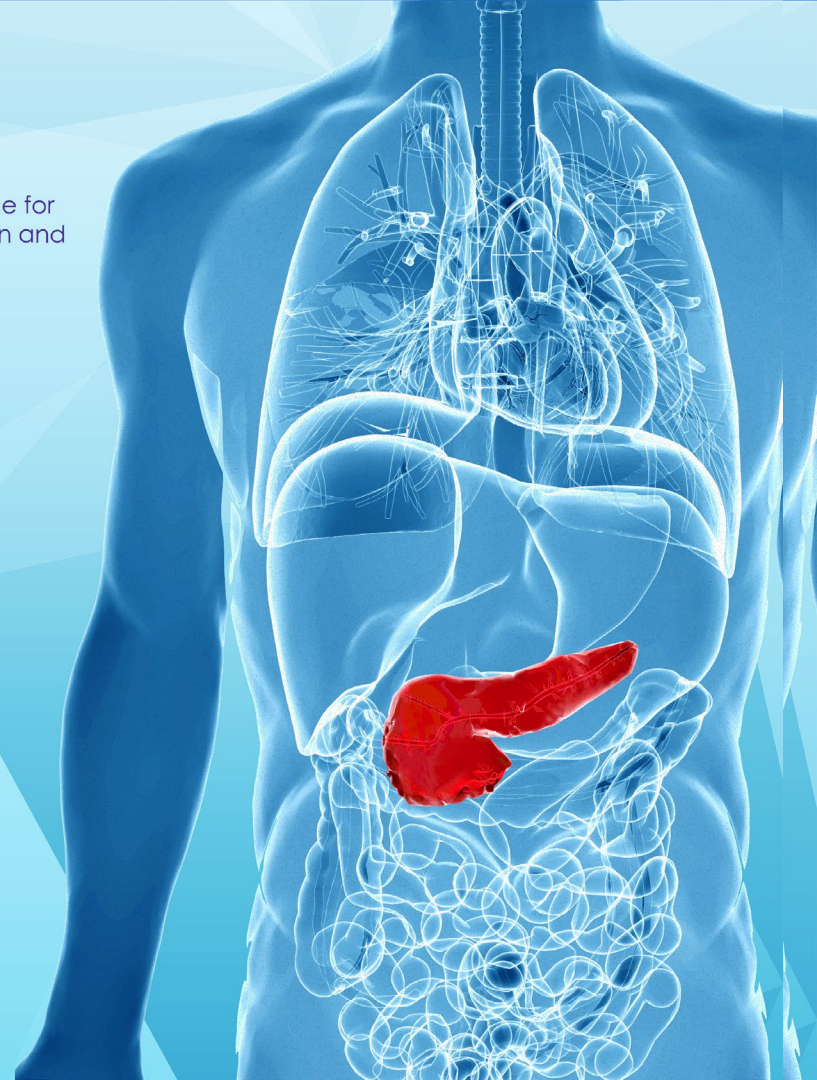


2020 CAPER

Collaborative Alliance for
Pancreatic Education and
Research

PANCREAS ACADEMY

OVERVIEW OF
ACUTE
PANCREATITIS



Overview of Acute Pancreatitis

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Conflicts of Interest

- No conflicts of interest to disclose.

Acute Pancreatitis

- ❑ An acute inflammatory event that originates within the pancreas and is associated with a wide variety of local and systemic complications
- ❑ Most common GI disease worldwide
- ❑ >270,000 hospital admissions per year in the US
- ❑ Annual cost \$2.6 billion in US

Vege et al, Gastroenterol. 2018
Peery et al, Gastroenterol. 2015
Das et al, Gastroenterol. 2016
Xiao et al, Lancet 2015

Outline of Lecture: Acute Pancreatitis (AP)

- ❑ Diagnosis
- ❑ Etiology
- ❑ Severity
- ❑ Management:
 - ❑ Intravenous fluids
 - ❑ Antibiotics
 - ❑ Nutrition
- ❑ Complications

DIAGNOSIS

DIAGNOSIS:

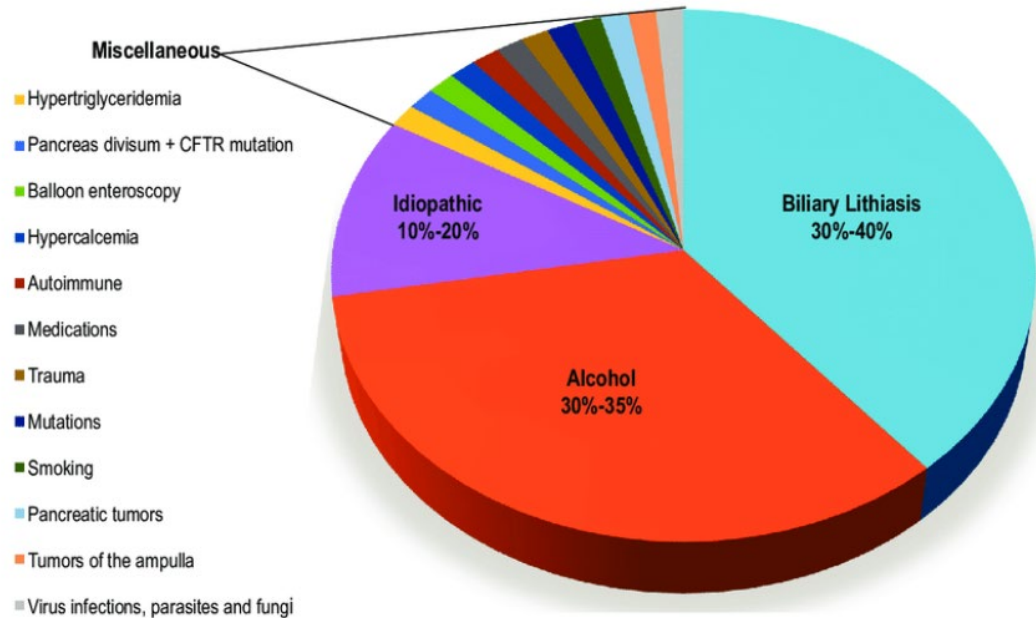
≥ 2 OF 3:

- ❑ Typical upper abdominal pain
- ❑ Amylase/lipase $>3\times$ ULN
- ❑ Imaging findings



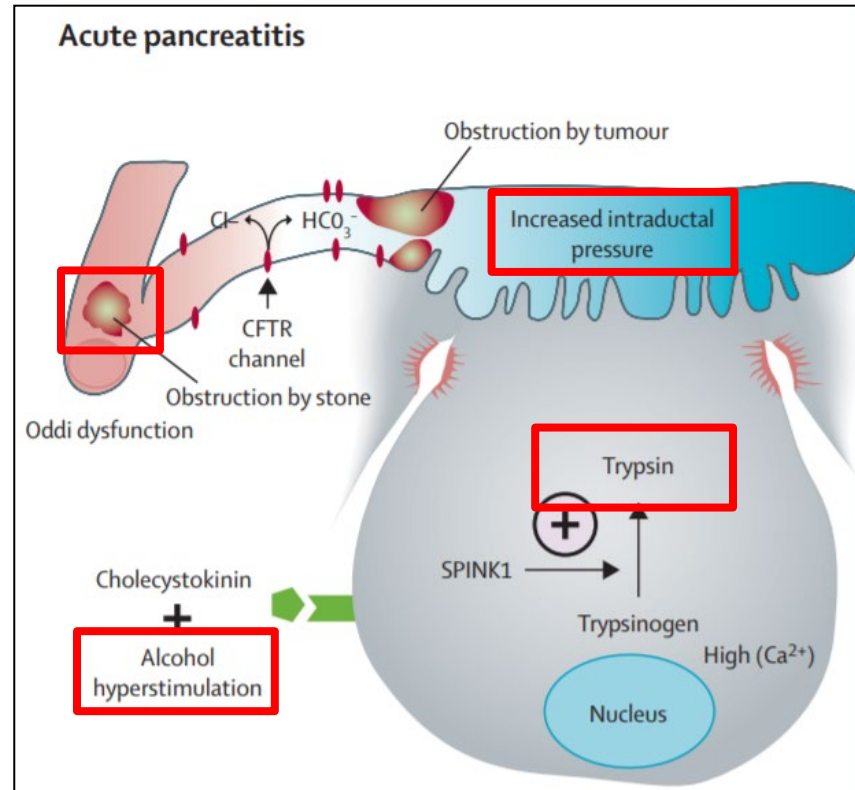
ETIOLOGY

Etiologies of AP

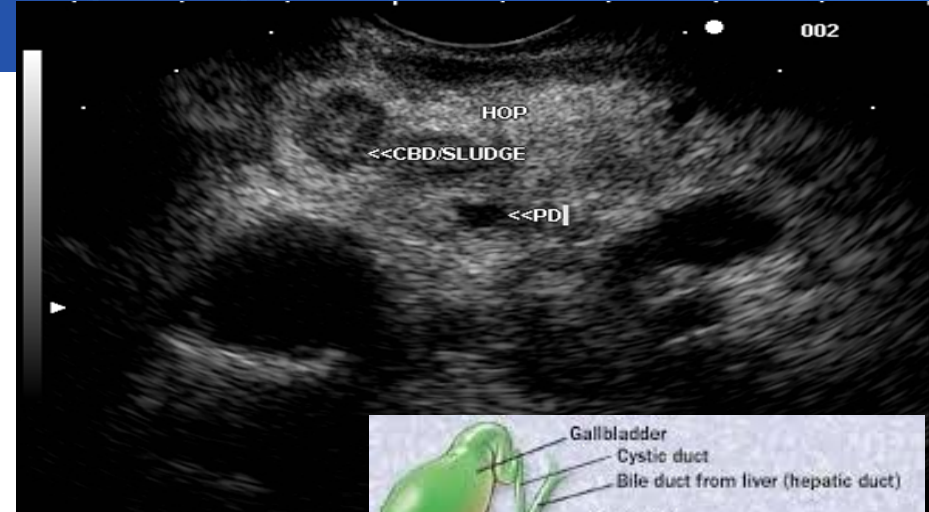
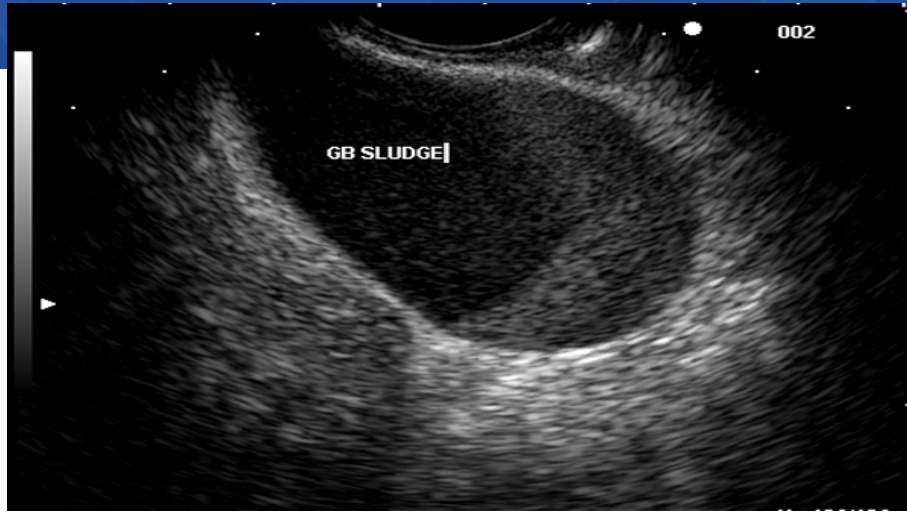


- ▶ Most Common:
 - ▶ Gallstones
 - ▶ Alcohol

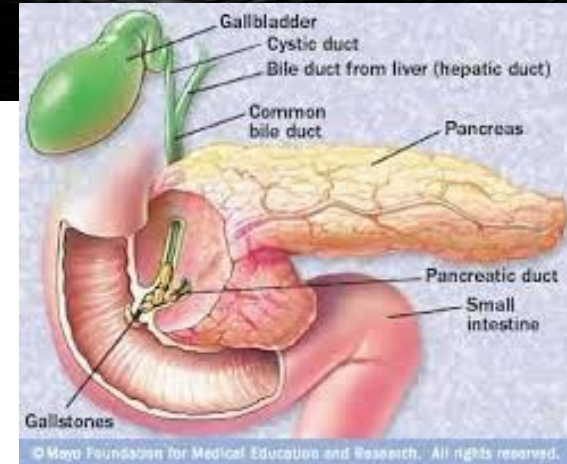
Pathophysiology of AP



Gallstones



- Most common cause of AP in US
- Gallstone passing through common bile duct may lodge in head of pancreas, causing transient pancreatic duct obstruction



Alcohol and AP

- ▶ Clear association between alcohol & AP
- ▶ No established threshold for volume of alcohol consumed and risk of AP
- ▶ Suspect elevated underlying susceptibility
- ▶ In general population: increased risk of all alcohol-related disorders with:
 - ▶ daily alcohol consumption of >3 drinks/day (female) or >4 drinks/day (male) (OR)
 - ▶ weekly alcohol consumption of > 7 drinks/week (women) or 14 drinks/week (men)
- ▶ Abstinence is best strategy



Other Causes

- ▶ Metabolic
 - ▶ Hypertriglyceridemia
 - ▶ Hypercalcemia
- ▶ Iatrogenic
 - ▶ Post-ERCP
- ▶ Autoimmune
- ▶ Medication-induced
 - ▶ HCTZ
 - ▶ Azathioprine
- ▶ Neoplastic
 - ▶ Pancreatic cancer
- ▶ Structural
 - ▶ Potential contribution of underlying pancreas divisum (ongoing clinical trial)
- ▶ Infectious
- ▶ Traumatic
- ▶ Inherited
 - ▶ Genetic
- ▶ Vascular
 - ▶ Ischemia

The top of the image features a solid blue header with a subtle geometric pattern of overlapping triangles and polygons in a lighter shade of blue.

SEVERITY

Dynamic Process:

- ▶ Rapid progression
- ▶ Early assessment is key
- ▶ Important to assess which patients will progress to severe disease
- ▶ Start supportive therapy immediately



Severity

- ▶ Majority (**80%**) of patients have a mild uncomplicated course and are discharged within a few days
- ▶ ~**20%** of patients develop a **severe clinical course** (systemic inflammatory response syndrome (SIRS), multi-organ failure, pancreatic necrosis)
 - ▶ Within the severe group, there is up to **30%** mortality
- ▶ Overall, **2%** of patients die
 - ▶ ≥50% of deaths occur within first 2 weeks of diagnosis

Prognostic scoring systems

Table 3. Performance of Clinical Scoring Systems and Laboratory Markers Using Admission Data From Training and Validation Cohorts

Score	Cut-off	Sensitivity	Specificity	PPV	NPV	AUC	Complete data ^a
APACHE-II	7	0.84 (± 0.11)	0.71 (± 0.06)	0.49 (± 0.11)	0.93 (± 0.08)	0.77 (± 0.07)	96%
BISAP	2	0.61 (± 0.20)	0.84 (± 0.04)	0.54 (± 0.10)	0.87 (± 0.10)	0.72 (± 0.10)	100%
Glasgow	2	0.85 (± 0.08)	0.83 (± 0.07)	0.61 (± 0.06)	0.95 (± 0.05)	0.84 (± 0.06)	98%
HAPS	1	0.70 (± 0.11)	0.53 (± 0.21)	0.32 (± 0.11)	0.85 (± 0.13)	0.62 (± 0.06)	99%
JSS	2	0.59 (± 0.13)	0.92 (± 0.05)	0.70 (± 0.16)	0.88 (± 0.07)	0.76 (± 0.07)	95%
Panc 3	1	0.76 (± 0.15)	0.52 (± 0.05)	0.34 (± 0.11)	0.87 (± 0.11)	0.64 (± 0.06)	99%
POP	9	0.57 (± 0.15)	0.76 (± 0.06)	0.43 (± 0.16)	0.85 (± 0.08)	0.67 (± 0.09)	99%
Ranson	2	0.66 (± 0.09)	0.78 (± 0.10)	0.49 (± 0.17)	0.88 (± 0.08)	0.72 (± 0.06)	98%
SIRS	2	0.70 (± 0.18)	0.71 (± 0.04)	0.43 (± 0.10)	0.88 (± 0.11)	0.70 (± 0.10)	98%
BUN	23	0.56 (± 0.10)	0.86 (± 0.05)	0.57 (± 0.14)	0.86 (± 0.05)	0.71 (± 0.03)	98%
Creatinine	1	0.77 (± 0.09)	0.59 (± 0.04)	0.38 (± 0.08)	0.89 (± 0.04)	0.68 (± 0.06)	98%
Validation cohort							
APACHE-II	7	0.97 (± 0.08)	0.44 (± 0.06)	0.14 (± 0.04)	0.99 (± 0.02)	0.71 (± 0.05)	100%
BISAP	2	0.62 (± 0.20)	0.76 (± 0.04)	0.20 (± 0.06)	0.96 (± 0.04)	0.69 (± 0.11)	100%
Glasgow	2	0.65 (± 0.24)	0.82 (± 0.05)	0.22 (± 0.08)	0.97 (± 0.02)	0.74 (± 0.10)	91%
HAPS	1	0.73 (± 0.26)	0.58 (± 0.09)	0.12 (± 0.06)	0.97 (± 0.02)	0.66 (± 0.09)	92%
JSS	2	0.42 (± 0.19)	0.89 (± 0.05)	0.23 (± 0.18)	0.95 (± 0.01)	0.66 (± 0.11)	91%
Panc 3	1	0.62 (± 0.31)	0.52 (± 0.05)	0.11 (± 0.05)	0.94 (± 0.04)	0.57 (± 0.16)	100%
POP	9	0.46 (± 0.31)	0.81 (± 0.04)	0.16 (± 0.12)	0.95 (± 0.02)	0.64 (± 0.16)	90%
Ranson	2	0.46 (± 0.28)	0.80 (± 0.03)	0.16 (± 0.11)	0.95 (± 0.02)	0.63 (± 0.15)	91%
SIRS	2	0.69 (± 0.16)	0.58 (± 0.04)	0.11 (± 0.03)	0.96 (± 0.03)	0.64 (± 0.01)	93%
BUN	23	0.65 (± 0.26)	0.81 (± 0.04)	0.21 (± 0.09)	0.97 (± 0.03)	0.73 (± 0.13)	96%
Creatinine	1	0.77 (± 0.20)	0.63 (± 0.07)	0.14 (± 0.12)	0.97 (± 0.02)	0.70 (± 0.11)	98%

SIRS Criteria

SIRS—defined by presence of two or more criteria:

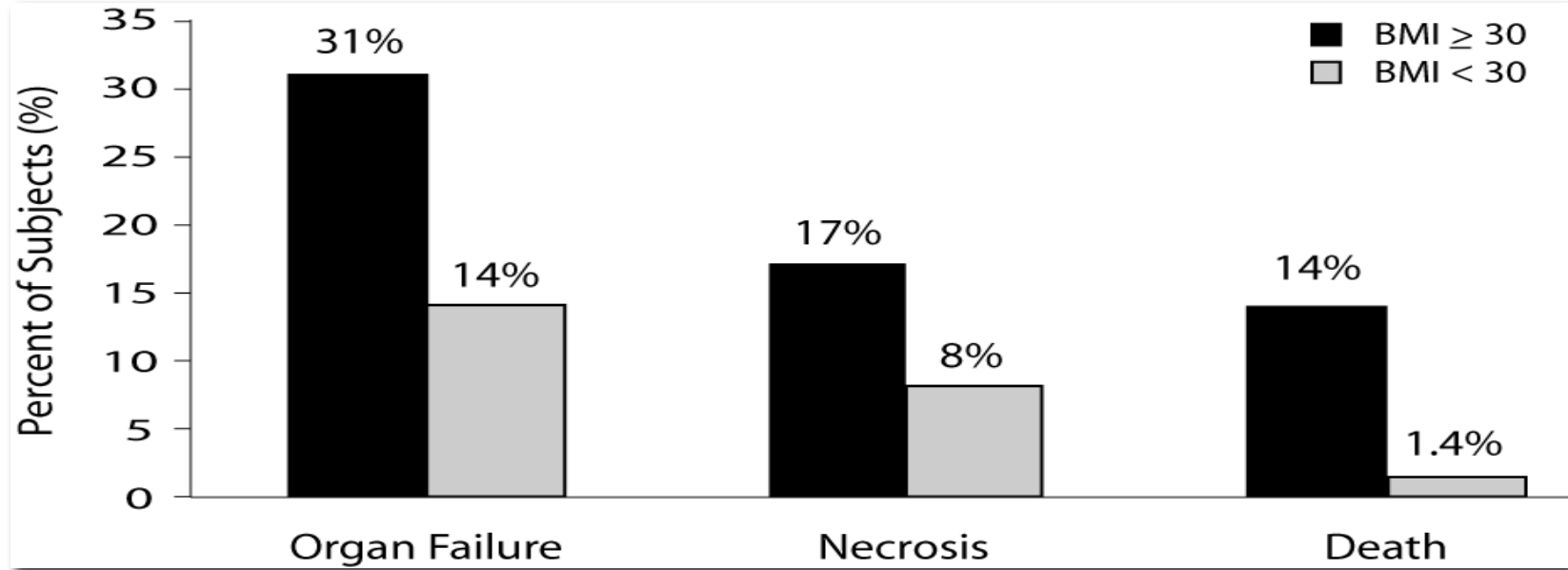
- ▶ Heart rate >90 beats/min
- ▶ Core temperature $<36^{\circ}\text{C}$ or $>38^{\circ}\text{C}$
- ▶ White blood count <4000 or $>12000/\text{mm}^3$
- ▶ Respirations $>20/\text{min}$ or $\text{PCO}_2 <32 \text{ mm Hg}^{13}$

Revised Atlanta Classification

- ▶ Mild acute pancreatitis
 - ▶ No organ failure
 - ▶ No local or systemic complications
- ▶ Moderately severe acute pancreatitis
 - ▶ Organ failure that resolves within 48 h (transient organ failure) and/or
 - ▶ Local or systemic complications without persistent organ failure
- ▶ Severe acute pancreatitis
 - ▶ Persistent organ failure (>48 h)
 - Single organ failure
 - Multiple organ failure

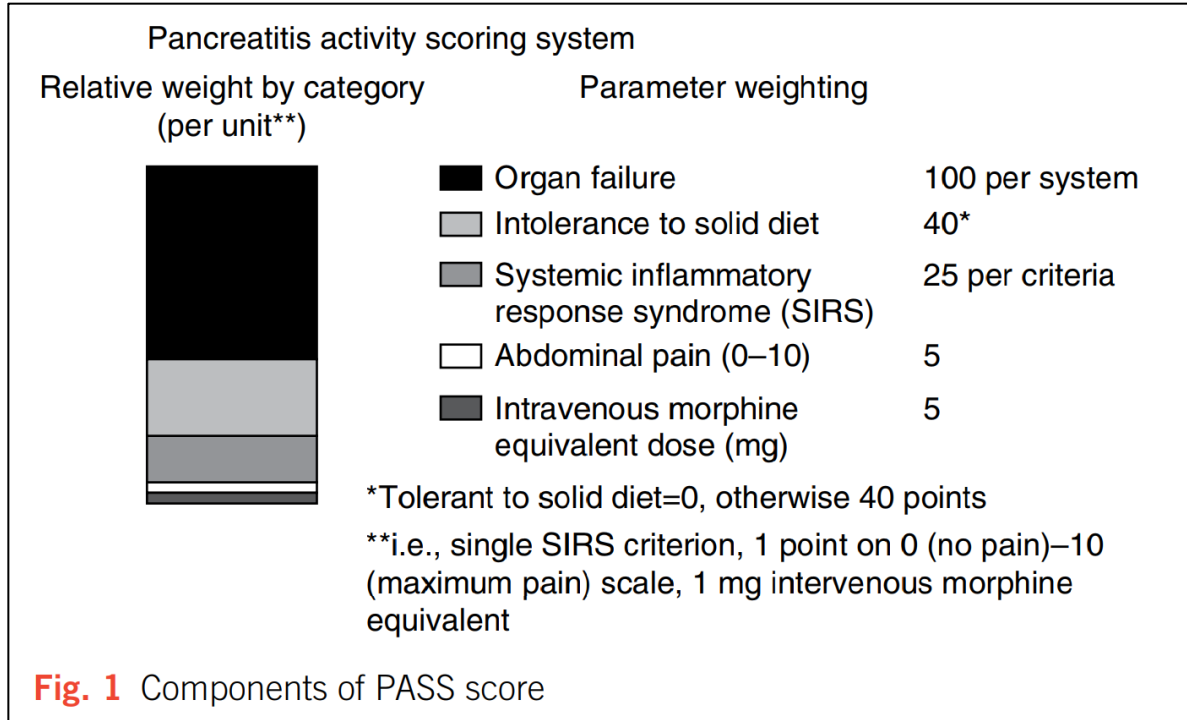
- Cardiovascular – Persistent Systolic BP <90 mm Hg
- Pulmonary - PaO₂ < 60 mm Hg
- Renal – Creatinine >2 mg/dL, after rehydration

Obesity: More Severe AP



Adipose tissue (fat) is known to release adipokines that worsen inflammation, including TNF- α , resistin, visfatin, adiponectin, etc.

Pancreatitis Activity Scoring System



- Designed to²¹ predict meaningful clinical outcomes and identify turning points in clinical course
- Ongoing work to validate in larger population

A blue header bar with a geometric pattern of overlapping triangles and polygons.

MANAGEMENT

Treatment of Acute Pancreatitis

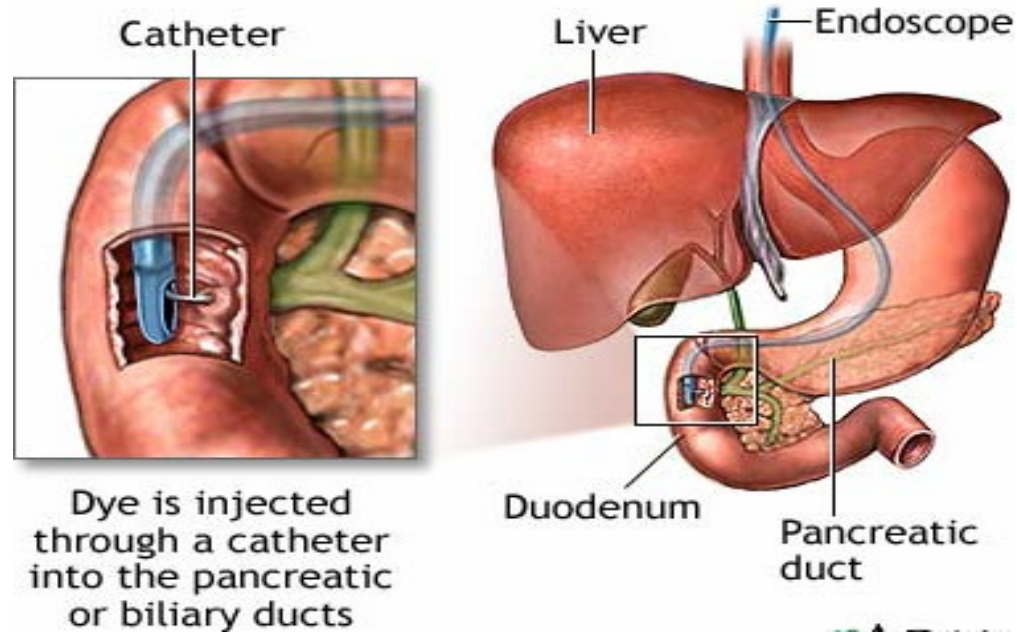
- No drug therapy available to treat acute pancreatitis
- Supportive care
 - Correct primary insult
 - Consider early ERCP
 - Cease alcohol use
 - Correct triglyceride or calcium levels
 - Fluid Resuscitation
 - Nutrition
 - Pain Control
- Prevention of future attacks

Role of Urgent ERCP

-Early ERCP in subjects with biliary pancreatitis and concomitant cholangitis or high suspicion of persistent bile duct stones is appropriate

- CT
- MRI/MRCP
- EUS

-Role of early ERCP in predicted severe gallstone pancreatitis in the absence of above is controversial



Fluid Resuscitation: Controversial Cornerstone of Therapy

- Fluid accumulates in the 'third space' in vascular leak
- Inadequate hydration can lead to hypotension, renal dysfunction, damage to pancreatic microcirculation
- Fluid Resuscitation:
 - 1-2 L bolus
 - continue 150-200 cc/hr of IVF for 48hr
 - **Lactated Ringers** preferred (theoretically decrease pancreatic acidosis, reduce trypsin activity)
- Optimal amount and composition remains unclear
- Adequacy assessed by improvement in vitals, urine output, correction of hemoconcentration (BUN, Cr, Hct)



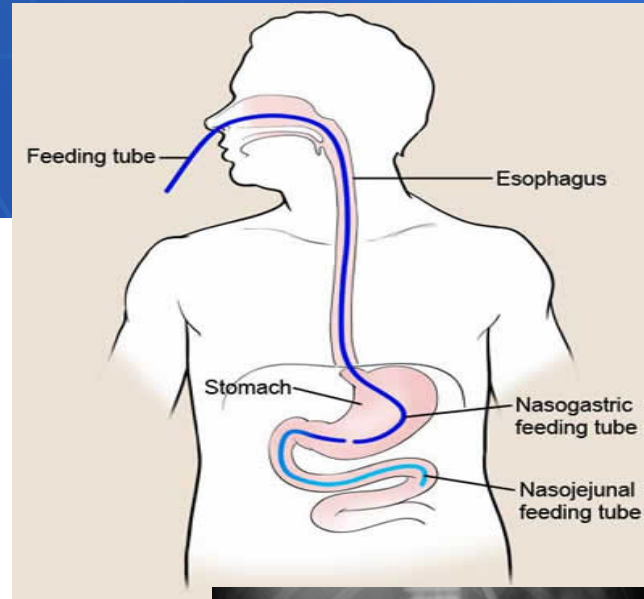
Comparison of AP Management Strategies

Variable	Europe (n = 409)	India (n = 366)	Latin America (n = 325)	North America (n = 512)	Total (n = 1612)	P value
Intravenous fluids						
Amount, median (IQR) ^a	2.5 (2.0–3.6)	3.2 (2.0–4.5)	3.0 (2.5–3.8)	3.0 (2.0–4.2)	3.0 (2.0–4.0)	< .001
Type of fluid, LR (%)	315 (77.0)	337 (92.3)	24 (7.4)	253 (49.4)	930 (57.7)	< .001
Inpatient pain management (%)						
NSAIDs	277 (67.7)	1 (0.3)	155 (47.7)	91 (17.8)	524 (32.5)	< .001
Tramadol	184 (45.0)	334 (91.3)	111 (34.2)	40 (7.8)	669 (41.5)	< .001
Opioids	41 (11.9)	90 (24.9)	167 (59.0)	454 (92.5)	752 (50.8)	< .001
Opioids at discharge (%)	1 (0.3)	2 (0.6)	17 (6.2)	314 (64.3)	334 (23.3)	< .001
Nutritional support (%)						
Enteral nutrition ^b	34 (31.8)	43 (19.9)	15 (15.3)	46 (34.8)	138 (25.0)	< .001
TPN ^b	3 (2.8)	59 (27.3)	4 (4.1)	9 (6.8)	75 (13.6)	< .001
ERCP ^c	29 (14.4)	17 (16.8)	34 (14.1)	76 (44.7)	156 (21.9)	< .001
Cholecystectomy ^d	52 (31.7)	6 (15.0)	101 (59.8)	52 (42.6)	211 (42.6)	< .001
Early pancreatic intervention ^b	9 (8.4)	50 (23.1)	5 (5.1)	9 (6.8)	73 (13.2)	< .001

- Acute Pancreatitis Patient Registry to Examine Novel Therapies in Clinical Experience (APPRENTICE)
- >1600 patients enrolled around the world
- Management strategies studied

Nutritional Support

- **An attempt at oral feeding (as tolerated)** is recommended by the AGA rather than keeping the patient nil per os (NPO)
- Nutritional support is required in AP pts predicted to remain fasting for >7 days
- Enteral feeding (NG or NJ) preferred to TPN
 - -maintains intestinal barrier;
 - -eliminates central line associated infections
- Large meta-analysis
 - reduction in infectious morbidity & hospital length of stay
 - trend toward reduced organ failure



McClave et al, JPEN 2006
Crockett et al, 2018

Prophylactic antibiotics

- Low quality evidence supporting the role of prophylactic antibiotics
- Guidelines from AGA, ACG, IAP recommend against routine use of prophylactic antibiotics
- **Infected pancreatic necrosis:** clear indication for antibiotic therapy

Crockett et al, Gastroenterol, 2018
Tenner et al, Am J Gastro, 2013
IAP/APA Working Group, Pancreatology, 2013
Cochrane database Rev 2010

COMPLICATIONS



Systemic Complications

- Cardiovascular
 - Hypotension, shock, vascular complications
- Pulmonary
 - Hypoxia, Pleural effusions, respiratory failure
- Renal
 - Oliguria, Azotemia, Acute tubular necrosis
- Metabolic
 - Hypocalcemia, hyperglycemia, hypertriglyceridemia, metabolic acidosis

Local Complications: Fluid Collections

- **Acute peripancreatic fluid collections (APFC):**
 - Common, occur early, located in or near pancreas, lack a defined wall; most regress, should be observed
 - 50% of fluid collections resolve
 - 10 -15% may progress into pseudocysts after forming capsule
- **Pancreatic Pseudocyst (PPC):**
 - Collection of clear pancreatic juice enclosed by a wall of fibrous or granulation tissue; requires >4 wks

- **Acute Necrotic Collection (ANC):**
 - ANC contains a significant amount of solid debris
- **Walled Off Necrosis (WON):**
 - Organized pancreatic necrosis, requires > 4 wks

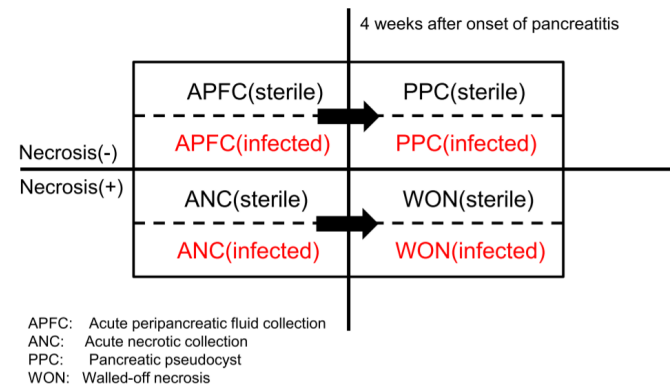
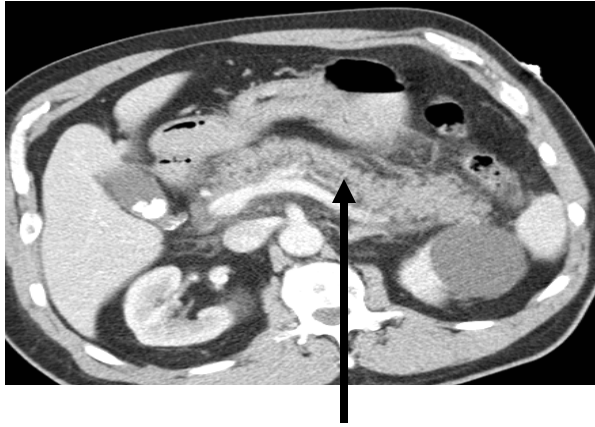
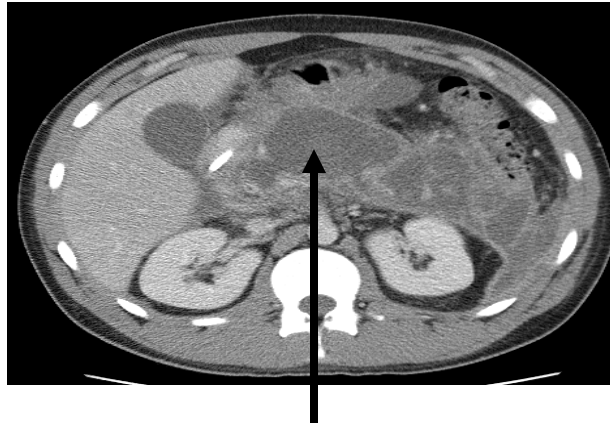


Fig. 3 Classification of pancreatic fluid collection by the revised Atlanta classification. *APFC* acute peripancreatic fluid collection, *ANC* acute necrotic collection, *PPC* pancreatic pseudocyst, *WON* walled-off necrosis

Pancreatic Necrosis: Evolution



Normally enhancing pancreas



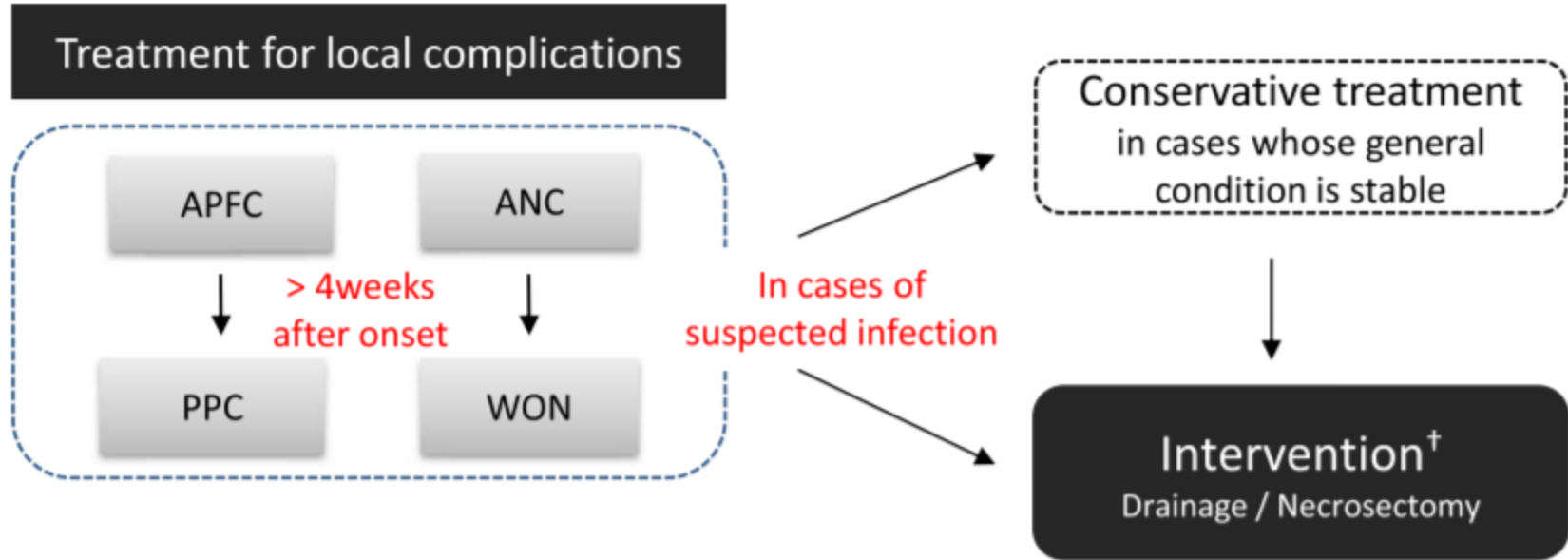
Non-enhancing necrosed pancreas



Capsule

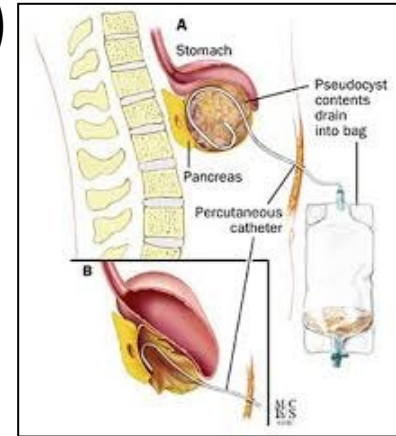
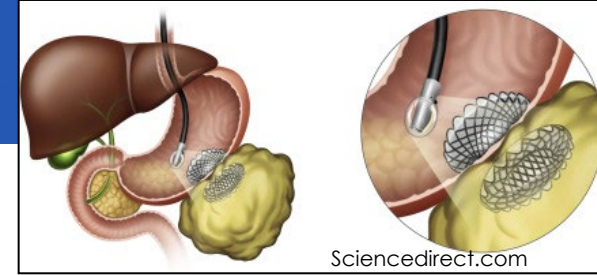
- Approx 10 - 20% of patients admitted with AP at tertiary medical centers have necrosis
 - Infectious complications occur in ~20-30%
 - occurs 2-5 weeks from occurrence of necrosis
 - New fevers, worsening abdominal pain, nausea, vomiting, growth of collection
 - Septic complications from infected necrosis account for most of late deaths in AP

Management of Fluid Collections

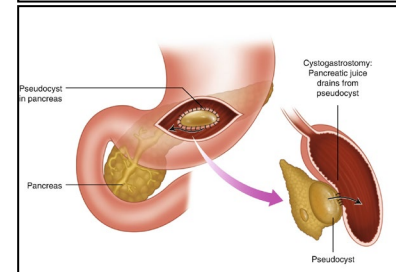


Drainage/Debridement

- **Internal Drainage:** Endoscopic Debridement
- Cystgastrostomy (pigtail stents, lumen-apposing stents)
- Endoscopic necrosectomy
- **External Drainage:**
- Drain placed by Ultrasound or CT guidance
- Drain placed surgically
- **Surgical Debridement**
- Minimally invasive approach is usually taken
- Avoid open necrosectomy
- High morbidity of open procedures



Johnshopkinsmedicine.edu



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

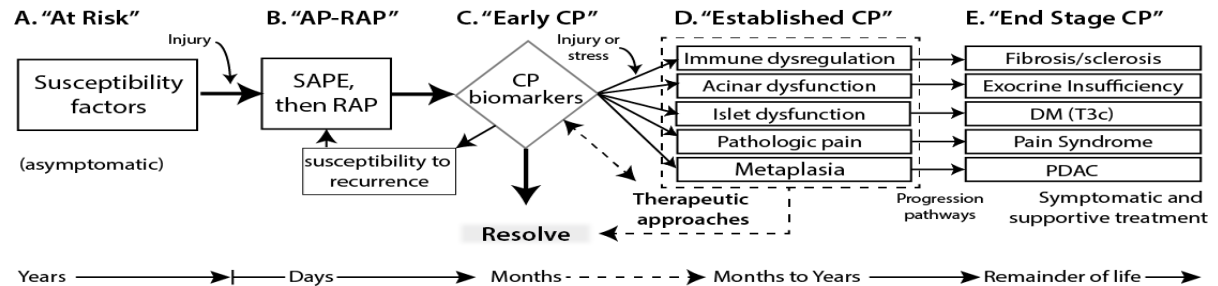
A Step-up Approach or Open Necrosectomy for Necrotizing Pancreatitis

- ▶ RCT n=88 pts
- ▶ Suspected or confirmed infected pancreatic necrosis
- ▶ Composite endpoint: new-onset organ failure, perforation, bleeding or death
- ▶ Step-Up therapy: 40% vs. Open Necrosectomy 69% ($p=0.006$)

Long-Term Sequelae of AP

➤ Recurrent Acute Pancreatitis and/or **Chronic Pancreatitis**

➤ Progression along spectrum



➤ Exocrine Pancreatic Insufficiency (EPI)

- Up to 40% of pts may experience within the 1 year after AP
- Fecal elastase-1 level, treat with pancreatic enzyme replacements

➤ Pancreatic Endocrine Insufficiency

- Type IIc Diabetes
- Brittle, hard to control

COVID-19 and AP

- ▶ Up to 50% of COVID-19 patients have at least one GI symptom
- ▶ Clinically severe acute pancreatitis is uncommon in COVID-19
- ▶ AP may be precipitated by vascular insult to pancreas in setting of hypotension, enzymes can be elevated from hemoconcentration, renal injury, or direct viral involvement of the pancreas
- ▶ Study of 52 patients at Wuhan University with COVID-19 pneumonia:
 - ▶ 9 (17%) had mild elevation ($<3\times$ ULN) in pancreatic enzymes
 - ▶ Higher incidence of anorexia and diarrhea in these patients
 - ▶ Elevated blood glucose levels were noted (possibly related to angiotensin-converting-enzyme 2 expression in pancreatic islet cells)

Table 1. Reported Digestive Manifestations of COVID-19

Digestive manifestation	Frequency reported (%)
Anorexia	30–40 ³⁻⁴
Diarrhea	2–50 ²
Nausea/vomiting	2–12 ^{3-4,11}
Abdominal pain	2–4 ³⁻⁴
Digestive symptoms only	3–23 ³⁻⁴
Abnormal liver tests	
Aminotransferases	14–53 ^{6,11}
Bilirubin	10–18
Virus detected in stool	50–55 ^{1,3,5}

COVID-19, coronavirus disease 2019.

Aloysius et al, Pancreatology, 2020
Hadi et al, Pancreatology, 2020
Wang et al, Gastroenterology, 2020
Aroniadis et al, Clin Gastro Hep, 2020

Summary

- Diagnosis: based on 2/3 criteria
- Etiologies: Gallstones and alcohol most common
- Severity: Revised Atlanta Criteria
 - 20% of pts develop severe disease
- Management:
 - Supportive Care: IV Fluids, Pain Control
 - Prevention of future attacks
- Complications
 - Necrosis, Fluid Collections, Infection, Vascular problems
 - Long-term, risk of EPI, DM, and CP

Thank You

A wide-angle aerial photograph of Pittsburgh, Pennsylvania, showing the city skyline across the Allegheny River. Several yellow steel arch bridges are visible, including the Roberto Clement Bridge in the foreground. The city's skyscrapers are clustered in the background, and a large fountain is visible on a small island in the river. The word "Questions?" is overlaid in yellow text on the lower right portion of the image.

Questions?