild* : lack of organ failure or systemic complications
- *Moderate* : transient organ failure and/or complications < 48hr
- *Severe* : persistent organ failure and systemic complications

Reference : 2012 revision of Atlanta classification of acute pancreatitis

Complication

Systemic complications (More common within the 1st week)	Local complications (Occurs after the 1st week)
Cardiovascular – shock, arrythmia	Acute fluid collection
Pulmonary – ARDS	Sterile pancreatic necrosis
Renal failure	Infected pancreatic necrosis
Disseminated intravascular coagulation	Pseudoaneurysm
GIT – ileus	Pancreatic abscess
Neurological – confusion, visual disturbances, encephalopathy	Splenic vein thrombosis
Subcutaneous fat necrosis	
Hyperglycemia	
Hyperlipidemia	
Hypocalcemia	

Which of the following is not considered adverse prognostic feature in acute pancreatitis?

- 1. WBC> 16,000
- 2. Amylase> 1000
- 3. Glucose> 200
- 4. PaO2< 60
- 5. Age> 55

Early prognostic signs

- Ranson's score
- APACHE II

Ranson's Criteria of Severity

Admission

- Age > 55 years
- WBC > 16,000 mm^3
- Glucose > 200 mg/dl
- LDH > 350 IU/L
- AST > 120 IU/L

After 48 hrs

- Hct decrease >10%
- BUN increase > 5 mg/dl
- Ca^{2+} < 8 mg/dl
- PaO_2 < 60 mm Hg
- Base deficit > 4 mEq/L
- Negative fluid balance > 6L

Ranson's Criteria (GB Pancreatitis)

- **At Admission**

  Age > 70 yr

  WBC > 18,000/mm^3

  Blood glucose > 220 mg/dL

  Serum lactate dehydrogenase > 400IU/L

  Serum aspartate aminotransferase >250IU/L
- **During Initial 48 hr**

  Hematocrit decrease of > 10%

  BUN increase of >2 mg/dL

  Serum calcium <8mg/dL

  Arterial pO_2 NA

  Serum base deficit > 5 mEq/Lio

  Fluid sequestration > 4L

APACHE II

- Measure at during the first 24 hours after admission
- Using a cutoff of ≥8
- The American Gastroenterological Association (AGA) recommends: Prediction of severe disease by the APACHE II system

Physiologic Variable	High Abnormal Range					Low Abnormal Range			
	+4	+3	+2	+1	0	+1	+2	+3	+4
Temperature - rectal (°C)	≥41°	39 to 40.9°		38.5 to 38.9°	36 to 38.4°	34 to 35.9°	32 to 33.9°	30 to 31.9°	≤29.9°
Mean Arterial Pressure - mm Hg	≥160	130 to 159	110 to 129		70 to 109		50 to 69		≤49
Heart Rate (ventricular response)	≥180	140 to 179	110 to 139		70 to 109		55 to 69	40 to 54	≤39
Respiratory Rate (non-ventilated or ventilated)	≥50	35 to 49		25 to 34	12 to 24	10 to 11	6 to 9		≤5
Oxygenation: A-aDO2 **or** PaO2 (mm Hg) a. FIO2 ≥0.5 record A-aDO2 b. FIO2 <0.5 record PaO2	≥500	350 to 499	200 to 349		<200 PO2>70	 PO2 61 to 70		 PO2 55 to 60	 PO2<55
Arterial pH (preferred) Serum HCO3 (venous mEq/l) (not preferred, but may use if no ABGs)	≥7.7 ≥52	7.6 to 7.69 41 to 51.9		7.5 to 7.59 32 to 40.9	7.33 to 7.49 22 to 31.9		7.25 to 7.32 18 to 21.9	7.15 to 7.24 15 to 17.9	<7.15 <15
Serum Sodium (mEq/l)	≥180	160 to 179	155 to 159	150 to 154	130 to 149		120 to 129	111 to 119	≤110
Serum Potassium (mEq/l)	≥7	6 to 6.9		5.5 to 5.9	3.5 to 5.4	3 to 3.4	2.5 to 2.9		<2.5
Serum Creatinine (mg/dl) Double point score for acute renal failure	≥3.5	2 to 3.4	1.5 to 1.9		0.6 to 1.4		<0.6		
Hematocrit (%)	≥60		50 to 59.9	46 to 49.9	30 to 45.9		20 to 29.9		<20
White Blood Count (total/mm3) (in 1000s)	≥40		20 to 39.9	15 to 19.9	3 to 14.9		1 to 2.9		<1
Glasgow Coma Score (GCS) Score = 15 minus actual GCS									

Biochemical marker

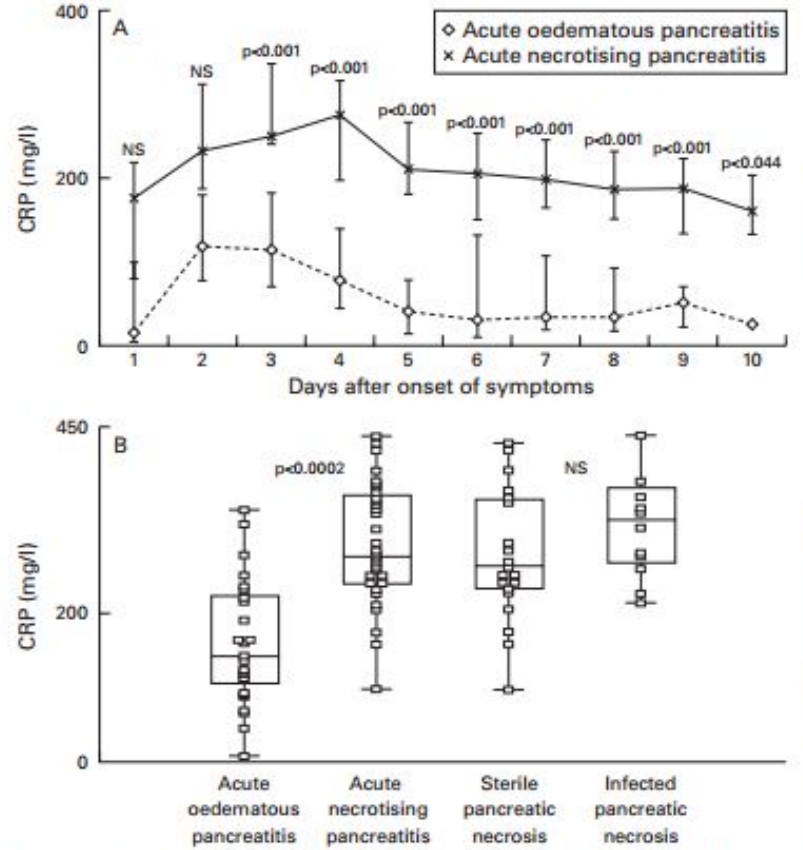


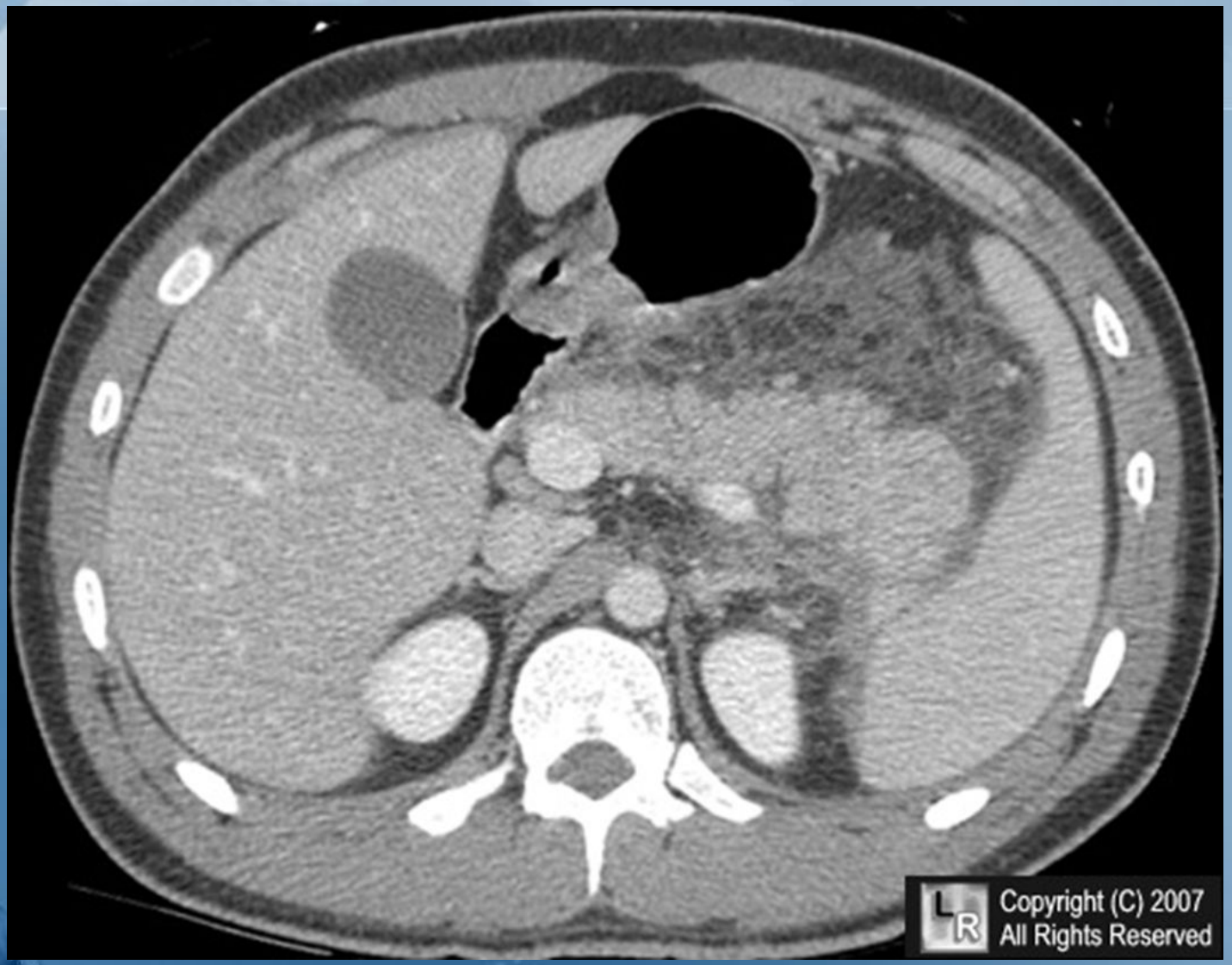
Figure 1 Median concentrations and quartile ranges for C reactive protein (CRP). (A) Acute oedematous pancreatitis compared with acute necrotising pancreatitis; (B) median peak values and ranges in patients with acute oedematous pancreatitis or acute necrotising pancreatitis and sterile pancreatic necrosis or infected pancreatic necrosis.

- CRP at 48hr
  - cutoff 150mg/L
  - Sens. 80%
  - Spec. 76%
- TAP
- Interleukins
- ???

CT severity score (Balthazar score)

≥6 = severe disease.

Grading based upon findings on unenhanced CT		
Grade	**Findings**	**Score**
A	Normal pancreas –without peripancreatic enhancement	0
B	Focal or diffuse enlargement of the pancreas, enhancement may be inhomogeneous on peripancreatic	1
C	Peripancreatic inflammation with intrinsic pancreatic abnormalities	2
D	Intrapancreatic or extrapancreatic fluid collections	3
E	Two or more large collections of gas in the pancreas or retroperitoneum	4
Necrosis score based upon contrast enhanced CT		
Necrosis, percent		**Score**
0		0
<33		2
33-50		4
≥50		6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Treatment

Treatment

- **General Considerations**
  - adequate IV hydration and analgesia
  - NPO
  - NG tube: not routinely used

  * But may be used in patients with ileus or intractable N/V
- Nutrition
  - Early enteral feeding
  - Nasojejunal tube feeding
  - PPN,TPN

Treatment

- Metabolic Complications
  - Correction of electrolyte imbalance - Ca,Mg
  - Cautiously for hyperglycemia
- Cardiovascular Care
- Respiratory Care
- Deep vein thrombosis prophylaxis

Prophylactic antibiotics

- Although this is still an area of debate
- Not indicated for mild attack
- suggest imipenem or meropenem for 14 days for patients with proven necrosis

TREATMENT OF ASSOCIATED CONDITIONS

- **Gallstone pancreatitis**
  - ERCP should be performed within 72 hours in those with a high suspicion of persistent bile duct stones
  - EUS & MRCP should be considered in case that clinical is not improving sufficiently
  - Cholecystectomy +/- IOC

Cholecystectomy??

- should be performed after recovery in all patient with gallstone pancreatitis
- Failure to perform a cholecystectomy is associated with a 25-30% risk of recurrent acute pancreatitis, cholecystitis, or cholangitis within 6-18 weeks

Cholecystectomy

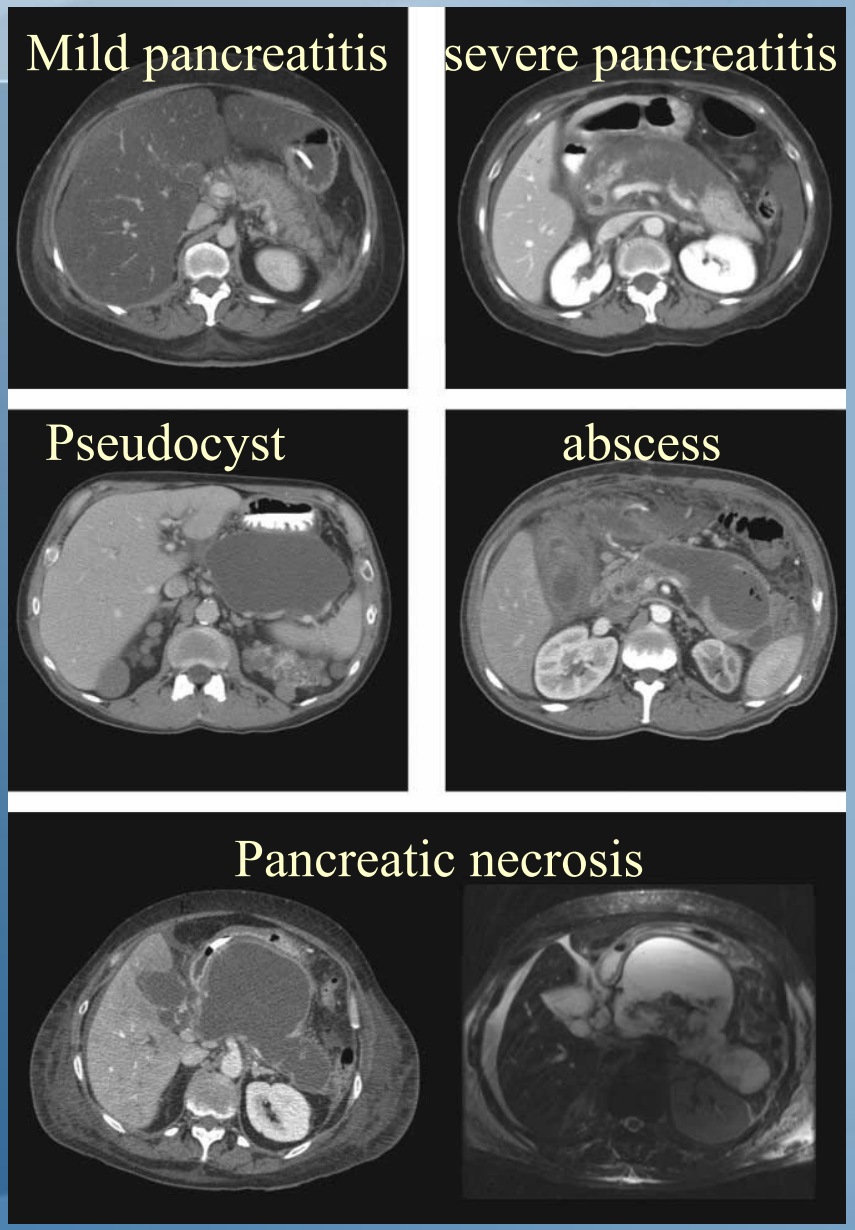
- In mild pancreatitis case, can usually be performed safely within 7 days after recovery
- In severe pancreatitis case ,delaying for at least 3 wks may be reasonable

- If high suspicion of CBD stones, preoperative ERCP is the best test that therapeutic intervention will be required
- If low suspicion,intraoperative cholangiogram during cholecystectomy may be preferable to avoid the morbidity associated with ERCP

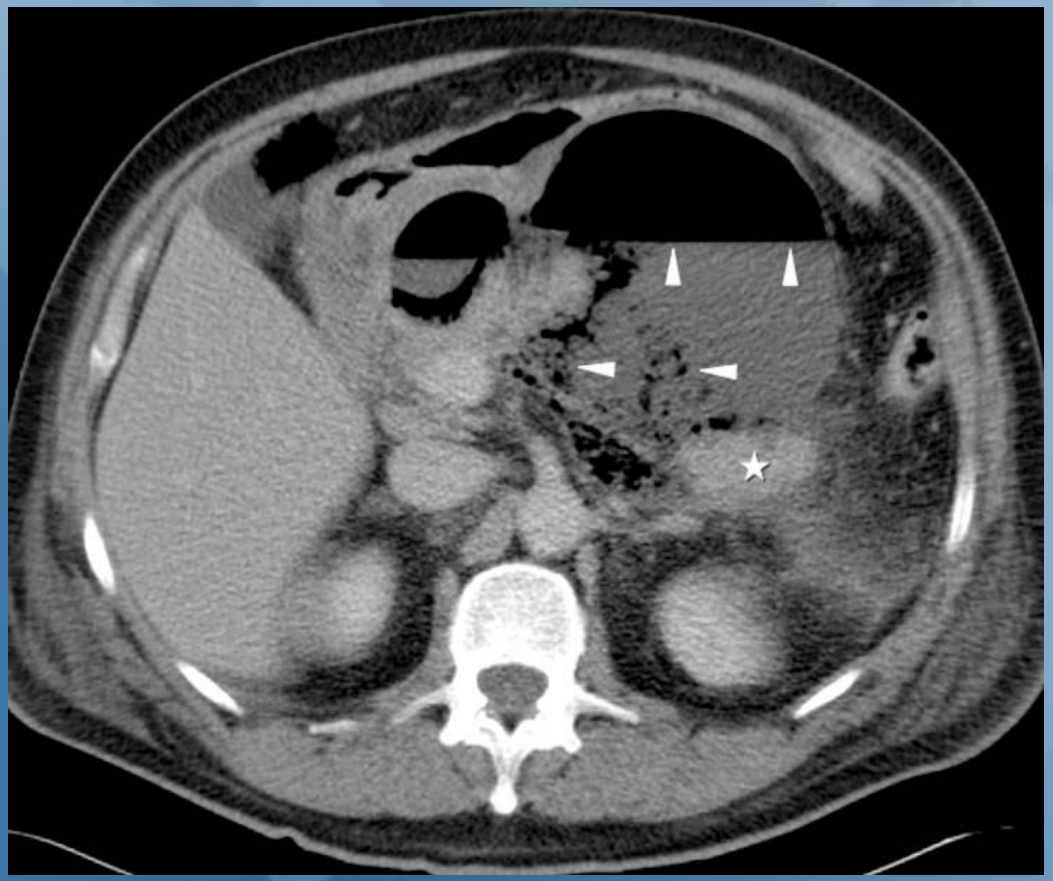
Complications

Local Complications

- Pseudocyst
- Abscess
- Necrosis
  - Sterile
  - Infected



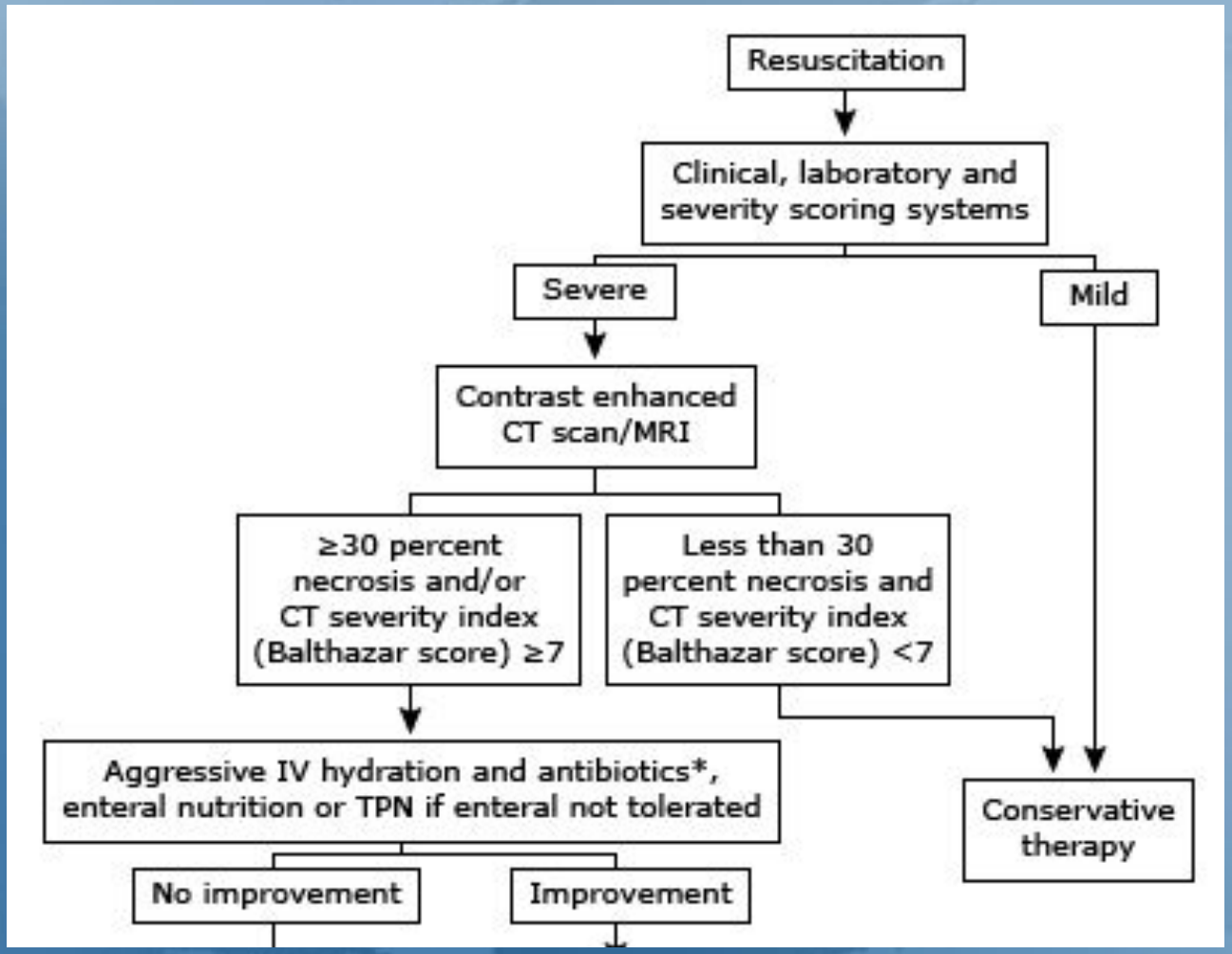
Infected pancreatic necrosis.

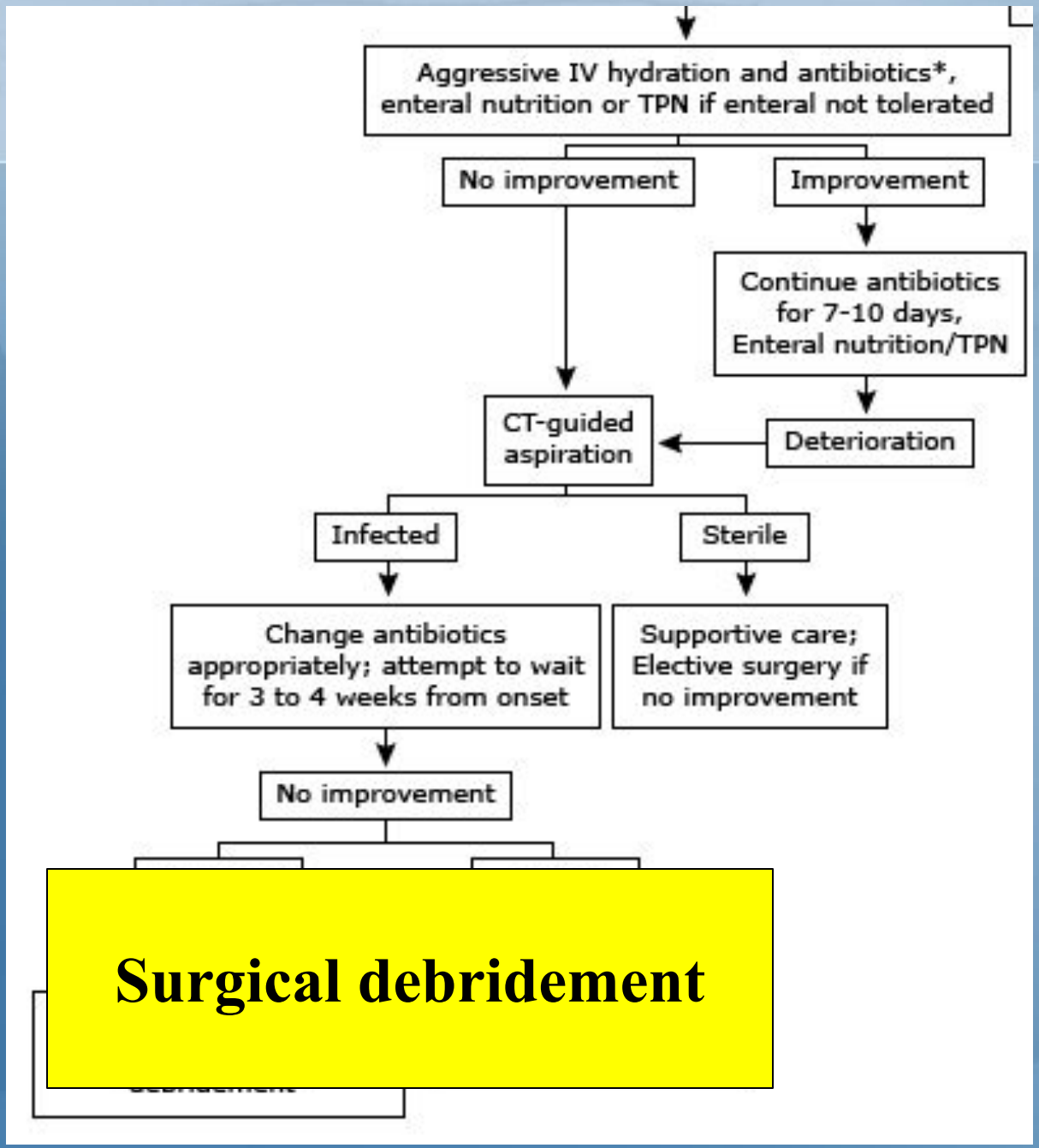


- The most common organisms include E.coli, Pseudomonas, Klebsiella, and Enterococcus

Guideline management of severe pancreatitis

AGA Guideline




Aggressive IV hydration and antibiotics*, enteral nutrition or TPN if enteral not tolerated
No improvement
Improvement
Continue antibiotics for 7-10 days, Enteral nutrition/TPN
Deterioration
CT-guided aspiration
Infected
Sterile
Change antibiotics appropriately; attempt to wait for 3 to 4 weeks from onset
Supportive care; Elective surgery if no improvement
No improvement
Surgical debridement

Management of pseudocyst

Management of pseudocyst

- **Watchful waiting:**

  - Operative intervention was recommended following an observation period of 6 wks

  - However, there are some reports support more conservative approach

Management of pseudocyst

- **Surgical drainage – gold standard**

  Open vs endoscopic

  –cystgastrostomy

  –Cystenterostomy

  –Cystojejunostomy, Cystoduodenostomy

  –Ressection

Management of pseudocyst

- **Percutaneous catheter drainage**
  - As effective as surgery in draining and closing both sterile and infected pseudocysts
  - Catheter drainage is continued until the flow rate falls to 5-10 mL/day
  - If no reduction in flow, octreotide (50 -200 µg SC q 8hr) may be helpful.
  - Should follow-up CT scan when the flow rate is reduced to ensure that the catheter is still in the pseudocyst cavity
  - more likely to be successful in patients without duct-cyst communication

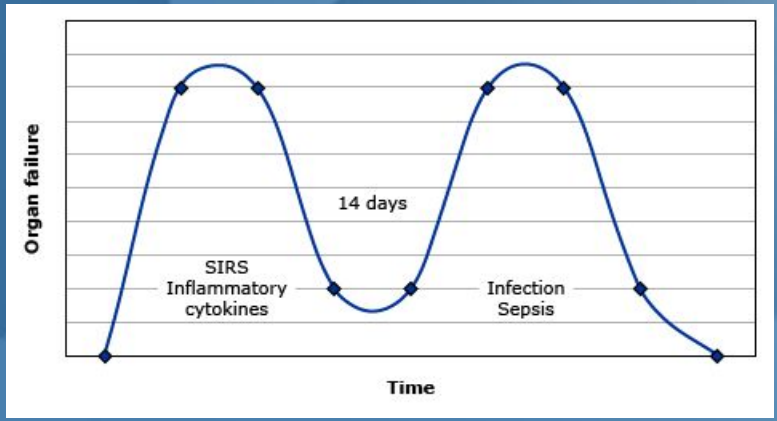
Management of local complication of pancreatitis

Indication for pancreatic debridement

- Infected pancreatic necrosis
- Symptomatic sterile pancreatic necrosis
  - chronic low grade fever
  - Nausea
  - Lethargy
  - Inability to eat
  - * Fail medical treatment

Timing of debridement

- The optimal timing is at least 3-4wks following the onset of acute pancreatitis.
- Delayed debridement allows
  - clinical stabilization of the patient
  - resolution of early organ failure
  - decreased inflammatory reaction, and necrotic areas are demarcated



Thank You