



Brigham and Women's Hospital

Founding Member, Mass General Brigham

Acute and Chronic Pancreatitis

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Fellowship

- Clinical focus: Pancreas
- Research focus: Acute Pancreatitis

I have no relevant disclosures



Agenda

1. Normal Physiology: *function, protection*

2. Acute Pancreatitis

- **Diagnosis:** *the revised Atlanta Classification*
- **Etiology:** *gallstones, alcohol, triglycerides*
- **Severity:** *classification, risk factors, early biomarkers*
- **Management:** *fluids, nutrition, antibiotics, necrosis*
- **Discharge:** *factors to consider*

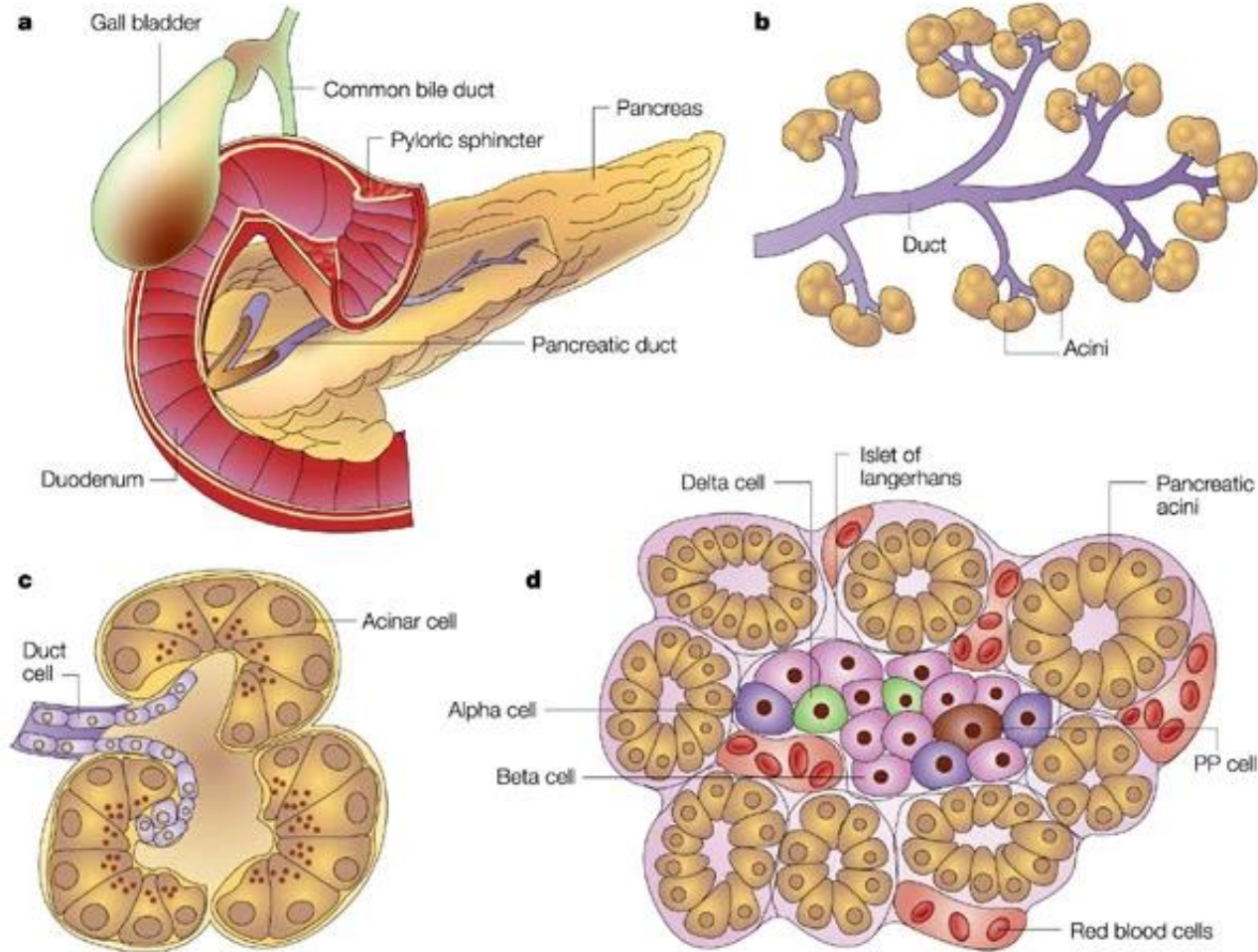
3. Chronic Pancreatitis

- **Definition and diagnosis**
- **Etiology:** *TIGAR-O*
- **Natural history and symptoms**
- **Management:** *pain, EPI*



Normal Physiology

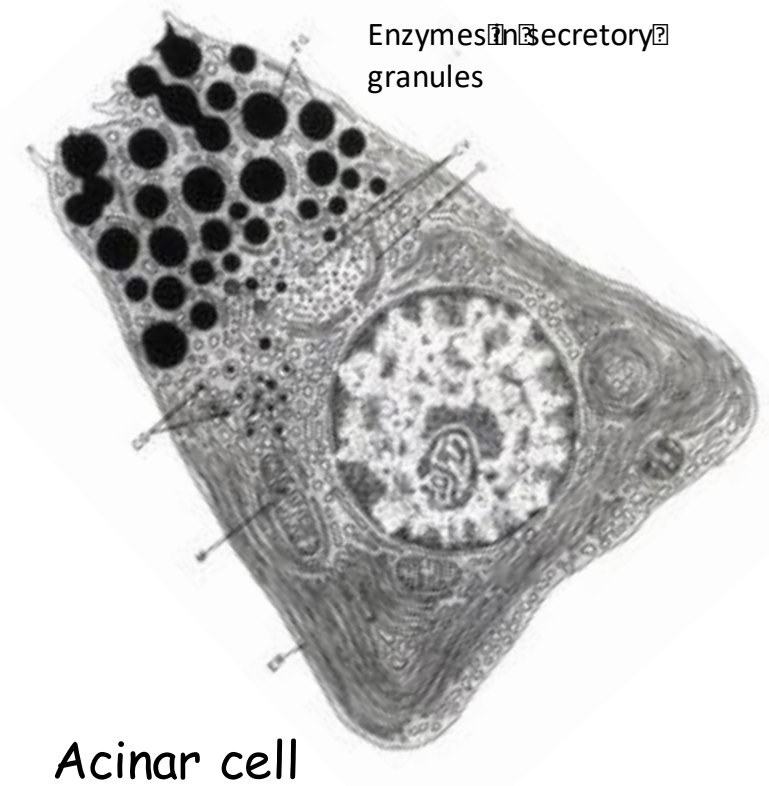
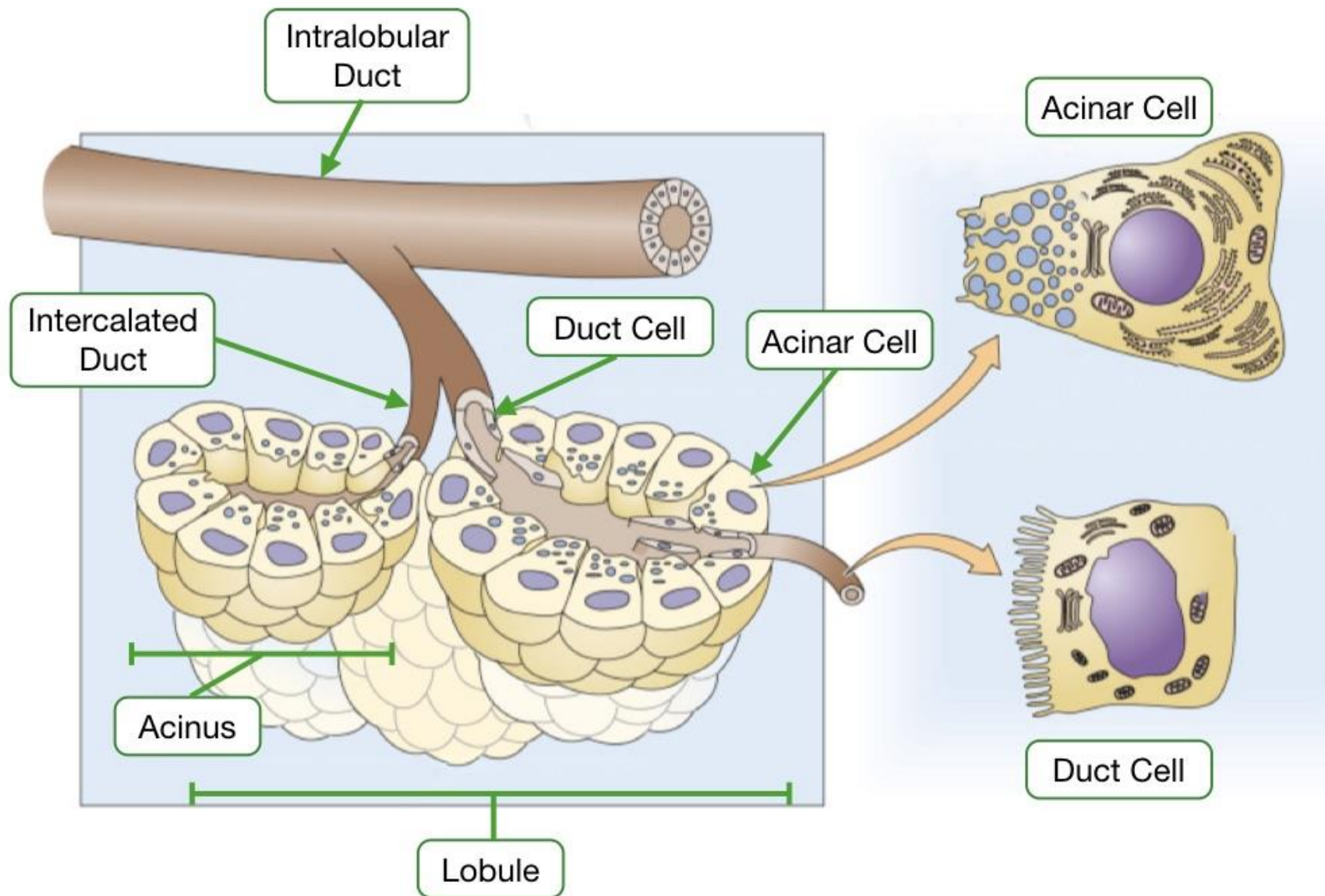




Nature Reviews | Cancer

Source: Bardeesy et al. *Nature Rev Ca*, 2002





Enzymes comprise of lipases, amylases, and proteases

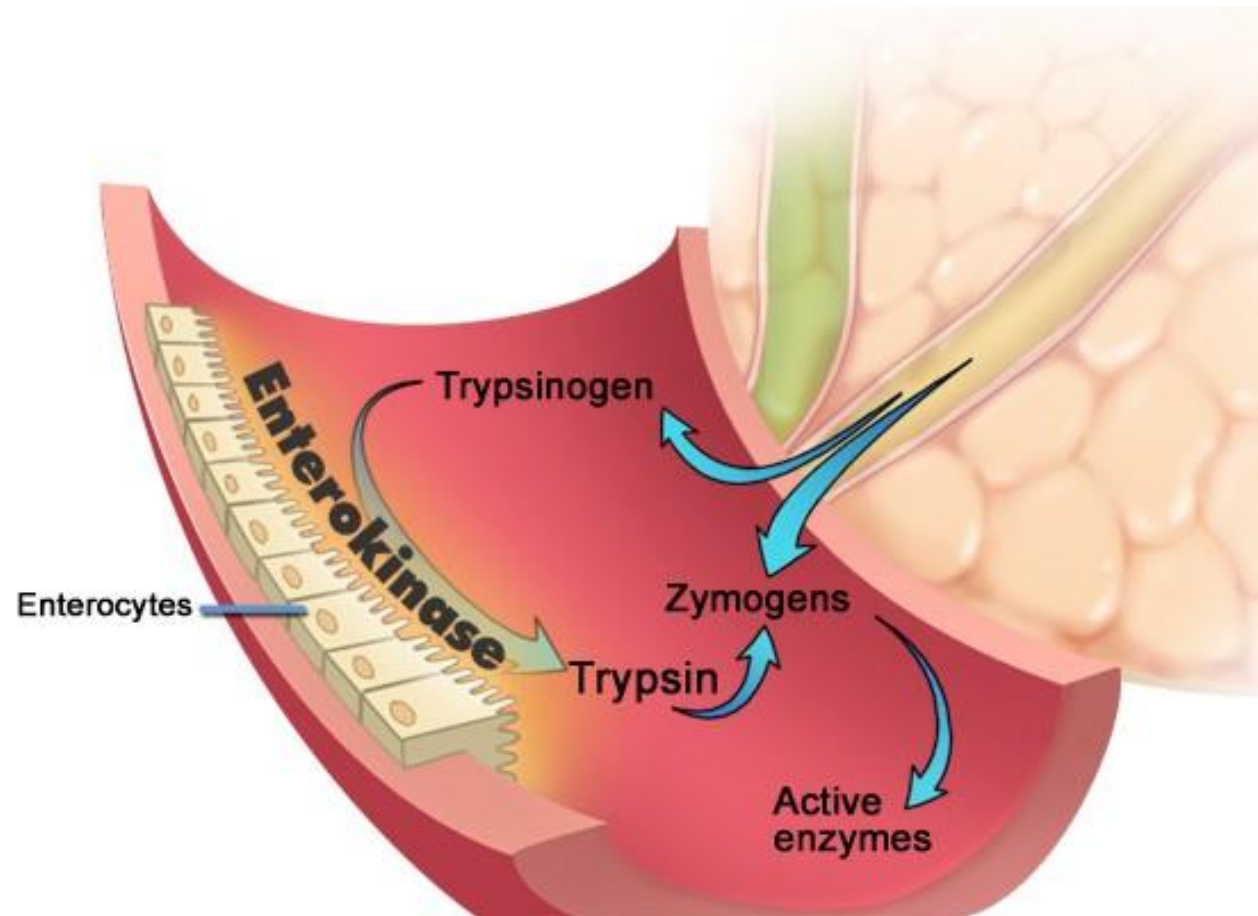
Source: https://medcell.org/tbl/histology_of_digestive_organs/reading.php



How does the pancreas protect itself from autodigestion?

- A. Most enzymes are synthesized in an inactive form
- B. Enzymes are stored in granules, away from the rest of the cell
- C. Enzyme and enzyme inhibitors are co-packaged together to prevent activation
- D. Some enzymes can inhibit themselves
- E. Enzymes are rapidly flushed out of the pancreas when secreted
- F. Enzymes are primarily activated in the duodenum, after leaving the pancreas





Source: Pancreapedia



Acute Pancreatitis



Acute Pancreatitis in the United States

- Third most common GI admission diagnosis: 288,000/year
- \$3 billion in aggregate costs/year
- \$26,000 in charges/hospitalization
- Incidence increasing >3% /year

Source: Peery et al. *Gastroenterol*, 2021

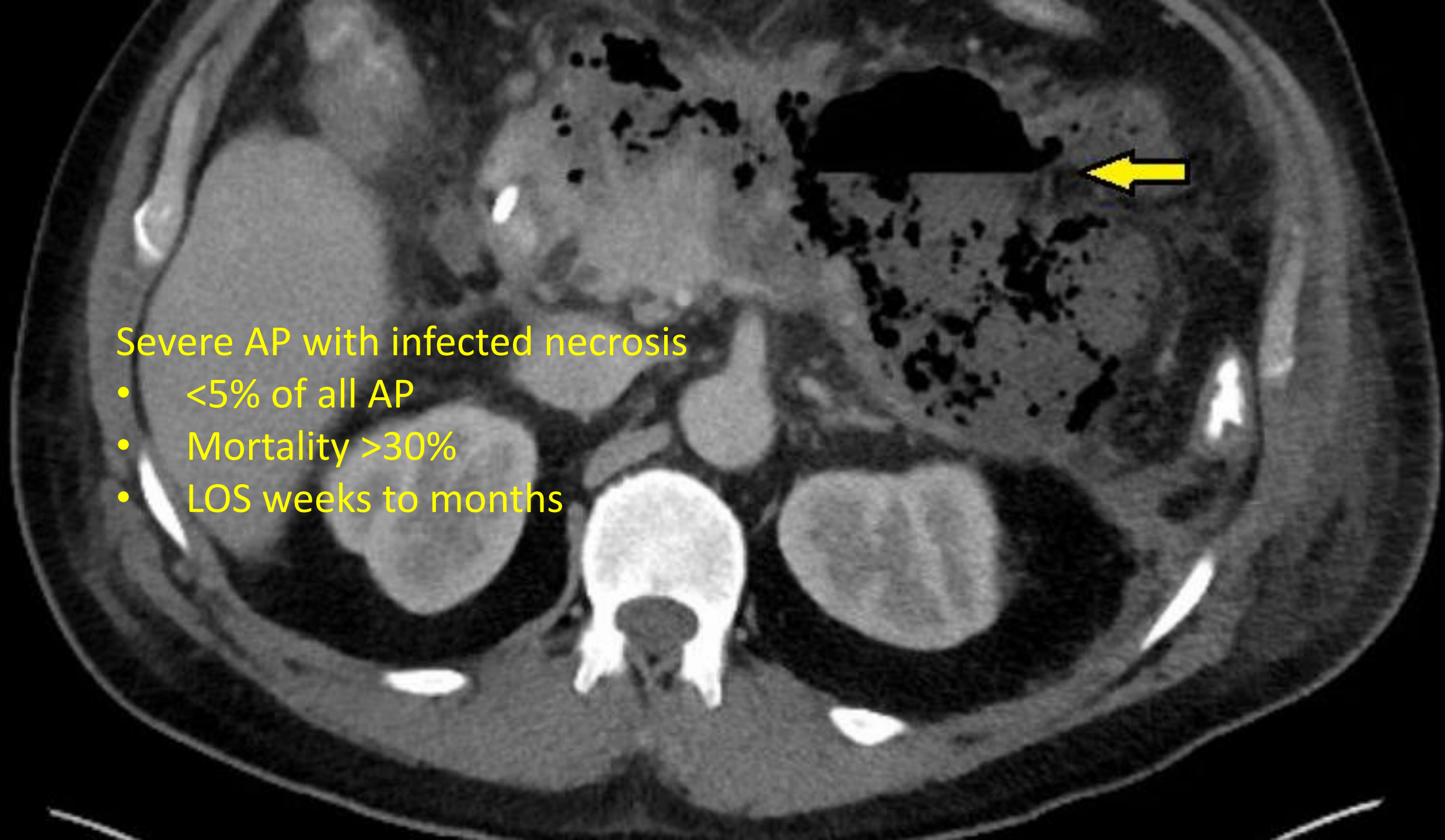




This is an axial CT scan of the abdomen. The image shows the liver, spleen, kidneys, and vertebral column. There is a subtle increase in the density of the lung bases, which is characteristic of mild interstitial pulmonary edema. A white arrow points to the right lung base, and a white arrowhead points to the left lung base. The text overlay provides clinical context for this finding.

Mild interstitial AP

- 85% of all AP
- Mortality <1%
- LOS 3-5 days



Severe AP with infected necrosis

- <5% of all AP
- Mortality >30%
- LOS weeks to months

Diagnosis



Diagnosis – Revised Atlanta Classification 2012

At least 2 of the following 3:

- Characteristic abdominal pain: acute, severe, epigastric pain, radiates to the back in 50%
- Serum amylase or lipase ≥ 3 x upper limit of normal
- CT or MRI characteristic of AP

Source: Banks et al. *Gut*, 2013



Etiology



Etiology

>75% can be explained by

- Biliary (gallstones) – ALT>150 U/L has 95% PPV
- Alcohol – chronic >50 g/day – send a phosphatidyl ethanol (PEth)
- Hypertriglyceridemia – fasting TG >1000 mg/dL

<1 % can be explained by

- Post ERCP – 5% risk, higher in certain individuals
- Drugs – idiosyncratic, mild, and almost never the cause

10-25% are “idiopathic”

- EUS may detect an etiology (30% gallstones, 2% neoplasms)
- MRCP or EUS in all cases of idiopathic pancreatitis
- Consider CCY following 2 episodes of idiopathic pancreatitis

Source: Forsmark et al. *NEJM*, 2016 / Ulmans et al. *Endoscopy*, 2020



Etiology

Take home points:

- Gallstones > EtOH > TG explain >75%
- Idiopathic: follow up MRCP/EUS, check PETH
- Almost never drug induced



Severity



Severity – Revised Atlanta Classification 2012

Mild: no organ failure*

Moderate: transient (<48h) organ failure or local complications

Severe: persistent (≥ 48 h) organ failure

*Organ failure (cardiac, respiratory, renal) defined per Modified Marshall Scoring System

Source: Banks et al. *Gut*, 2013 / Marshall et al *Crit Care Med*, 1995



Severity - Local Complications

(Peri)pancreatic Fluid collections:

- Interstitial AP: Acute peripancreatic fluid collection (APFC) → pseudocysts
- Necrotizing AP: Acute necrotic collection (ANC) → Walled off necrosis (WON)

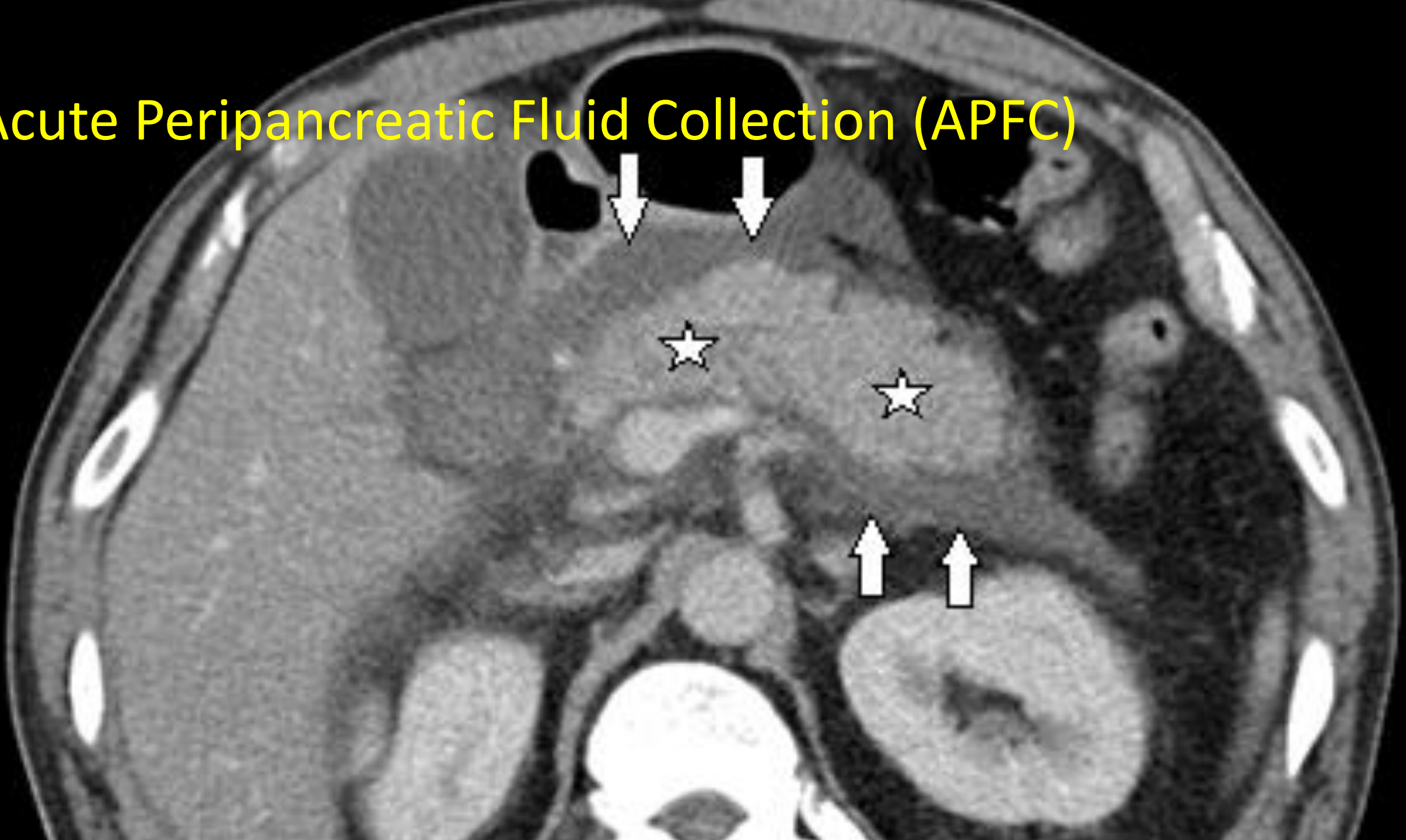
Other local complications:

- Gastric outlet obstruction
- Splenic / portal vein thrombosis

Source: Banks et al. *Gut*, 2013



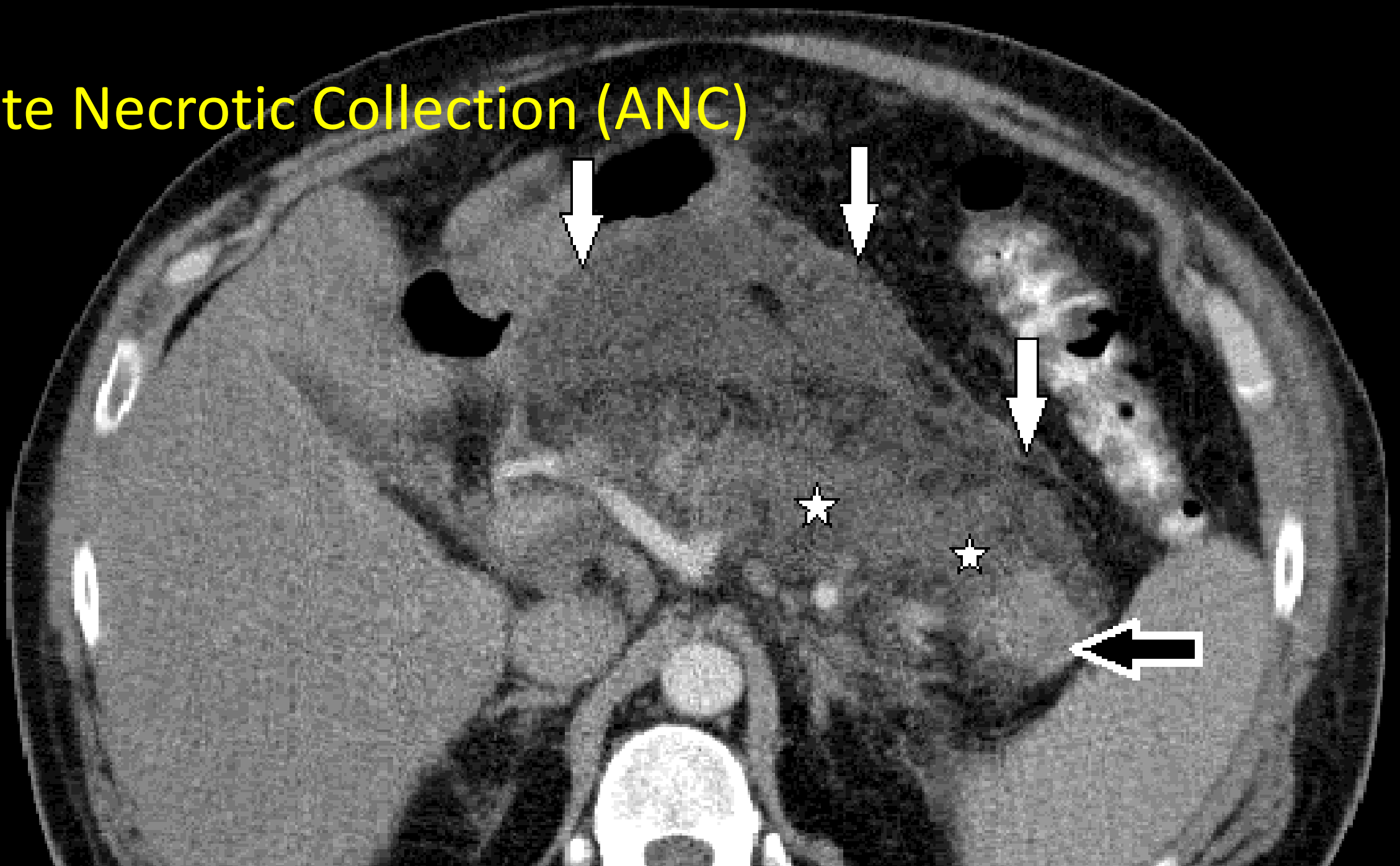
Acute Peripancreatic Fluid Collection (APFC)



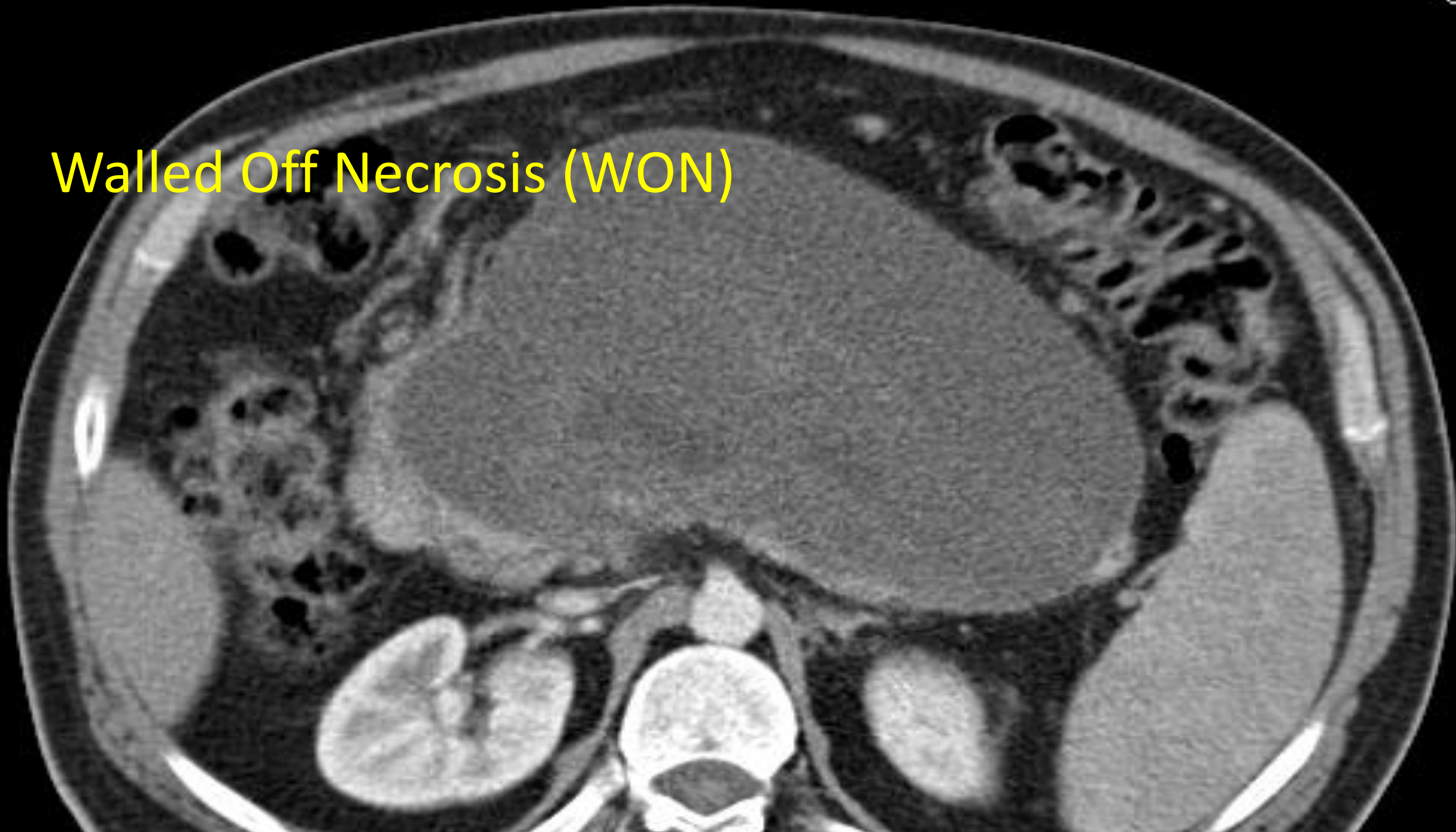
Pseudocyst



Acute Necrotic Collection (ANC)



Walled Off Necrosis (WON)



Severity - RAC 2012

Mild: no organ failure*

Moderate: transient (<48h) organ failure or local complications

Severe: persistent (≥ 48 h) organ failure

*Organ failure (cardiac, respiratory, renal) defined per Modified Marshall Scoring System

Source: Banks et al. *Gut*, 2013 / Marshall et al *Crit Care Med*, 1995



Severity - RAC 2012

Mild (no OF): mortality 0%

Moderate (transient OF): mortality 1-3%

Severe (persistent OF):

- Single POF: mortality 20%
- Double POF: mortality 30%
- Triple POF: mortality 60%

Source: Banks et al. *Gut*, 2013 / Scheepers et al. *Gut*, 2019



Severity – Predictors of Severity

- Older age
- Comorbidities
- Obesity
- First episode (0% mortality for recurrent AP)
- SIRS
- BUN > 25 mg/dl
- HCT > 44%



Severity

Take home points:

- Mortality in recurrent AP \sim 0%
- Evaluate for markers of severity (SIRS, BUN) at admission
- Monitor for signs of organ failure \rightarrow ICU



Management



A 50M presents with severe epigastric pain radiating to the back, lipase 3000, ALT 300, Tbili 0.8, WBC 9. He is afebrile, HR 90, BP 120/80, RR 12, 98%. RUQUS shows gallstones, CBD 6mm. Best practice(s) are to:

- A. Order CT scan for diagnostic confirmation
- B. Keep patient NPO until pain has resolved
- C. Administer prophylactic antibiotics to reduce risk of cholangitis
- D. Proceed to ERCP for suspected choledocholithiasis
- E. Consult surgery for same admission cholecystectomy
- F. Bolus IVF 20cc/kg

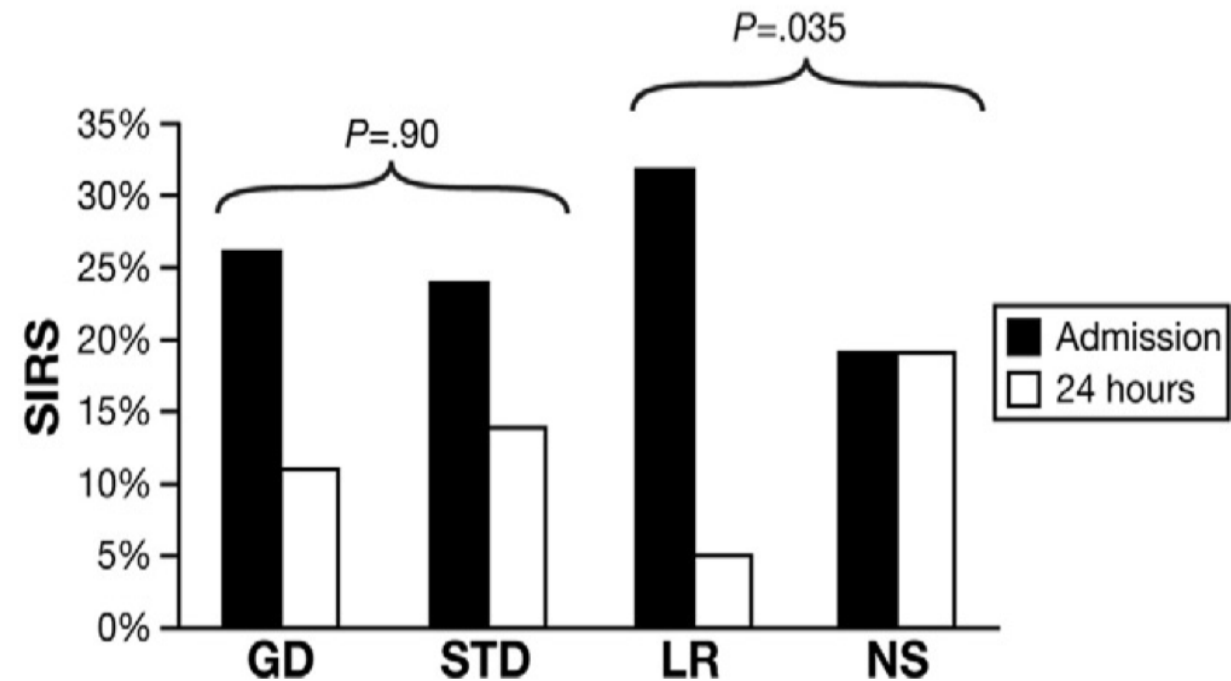


Management – Fluid Resuscitation

Lactated Ringers is *probably* better than Normal Saline

Single center RCT: n=40, **LR** vs. **NS**

- Primary outcome: SIRS at 24h lower in LR group



Source: Wu et al. *Clin Gastroenterol Hepatol*, 2011



Management – Fluid Resuscitation

Moderate >> Aggressive resuscitation for mild AP

Multicenter RCT: n=249, Aggressive (bolus 20 cc/kg → 3 cc/kg/hr) vs. Moderate (bolus 10 cc/kg if hypovolemic → 1.5 cc/kg/hr) IVF for mild acute pancreatitis (WATERFALL trial)

- Primary outcome: development of moderate/severe AP
- Safety checkpoint: fluid overload



Management – Fluid Resuscitation

Multicenter RCT: n=249, **Aggressive** vs. **Moderate IVF** for mild acute pancreatitis (WATERFALL trial)

	Aggressive IVF (n=122)	Moderate IVF (n=127)	
Volume first 48h	7.8 (6.5-9.8) L	5.5 (4-6.8) L	
Primary outcome (mod/sev AP)	22%	17%	RR 1.3 (0.78-2.18)
Necrosis	14%	7%	RR 1.95 (0.87-4.38)
Fluid overload	21%	6%	RR 2.85 (1.36-5.94)

Source: De Madaria et al. *NEJM*, 2022



Management – Fluid Resuscitation

Take home points:

- Early moderate goal-directed IVF resuscitation for mild AP
 - 10 ml/kg bolus (no bolus if euvolemic) → 1.5 cc/kg/hr then adjust
- Lactated ringers is preferred



Management – Nutrition

AP may lead to >10% loss in body weight

- Anorexia
- Catabolic state/ negative nitrogen balance
- Gut barrier dysfunction
- Exocrine pancreatic insufficiency
- Iatrogenic malnutrition



Management – Nutrition

1. Early (< 24h) oral feeding as tolerated > NPO
 - Protects gut-mucosal barrier and reduces bacterial translocation
 - 11 RCTs: ↓ intervention for necrosis, no difference mortality, pOF, necrosis
2. Enteral > Parenteral nutrition (if cannot tolerate oral feeding)
 - 12 RCTs: ↓ infected necrosis and OF, no difference in mortality
3. NGT = NJT (predicted severe or necrotizing AP requiring enteral feeding)
 - 3 RCTs: No difference in mortality, OF (including respiratory failure), necrosis

Source: Crockett et al. *Gastroenterol*, 2018



Management – Nutrition

Take home points:

- Avoid routine NPO orders
- Feed when patient is hungry, OK to start with a solid diet
- If unable to tolerate oral feeding, use NG or NJ



Management – Antibiotics

14 RCTs assessing outcomes of antibiotic ppx – 841 patients

- No reduction in mortality, infected necrosis, non-pancreatic infections, need for surgical interventions

Take home points:

- No role for antibiotic prophylaxis
- Reserve for cholangitis or documented infected necrosis



Management – Same Admission CCY

Multicenter RCT: n=266, **Same-Admission** vs. **Interval CCY** for mild gallstone pancreatitis (PONCHO trial)

- Primary composite outcome: 6 m readmission for biliary complication + mortality

	Same admission (n=128)	Interval (n=136)	
Time to CCY	1 day	27 days	
Primary outcome	5%	17%	RR 0.28 (0.12-0.66)
Reporting colic while waiting	3%	51%	RR 0.06 (0.02-0.19)
Cost to prevent 1 readmission	-€1918		

Source: Da Costa et al. *Lancet*, 2015 / Da Costa et al. *Br J Surg*, 2016



Management – Necrosis

Sterile necrosis / pseudocysts

- Almost never require early intervention
- Only require intervention if symptomatic (persistent pain, anorexia, nausea) later in disease course (WON, 4-6 weeks)
- Do not require intervention if asymptomatic (1/3 will resolve)

Source: Freeman et al. *Pancreas*, 2012



Management – Infected Necrosis

Infected necrosis

- Peaks 2-4 weeks after presentation
- Suspected in sepsis, SIRS, or OF >7 days after onset
- Proven by Cx/gram stain or gas within necrotic collection

Treatment has evolved

- Early surgery → delayed surgery → surgical step up → endoscopic step up



Management – Infected Necrosis (in 2018)

RCT: n=66, **endoscopic step-up** (EUS drainage → EUS necrosectomy) vs. **min invasive surgery** (laparoscopic or VARD) (MISER TRIAL)

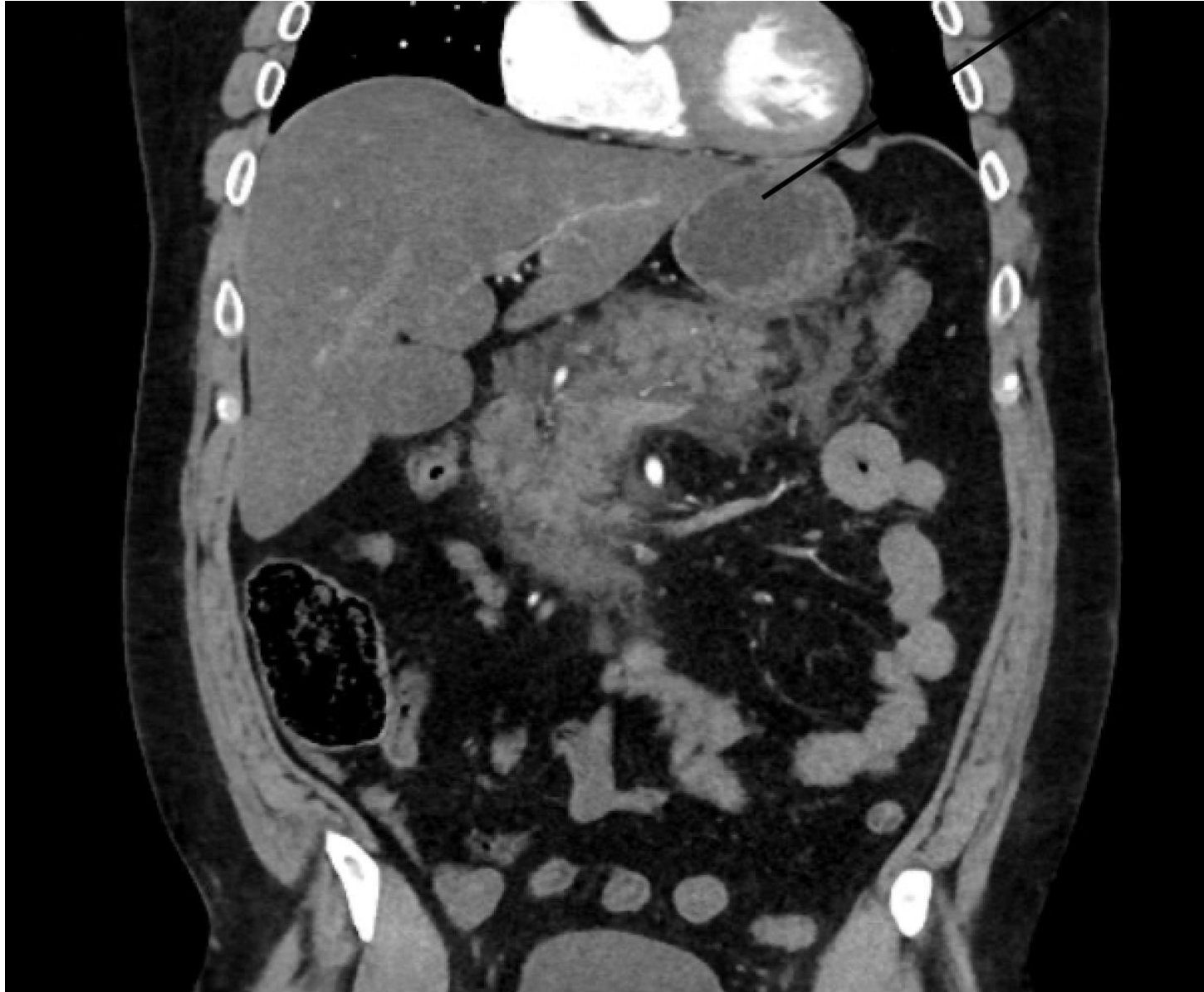
- Primary composite outcome (OF, visceral perforation, systemic dysfunction, enterocutaneous fistula, bleeding, perforation)

	Endoscopic (n=34)	MI Surgery (n=32)	
Primary outcome	12%	41%	RR 0.29, (0.11-0.80)
Multi organ failure	6%	9%	RR 0.63 (0.11-3.51)
Enterocutaneous fistula	0	28%	p = 0.001
Necrosectomy	32%	97%	p < 0.001
Total costs pp	\$75,830	\$117,492	p < 0.039

Source: Bang et al. *Gastro*, 2018 (MISER trial)

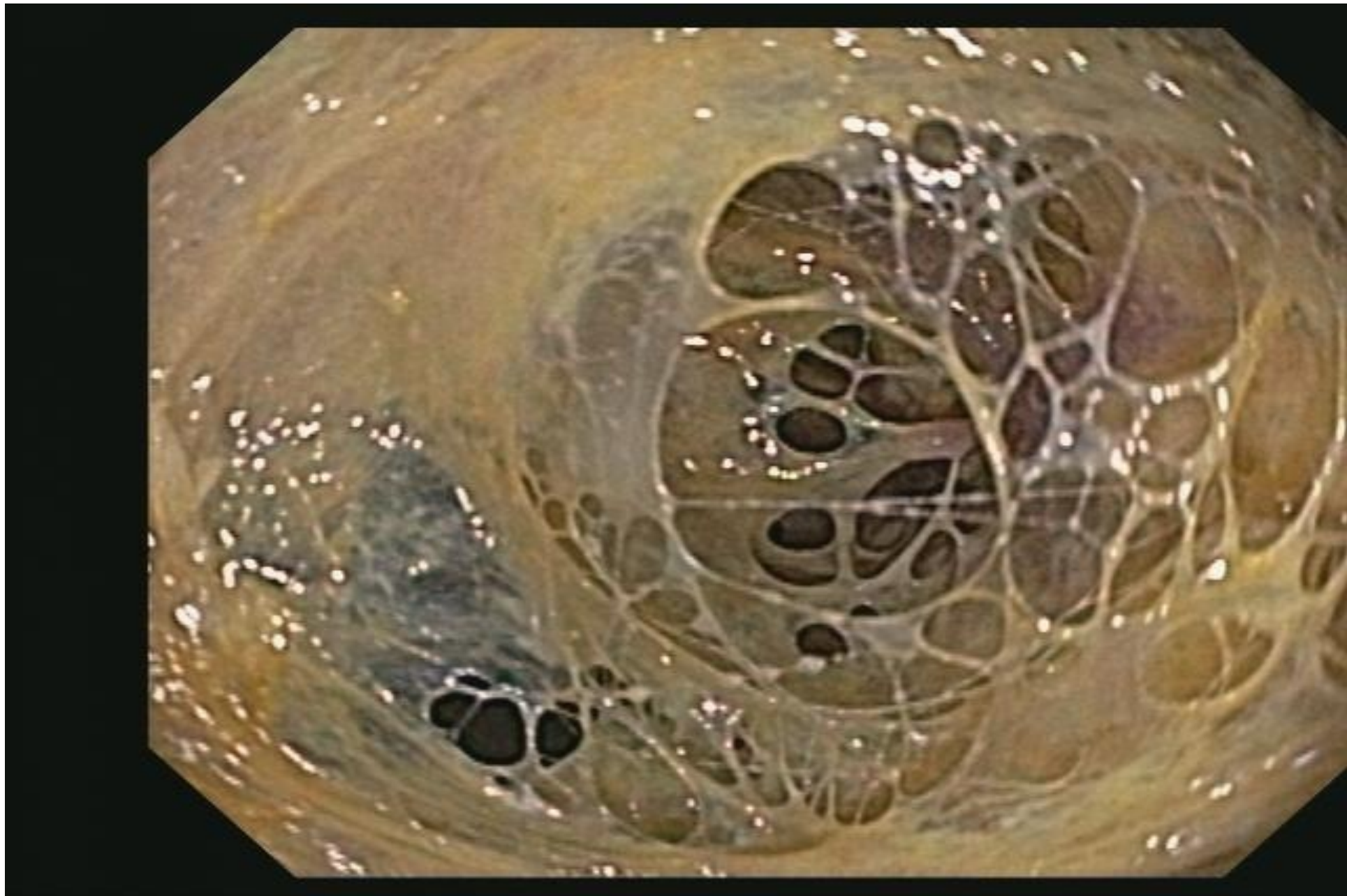


Day 0



Day 27





Day 51



Discharge



Discharge – Impact of Alcohol and Smoking after AP

Very heavy alcohol use (≥ 5 /day) increases risk of CP (OR 3.1)

Smoking (>35 pack years) increases risk of CP (OR 4.6)

RCT: n=120 EtOH AP, **initial only** vs **repeat** (q6 m x2 years) alcohol cessation counseling by RN

- Reduced recurrent AP (21% vs. 8%) in repeat counseling arm

Take home point:

- Provide smoking and alcohol cessation counseling

Source: Yadav et al. *Arch Int Med*, 2009 / Nordback et al. *Gastroenterol*, 2009



Chronic Pancreatitis



Definition and Diagnosis



Definition - Chronic Pancreatitis

Pathologic fibro-inflammatory syndrome of the pancreas in individuals with genetic, environmental and/or other risk factors who develop persistent pathologic responses to parenchymal injury or stress.

Common features of established and advanced CP:

- Fibrosis on histology
- Pancreatic atrophy, duct distortion and strictures, calcifications on imaging
- Pain syndromes
- Pancreatic exocrine and endocrine dysfunction
- Dysplasia

Source: Whitcomb et al. Pancreatology, 2016.



Diagnosis

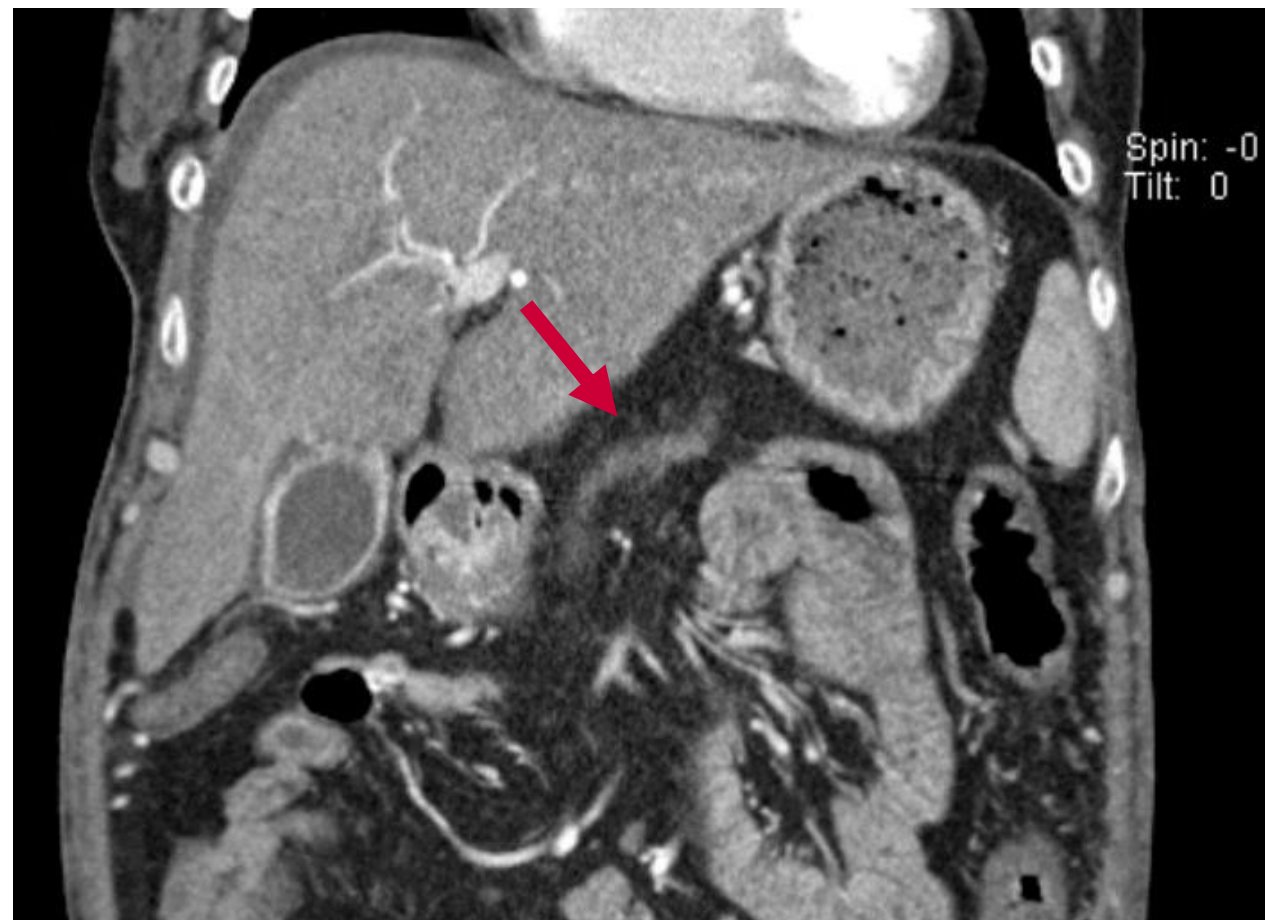
Take a history!

- History of acute pancreatitis
- Characteristic pain or maldigestion
- Genetic or environmental risk

In those with high pre-test probability, then imaging can confirm diagnosis



Diagnosis – Imaging



Etiology



Etiology – TIGAR-O

Toxic-Metabolic: Alcohol, Smoking, Hypercalcemia, Hypertriglyceridemia

Idiopathic

Genetic: *PRSS1*, *SPINK1*, *CFTR*, *CTRC*

Autoimmune

Recurrent/Severe AP: etiology in 60%

Obstructive: Pancreas divisum, Sphincter of Oddi Dysfunction, Duct obstruction



Natural History and Symptoms



Natural History and Symptoms

Abdominal or back pain – ETOH cessation may improve pain

Nausea vomiting

Exocrine pancreatic insufficiency

- Bloating
- Steatorrhea
- Weight loss
- Fat sol vitamin deficiency

Diabetes type 3c: duration of CP associated with islet cell loss

Pancreatic cancer: ~3-5% lifetime, higher in certain genetic conditions

Source: Gardner et al. Am J Gastroenterol, 2020



Management



Management – Surgery leads to better long term pain relief for obstructive CP

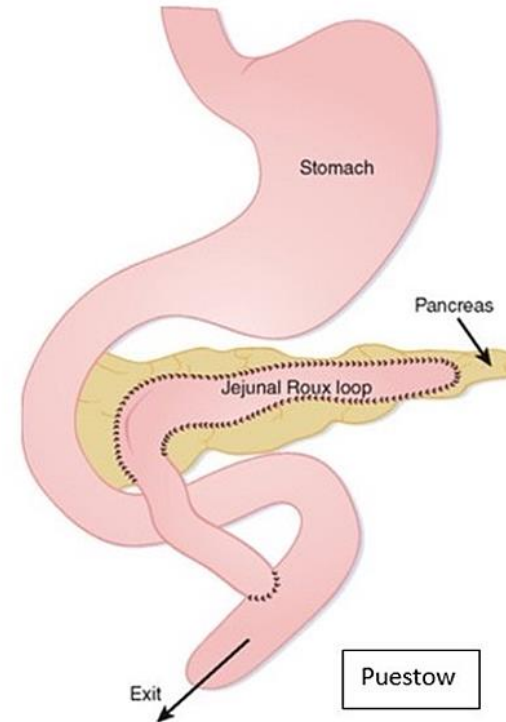
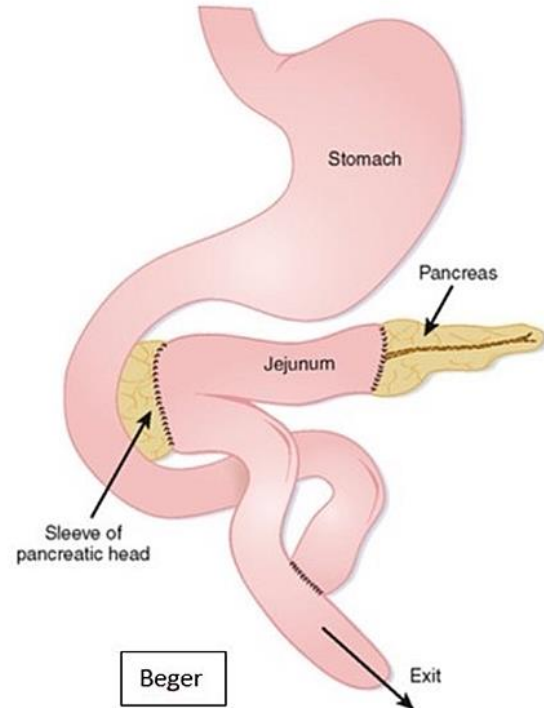
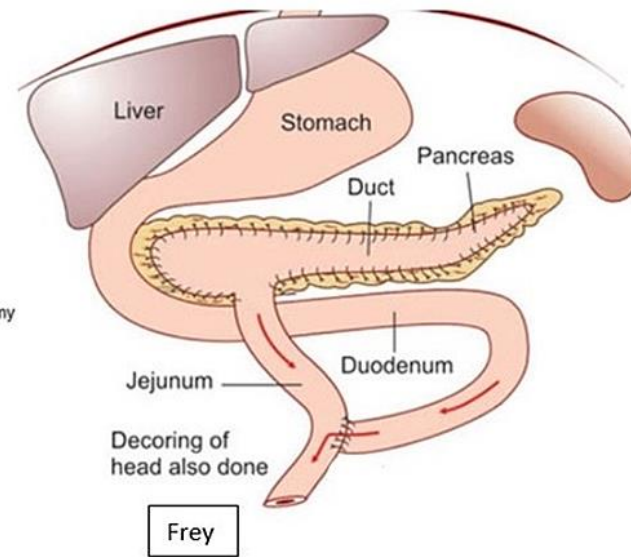
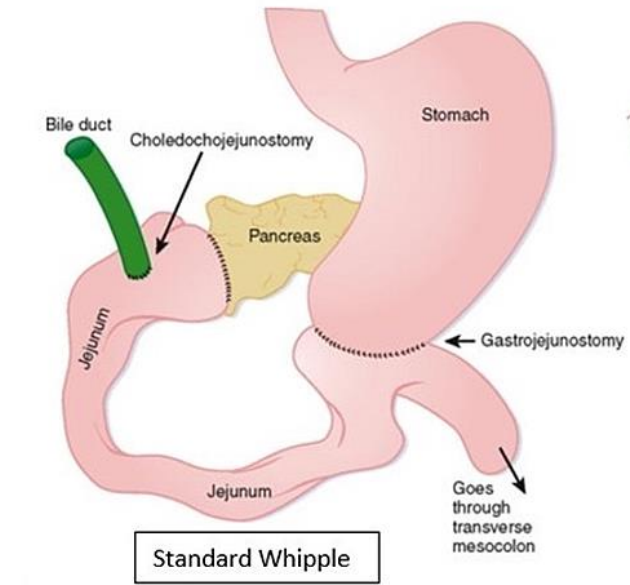
Long term outcomes of Multicenter RCT: n=61, **early surgery** vs. **endoscopy** (ESCAPE TRIAL), mean follow up 98 months

- Primary outcome: Izbicki pain score

	Early surgery (n=31)	Endoscopic (n=30)	
Primary outcome (Izbicki pain score)	33	51	P = 0.03
Complete pain relief	14%	6%	P = 0.04
VAS score pain	29	47	p = 0.02
Satisfaction (very satisfied)	22%	10%	p = 0.003
No difference: SF-36 QoL score, pancreatic function, smoking or alcohol use			

Source: van Veldhuisen et al. JAMA Surgery, 2024





Source: Ashraf et al. Cureus, 2021



Management – Pain in CP

Antioxidants may reduce pain

- Selenium, ascorbic acid, β -carotene, α -tocopherol, methionine

Pancreatic enzymes are ineffective for pain control

- May help anecdotally

Celiac plexus block may be considered

- Effective in 60%, duration 3-6 months

Opiates (when other options exhausted)



Management – EPI

EPI should be screened for in all CP patients

- Represents 90% loss of pancreatic acinar function
- Weight loss, steatorrhea, diarrhea, malnutrition, osteopenia
- Fecal elastase -1 most readily available diagnostic test

PERT improves fat and protein absorption, symptoms, and QoL

- Starting dose 40,000-50,000 U lipase with each meal

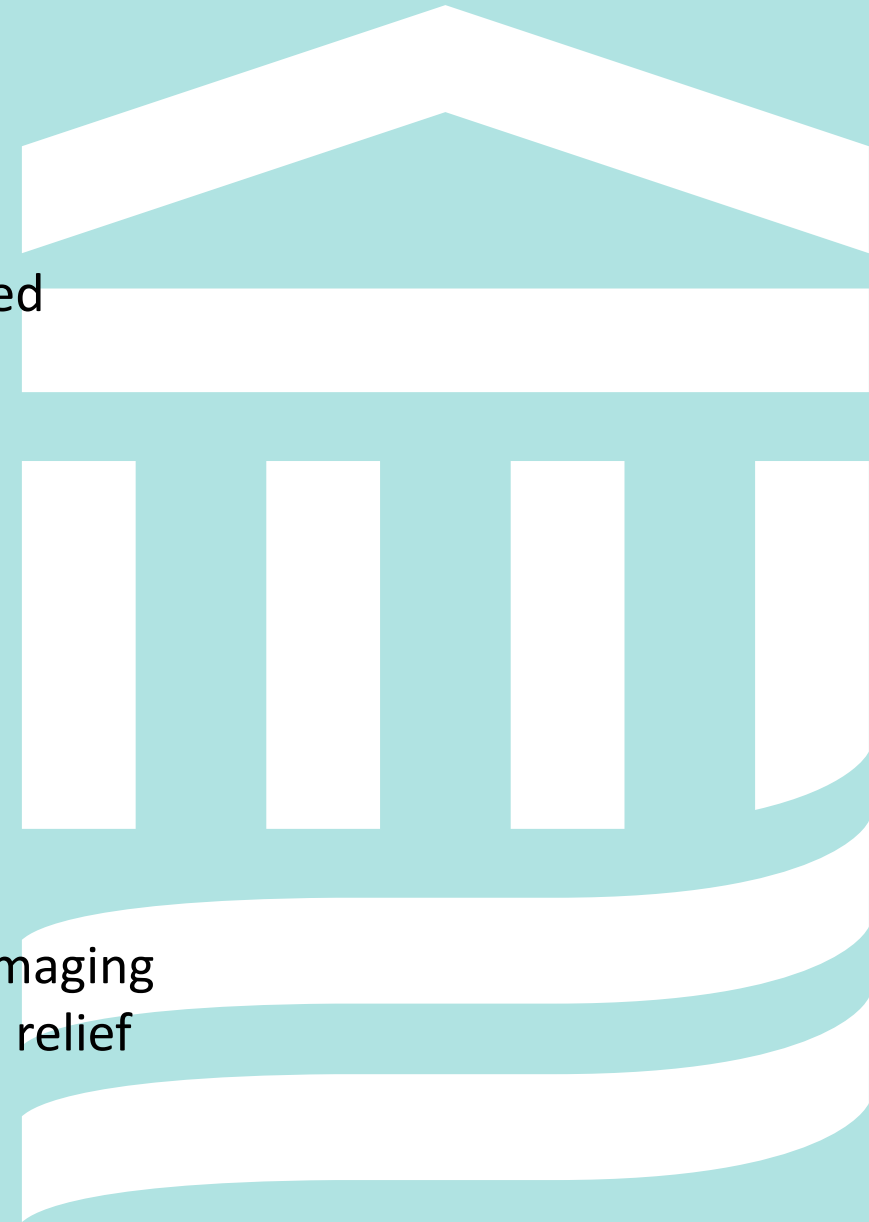
Evaluate periodically for

- Fat soluble vitamin, An, Mg deficiency
- Osteoporosis



Take Home Points

1. Pancreatitis occurs when protective mechanisms are overwhelmed
2. Evaluate for early markers of severity
3. Document persistent organ failure
4. Provide early, moderate, goal directed fluid resuscitation
5. Initiate early oral feeding when tolerated, regardless of severity
6. Choose enteral rather than TPN if unable to tolerate orals
7. Avoid prophylactic antibiotics
8. Drain +/- debride (EUS guided) infected or symptomatic necrosis
9. Perform early cholecystectomy for mild gallstone pancreatitis
10. Discontinue smoking and alcohol
11. Diagnose chronic pancreatitis by clinical suspicion + compatible imaging
12. Consider surgery > endoscopic decompression for long term pain relief
13. Dose PERT appropriately



BWH Center for Pancreatic Disease

Post-discharge follow up:

djin@bwh.harvard.edu / 617-732-6389

Clinic admin: Donna Shah



References

Banks PA, et al. Classification of Acute Pancreatitis – 2012: Revision of the Atlanta Classification and Definitions by International Consensus. *Gut*, 2013.

Tenner S, et al. ACG Guidelines: Management of Acute Pancreatitis. *Am J Gastroenterol*, 2024.

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