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Triggers and Treatment of Acute Pancreatitis

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Disclosures

Rick Davis, PA-C

No financial relationships to disclose.

Acute Pancreatitis: Inflammatory Disorder of the Pancreas

- Acute pancreatitis
- Acute relapsing pancreatitis
- Acute on chronic pancreatitis
- Among most common GI disorders to cause hospitalization
- Global incidence of 34/100,000 person-years

Acute Pancreatitis: Etiologies

- Gallstone
- EtOH
- Trauma (e.g., ERCP, surgical resection, biopsy)
- Malignant/pre-malignant lesions
- Metabolic (hypertriglyceridemia; hypercalcemia)

Acute Pancreatitis: Etiologies (Cont'd)

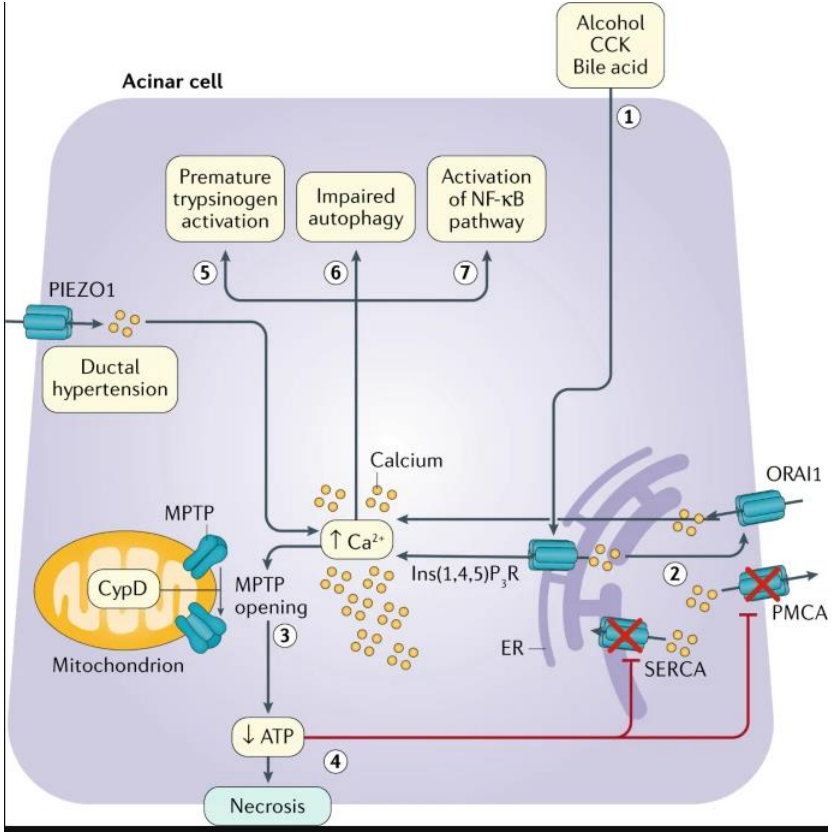
- Genetic: PRSS1, SPINK1, CFTR
- Medications: e.g., mesalamine, azathioprine, losartan
- Infections: viral, bacterial, parasitic
- Idiopathic

Acute Pancreatitis: Pathophysiology

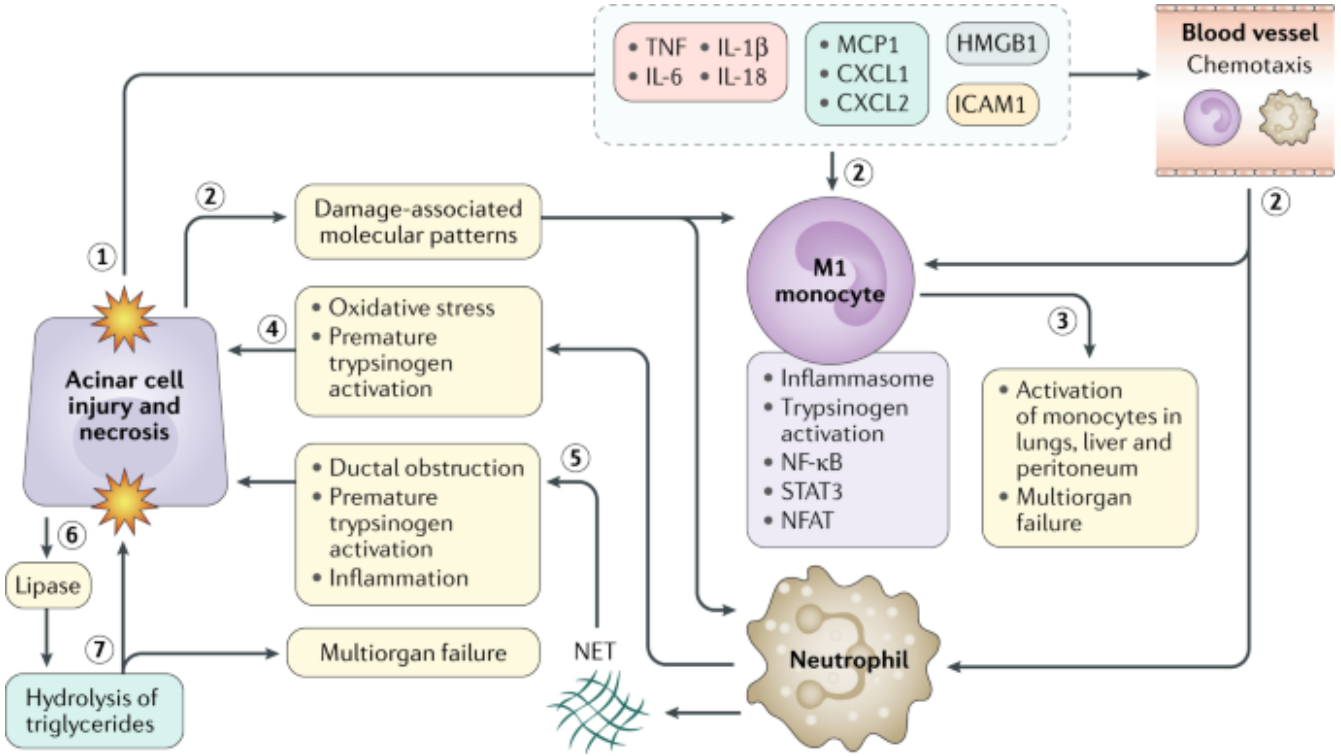
- Pathologic elevation of Ca++ concentration in acinar cells
- Mediates pro-cell death, pro-inflammatory pathways
- Activates NFkB and mitochondrial dysfunction
- Ductal obstruction with gallstones or ERCP can cause increased Ca++ entry to cells via plasma membrane receptors activated by pressure

Nat Rev/Gastro Hepatol. 2019;16: 479-96.

Acute Pancreatitis: Pathophysiology Ca++ Mediated Mitochondrial Dysfunction and Cell Death



Immune Response to Acinar Cell Injury and Necrosis in Acute Pancreatitis



Nat RevGastro Hepatol. 2019;16: 479-96.

Acute Pancreatitis: Clinical Presentation

Acute onset of epigastric abdominal pain

- Sharp with radiation to back and sudden onset frequently with biliary cause
- Indolent, aching pain frequently with EtOH, metabolic

Nausea +/- vomiting

Anorexia

Acute Pancreatitis: Diagnostic Criteria

Revised Atlanta Classification (2012)

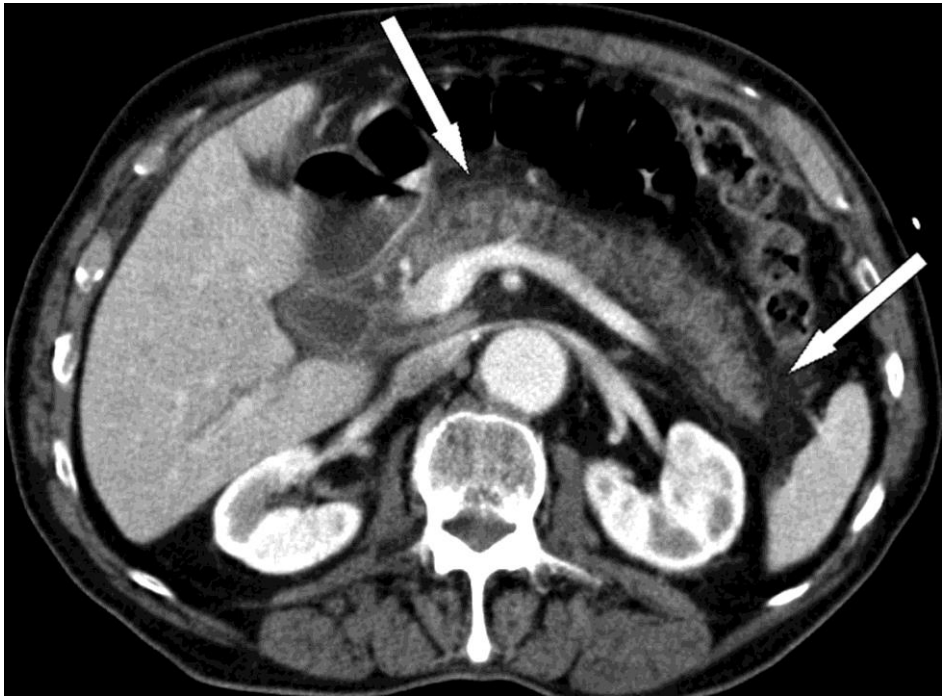
- Two of three of following:
- Pancreatic enzymes, amylase/lipase > 3x ULN
- Typical abdominal pain of acute pancreatitis
- Findings of acute pancreatitis on cross-sectional imaging

Revised Acute Pancreatitis: Types
Atlanta Classification

- Interstitial edematous pancreatitis
  - Diffuse or localized enlargement of pancreas
  - Homogenous enhancement of parenchyma
  - Peripancreatic fluid collections
    - < 4 wks: Adjacent to pancreas (APFC)
    - > 4 wks: Pseudocyst

Gut. 2013;62: 102-111

A 63-Year-Old Man With Acute Interstitial Oedematous Pancreatitis



Peter A Banks et al. *Gut*. 2013;62:102-111.

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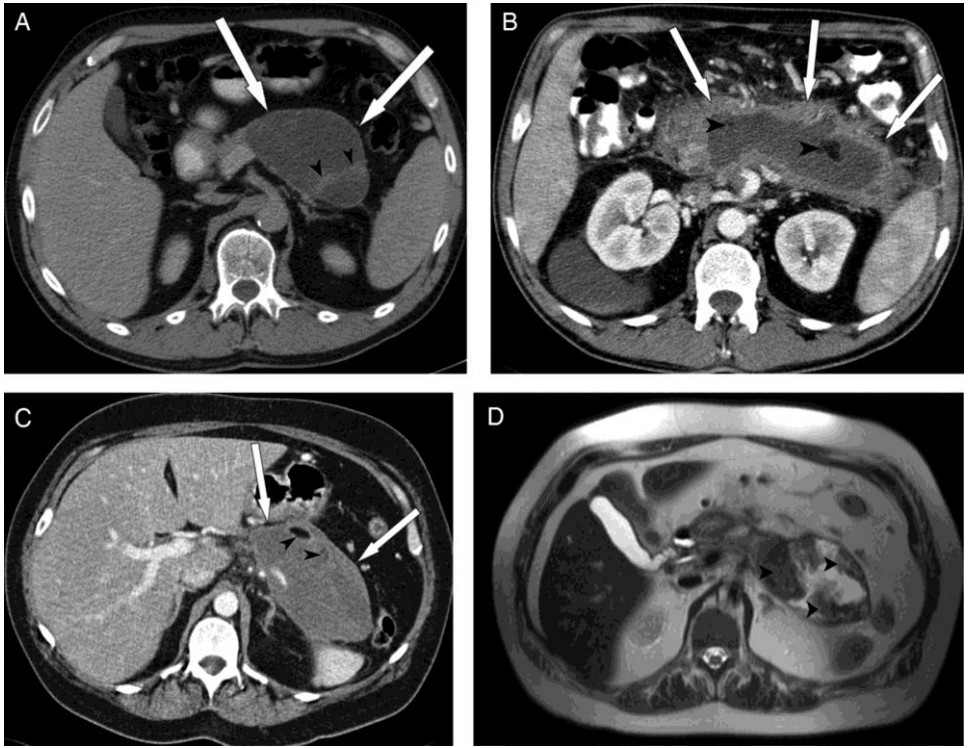
Revised Acute Pancreatitis: Types
Atlanta Classification

- Necrotizing pancreatitis:
  - Necrosis of parenchyma +/- peripancreatic tissue
  - Variable contrast enhancement first few days
  - Non-enhancing areas > 1 wk considered necrosis
- Collections:
  - < 4 wk: Acute Necrotizing Collection (ANC)
    - Pancreatic/peripancreatic tissues; heterogenous non-liquid density, locations
  - > 4 wk: Walled Off Necrosis (WON)
    - Mature, encapsulated, well-defined wall, heterogenous liquid/non-liquid

Gut. 2013;62: 102-111

(A–C) Three Different Patients With Walled-Off Necrosis (WON) After an Acute Attack of Necrotising Pancreatitis



Peter A Banks et al. *Gut*. 2013;62:102-111.

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Acute Pancreatitis: Grades of Severity
Revised Atlanta Criteria

- Mild:
  - No organ failure
  - No local or systemic complications
- Moderately Severe:
  - Organ failure, resolves < 48h
  - Local or systemic complications, no persistent organ failure
- Severe:
  - Persistent organ failure (> 48h); single or mulit-organ failure

Acute Pancreatitis: Prediction of Severity

- SIRS: Systemic Inflammatory Response Syndrome
- BISAP: Bedside Index for Severity in Acute Pancreatitis
- APACHE II: Acute Physiology and Chronic Health Evaluation (ICU patients, not specific to acute pancreatitis)
- Ranson criteria (48h after admission)

Acute Pancreatitis: SIRS
Severe Inflammatory Response Syndrome

- *Systemic Inflammatory Response Syndrome* (SIRS) is the occurrence of at least two of the following criteria: fever >38.0°C or hypothermia <36.0°C, tachycardia >90 beats/minute, tachypnea >20 breaths/minute, leucocytosis >12*10^9/l or leucopoenia <4*10^9/l

Crit Care Med. 2008;17: 296-327.

From: **Acute Pancreatitis: A Review**

Table 2. Comparison of APACHE II, BISAP, and Ranson Scores Based on the Revised Atlanta Classification Definitions of Severity

	APACHE II	BISAP (2008, Gut)	Ranson
Variables	• Age • Temperature • Mean arterial pressure • pH • Heart rate • Respiratory rate • Sodium • Potassium • Creatinine • Acute kidney failure • Hematocrit • WBC count • Glasgow Coma Scale • F_{IO_2}	• BUN >25 mg/dL (>8.9 mmol/L) • Impaired mental status • >2 SIRS criteria • Age >60 y • Pleural effusion present	Admission: • Age >55 y • WBC count >16 000/μL • Lactate dehydrogenase >350 U/L • AST >250 U/L • Glucose >200 mg/dL Within 48 h: • Fall in hematocrit >10% • Increase in BUN >5 mg/dL • Calcium <8 mg/dL • Pao_2 <60 mm Hg • Base deficit >4 mEq/L • Fluid loss >6 L
Original purpose	Severity of disease and mortality in ICU patients	Prediction of mortality in AP	Prediction of mortality in AP
Prediction of severity, AUC (SE)[22]	• 0.82 (0.03)	Score ≥3 • 0.87 (0.16)	• 0.83 (0.08)
Prediction of severity[22] • Sensitivity (95% CI) • Specificity (95% CI)	Score ≥8 • 0.83 (0.77-0.88) • 0.59 (0.56-0.63)	Score ≥3 • 0.51 (0.43-0.60) • 0.91 (0.89-0.92)	Score ≥3 • 0.66 (0.59-0.72) • 0.78 (0.76-0.81)
Prediction of mortality, AUC (SE)[22]	• 0.83 (0.16)	Score ≥3 • 0.87 (0.03)	• 0.92 (0.05)
Prediction of mortality[22] • Sensitivity (95% CI) • Specificity (95% CI)	Score ≥8 • 0.95 (0.77-1.00) • 0.68 (0.63-0.73)	Score ≥3 • 0.56 (4.23-7.55) • 0.91 (0.90-0.91)	Score ≥3 • 0.93 (0.78-0.99) • 0.69 (0.65-0.79)
Advantages	• Can be calculated within 24 h	• 5 Variables • Easy to calculate (1 point per variable) • Can be calculated within 24 h • Specific to AP	• Comprehensive • Specific to AP
Limitations	• Designed for patients admitted to ICUs • Large set of mandatory variables • Not specific to AP	• Lower sensitivity and specificity for predicting disease severity than APACHE II	• At least 48 h to calculate score • All data points not collected routinely in non-ICU patients

Abbreviations: AP, acute pancreatitis; APACHE II, Acute Physiology and Chronic Health Evaluation II; AST, aspartate aminotransferase; AUC, area under curve; BISAP, Bedside Index of Severe Acute Pancreatitis; BUN, blood urea nitrogen; F_{IO_2}, fraction of inspired oxygen; ICU, intensive care unit; Pao_2, partial pressure of arterial oxygen; SIRS, systemic inflammatory response syndrome; WBC, white blood cell.

JAMA. 2021;325(4):382-390. doi:10.1001/jama.2020.20317.

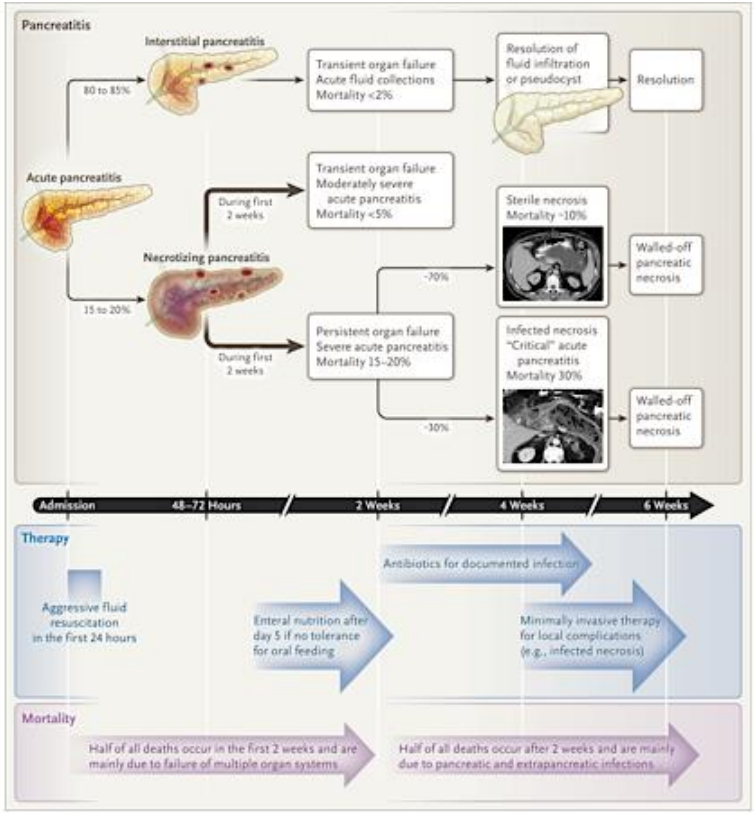
Acute Pancreatitis: BISAP Bedside Index for Severity in Acute Pancreatitis Score

- BUN > 25 mg/dl
- Impaired mental status
- > 2 SIRS criteria
- Age > 60
- Pleural effusion present
- Score >/= 3 increased risk of severe pancreatitis; specific to acute pancreatitis [sens 0.51;spec 0.91]

Acute Pancreatitis: BISAP Score

- Developed in 2008
- Specific for acute pancreatitis
- Score >/= 3 associated with developing organ failure and pancreatic necrosis
- Lowest score with < 1% mortality
- Highest score with > 20% mortality

Time Course and Management of Acute Pancreatitis



NEJM. 2016;375: 1972-81.

From: **Acute Pancreatitis: A Review**

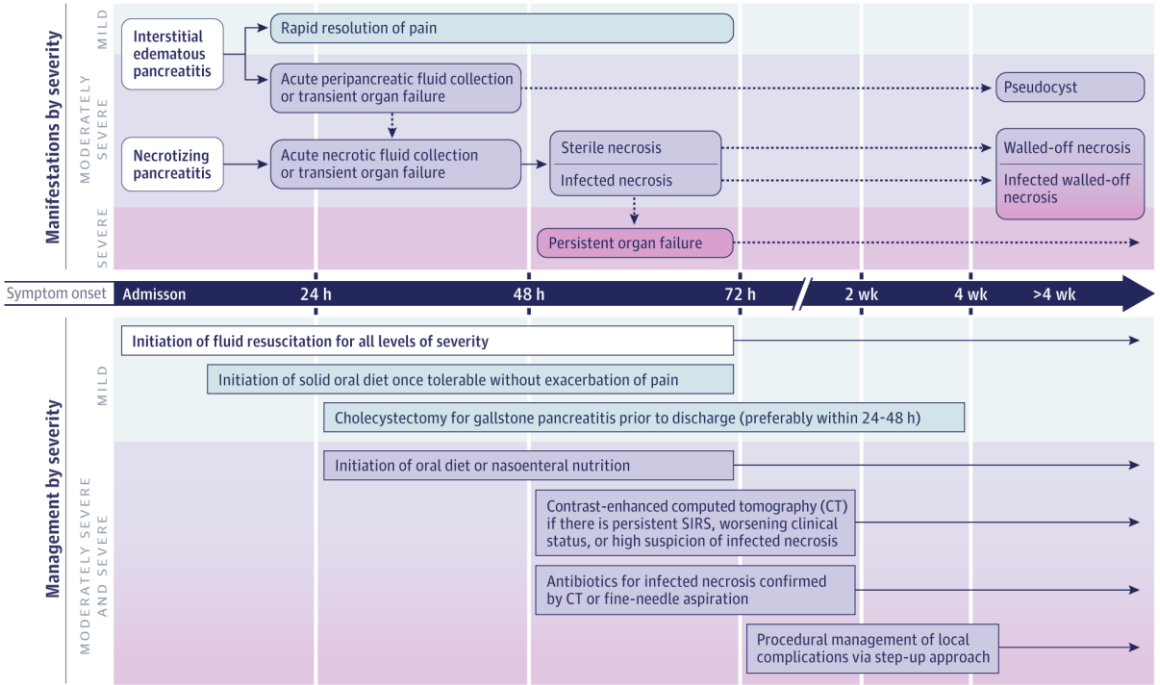
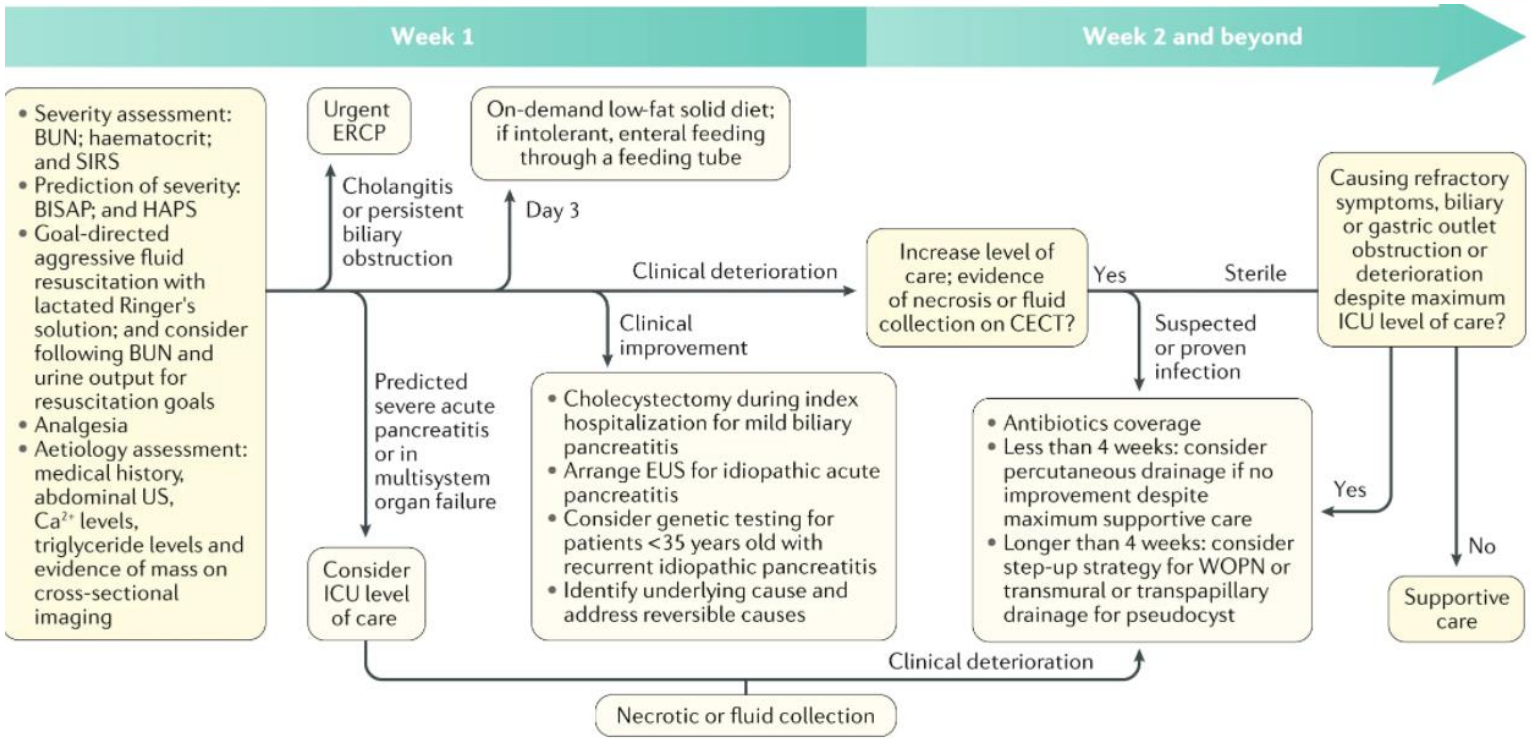


Figure Legend:
Timeline, Manifestations, and Management of Acute Pancreatitis SIRS indicates systemic inflammatory response syndrome.

JAMA. 2021;325(4):382-390. doi:10.1001/jama.2020.20317.



Nat Rev/Gastro Hepatol. 2019: 16: 479-96.

Acute Pancreatitis: Management

- Fluid resuscitation to restore tissue perfusion
  - Recent data suggesting Lactated Ringers solution superior to NS, [weak/moderate evidence]
  - Monitor VS, measure urine output, BUN, Hct
- Nutritional support
  - Enteral nutrition as soon as tolerated with low fat oral diet [AGA recs within 24h] if severe, n-g or n-j tube feeds
  - Prevent bacterial translocation, infection

From: **Acute Pancreatitis: A Review**

Table 3. Comparison of Guidelines for Fluid Resuscitation, Nutrition, and Timing of Cholecystectomy

Recommendation	IAP and APA (2013)[37]	AGA (2018)[38]	ACG/Acute Pancreatitis Task Force on Quality (2019)[39]	Quality Improvement Expert Panel (2019)[40]
Rate and/or targets of intravenous fluid resuscitation	Moderate-quality evidence Goal-directed intravenous fluid therapy with 5-10 mL/kg/h Heart rate <120/min; mean arterial pressure, 65-85 mm Hg; urinary output >0.5-1 mL/kg/h; hematocrit, 35%-44%	Very low quality of evidence Goal-directed therapy for fluid management No recommendation on rate, volume, or duration	Moderate-quality evidence Bolus and maintenance fluid resuscitation with titration according to interval assessment of vital signs, urine output, BUN, and hematocrit during the first 48 h No recommendation on rate or volume	Quality of evidence: B[a] ≥3 mL/kg/h, should be initiated unless prohibitive comorbidities exist (eg, heart or kidney failure) Trend BUN, hematocrit, creatinine every 8-12 h for the first 24-48 h
Type of fluid for initial resuscitation	Moderate quality of evidence Lactated Ringer solution	Low quality of evidence No recommendation	Moderate-quality evidence Lactated Ringer solution unless contraindicated	Quality of evidence: B[a] Lactated Ringer solution
Timing of enteral nutrition	Moderate quality of evidence In mild AP, oral feedings can be restarted once abdominal pain is decreasing and inflammatory markers are improving	Moderate quality of evidence Early nutrition within 24 h	High quality of evidence Within 48-72 h unless it is not tolerated or is contraindicated (ie, bowel obstruction or paralytic ileus)	Quality of evidence: B[a] In mild AP, oral feedings should be started within 24 h of symptom control
Route of nasoenteral nutrition (nasogastric vs nasojejunal)	High-quality evidence Nasogastric or nasojejunal	Low-quality evidence Nasogastric or nasojejunal for predicted severe or necrotizing AP	Nasogastric or nasojejunal[b]	Quality of evidence: B[a] Nasojejunal nutrition for severe AP if oral nutrition not tolerated within 3-5 d
Type of nutrition	Moderate-quality of evidence Elemental or polymeric enteral nutrition formulations	No recommendation	High-quality evidence Low-fat solid diet	No recommendation
Timing of cholecystectomy for biliary AP	Low-quality evidence Initial admission for mild AP Low-quality evidence Cholecystectomy in biliary AP complicated by collections should be deferred until collections resolve or if they persist beyond 6 weeks	Moderate-quality evidence Initial admission	High-quality evidence Surgery consultation to consider cholecystectomy prior to discharge Moderate-quality evidence Cholecystectomy in biliary AP complicated by necrosis or collections should be deferred until inflammation subsides or collections resolve/stabilize	Quality of evidence: B[a] Within 2 wk for mild AP

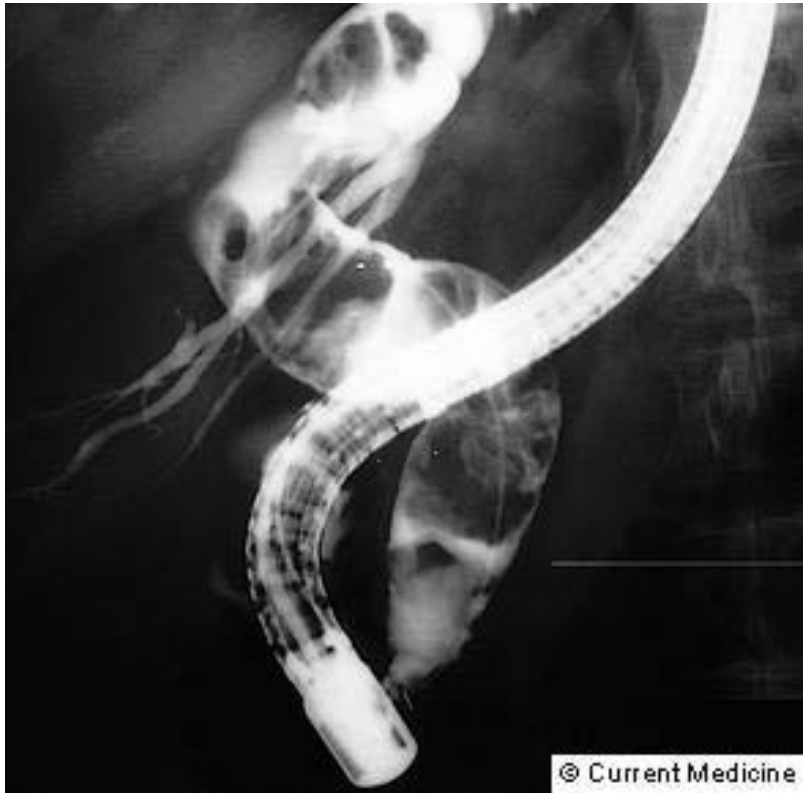
Abbreviations: ACG, American College of Gastroenterology; AGA, American Gastroenterological Association; AP, acute pancreatitis; APA, American Pancreatic Association; BUN, blood urea nitrogen; IAP, International Association of Pancreatology.

[a] Limited or conflicting evidence from single randomized trial or nonrandomized studies; [b] Quality of evidence for recommendation not provided.

JAMA. 2021;325(4):382-390. doi:10.1001/jama.2020.20317.

Acute Pancreatitis: Endoscopic Interventions

- ERCP: Sphincterotomy, stent placement for obstructive cholangitis, choledocholithiasis
- EUS-guided trans-gastric drainage of pseudocyst
- EUS-guided trans-gastric necrosectomy of Walled Off Necrosis (WON)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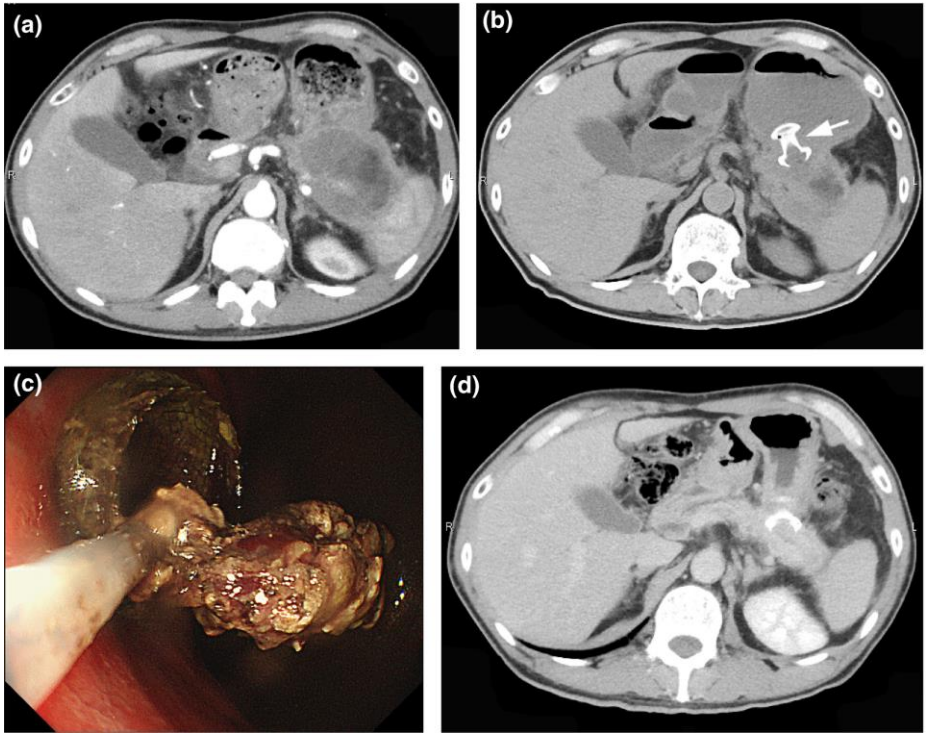
Endoscopic Management of Walled-Off Pancreatic Necrosis



Digestive Endoscopy. Volume: 33, Issue: 3, Pages: 335-341, First published: 19 April 2020, DOI: (10.1111/den.13699).

Acute Pancreatitis: Clinical Pearls

- Confirm diagnosis at consultation of acute pancreatitis correctly
- Predict severity of disease
- Necrotizing pancreatitis can be a late complication
- Do initiate fluid resuscitation but monitor for fluid overload, I/Os
- Consider Lactated Ringers > NS if not contraindicated
- Don’t give empiric antibiotics, only if signs of infected necrosis
- Initiate low fat enteral feeding early as tolerated

Acute Pancreatitis: Clinical Pearls

- Treat underlying etiology early
- Repeat cross sectional imaging if clinical worsening
- Involve supervising gastroenterologist early especially if predictive scores or signs of severe disease and need for critical care
- Consult surgery for biliary etiology
- ERCP only if cholangitis/choledocholithiasis while hospitalized

Acute Pancreatitis: Sequelae

- Risk factors for recurrent pancreatitis:
  - EtOH acute pancreatitis
  - Biliary pancreatitis w/o cholecystectomy
  - Tobacco smoking
- Risk factors for progression to chronic pancreatitis:
  - Recurrent acute pancreatitis
  - Pancreatic necrosis
  - Tobacco smoking
  - EtOH acute pancreatitis

Acute Pancreatitis: References

- Mederos MA et al. Acute Pancreatitis, A Review. *JAMA*. 2021;325: 382-90.
- Lee PJ and GI Papachristou. New insights into acute pancreatitis. *Nat Rev Gastro Hepatol.* 2019;16: 479-96.
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