Acute pancreatitis

Definition

Acute reversible inflammation and autodigestion of the pancreatic parenchyma, Presents with abdominal pain, and is associated with raised pancreatic enzymes in the blood.

Revised Atlanta classification and definitions (Banks et al. 2012)

The diagnosis of acute pancreatitis (AP) requires 2 of the following 3 features

1.Abdominal pain- acute onset of a persistent, severe epigastric pain which radiates to the back

2.Serum lipase/amylase activity of at least 3x greater than the upper limit of normal.

3.Characteristic findings of acute pancreatitis on CECT or MRI or transabdominal US.

* If the abdominal pain strongly suggests that acute pancreatitis is present but the amylase/lipase is less than 3x upper limit of normal (as may be the case with a late presentation) imaging may be needed to confirm the diagnosis.

Epidemiology

- Incidence has increased in past 20 years
- Most patients (80%) – mild and self-limited course but 10 – 20% of patients have a rapidly progressive inflammatory response with increased LOS, morbidity and mortality
- Mortality < 1% in mild pancreatitis but increases to 10 – 30% in severe acute pancreatitis – MODS is the most common cause
- Bimodal pattern of mortality
    - Early phase – MODS secondary to inflammatory cascade triggered by pancreatic inflammation
    - Late phase (> 2weeks) – usually secondary to septic complications (infected necrosis)

Etiology (Mnemonic: I GET SMASHED)

Idiopathic (15-25%)

Gallstones (38%)

Ethanol (36%)

Trauma

Steroids

Mumps and other infections (CMV, mycoplasma, Varicella zoster virus)

Autoimmune: SLE, Sjogren's syndrome

Scorpion toxin and other toxins

Hypercalcaemia, hypertriglyceridemia (metabolic causes)

ERCP (2-5%)- Post ERCP

Drugs (1-2%) – steroids, NSAIDS, diuretics, ARVs particularly stavudine

Rare causes: neoplasm (pancreatic/ampullary tumor), congenital (pancreatic divisum), genetics.

Pathophysiology

Acute pancreatitis is caused by unregulated activation of trypsin within pancreatic acinar cells, activating pro-enzymes leading to auto-digestion and an inflammatory response and can result in a progression to systemic inflammatory response syndrome (SIRS).

Gallstones

- Most common in Western world
- Responsible for 40% of cases in USA
- More common in women 50 – 70year old women
- Mechanisms – 2 theories:
    - Obstructive theory – increased pressure in pancreatic duct due to continuous secretion of pancreatic juice in the presence of pancreatic duct obstruction
    - Reflux theory – stones impacted in the Ampulla of Vater – common channel forms that allows reflux of bile salts into pancreas. Bile salts cause direct acinar cell destruction and necrosis.

Alcohol

- Second most common cause worldwide
- Most common cause in South Africa
- 35% of cases in USA
- Young men - 30 – 45 years old
- Only 5 – 10% of patients who drink develop acute pancreatitis
- Factors that contribute to development of acute pancreatitis
    - Concomitant smoking
    - Genetic predisposition
    - Heavy alcohol abuse (controversial – disproven in some recent studies)
- Triggers pro-inflammatory pathways in pancreas
    - Increases expression and activity of caspases (proteases that mediate apoptosis)
    - Decreased perfusion of pancreas
    - Sphincter of Oddi spasm
    - Obstructs pancreatic ducts by precipitation of protein inside ducts.

Clinical manifestations

- Cardinal symptom is epigastric and/or peri-umbilical pain that radiates to the back
- Associated nausea/vomiting that does not relieve the pain
- Commonly dehydration, poor skin turgor, tachycardia, hypotension and dry mucous membranes.
- The findings on abdominal examination vary according to the severity of the disease
    - Mild pancreatitis – normal/only mild epigastric tenderness.
    - Severe pancreatitis – significant abdominal distention, associated with generalised rebound tenderness and abdominal rigidity.
- Importantly – the nature of the pain described by the patient may not correlate with the physical examination or the degree of pancreatic inflammation – can have minimal examination findings with severe pancreatitis.
- **Rare findings** – flank and peri-umbilical ecchymoses (Grey Turner and Cullen's signs respectively) – retroperitoneal bleeding associated with severe pancreatitis
- Jaundice may be present – concomitant choledocholithiasis or significant edema of the head of the pancreas.
- May have dullness to percussion and decrease air entry in L (less commonly R) hemithorax – pleural effusion secondary to acute pancreatitis.

Two types of acute pancreatitis

1. **Interstitial edematous pancreatitis**

- The majority of patients with acute pancreatitis have diffuse enlargement of the pancreas secondary to inflammation and edema
- CT – homogenous enhancement of pancreas, peri-pancreatic fat stranding, some peri-pancreatic fluid may be present
- Clinical symptoms usually resolve within the first week

2. **Necrotising pancreatitis**

- 5 – 10% of patients develop necrosis of pancreatic parenchyma or peri-pancreatic tissue or both
- impairment of pancreatic perfusion and signs of peri-pancreatic necrosis develop over several days
- Early CT scan may underestimate degree of necrosis – difficult to differentiate edema from necrosis
- After the first week any non-enhancing area of pancreatic parenchyma can be considered to be parenchymal necrosis
- Pancreatic necrosis has a variable natural history – may remain solid/liquefy, remain **sterile/ become infected**, persist/disappear over time.

Classification according to severity of acute pancreatitis

Important to define and stratify severity of acute pancreatitis

- Identify potentially severe acute pancreatitis to allow early aggressive treatment
- Assess the need for high care or ICU admission
- Identify patients that need referral to specialized centers

1. **Mild acute pancreatitis**

- Absence of organ failure
- Absence of local/systemic complications
- Can usually be discharged in the early phase
- Don't require imaging
- Low mortality

2. **Moderately severe acute pancreatitis**

- Transient organ failure (<48 hours)
- Local or systemic complications in the absence of persistent organ failure
- May resolve without intervention or may require prolonged specialist care
- Mortality is far less than that of severe acute pancreatitis

3. **Severe acute pancreatitis**

- Persistent organ failure (>48 hours)
- Organ failure that develops during early phase due to SIRS
- If SIRS is present there is an increased risk of persistent organ failure – treat as if it is severe acute pancreatitis
- Persistent organ failure may be single or multiple
- These patients usually also have local complications
- Mortality 36 – 50%
- If infected necrosis is also present the mortality is very high
- **Criteria for SIRS – 2/more of:**
    - HR > 90bpm
    - Temp < 36°C/> 38.3°C
    - WCC < 4000/> 12 000
    - RR > 20 per min/PCO2 < 32 mmHg

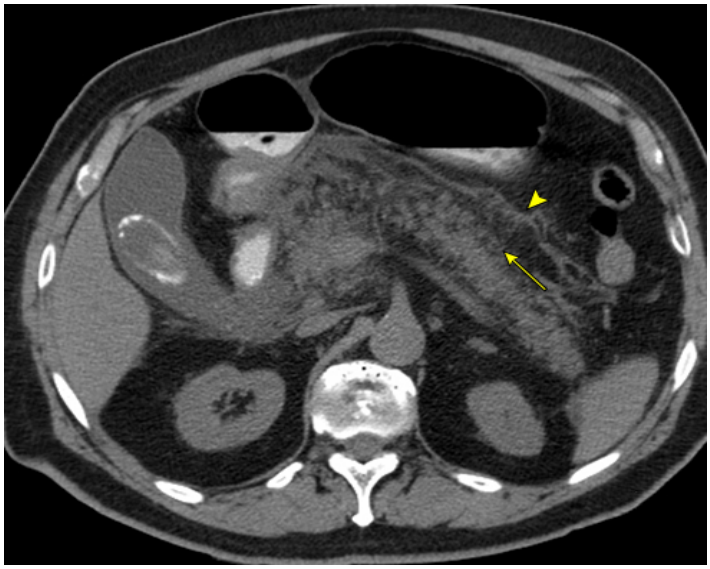
Risk factors for severe pancreatitis:

- Age > 60 years
- Comorbid illness
- History of chronic alcohol consumption
- Obesity

Local complications:

1. **Acute peri-pancreatic fluid collection**

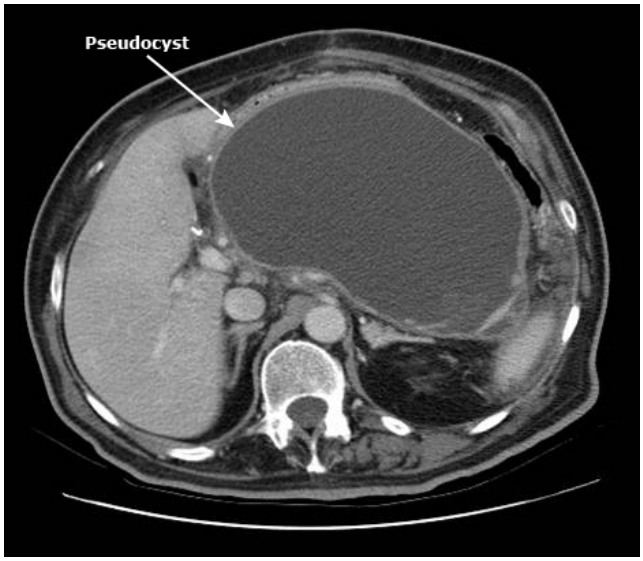
- Usually develops in the early phase
- No well-defined wall, homogenous, confined by normal fascial planes in retroperitoneum, may be multiple
- Most remain sterile and resolve spontaneously
- If it persists more than 4 weeks – likely to develop into pancreatic pseudocyst
- Does not require treatment if it resolves or is asymptomatic.



The computed tomography (CT) scan in a 75-year-old man with acute interstitial pancreatitis reveals heterogeneous appearance of the pancreas (arrow) and peripancreatic fat stranding (arrowhead).

2. **Pancreatic pseudocyst**

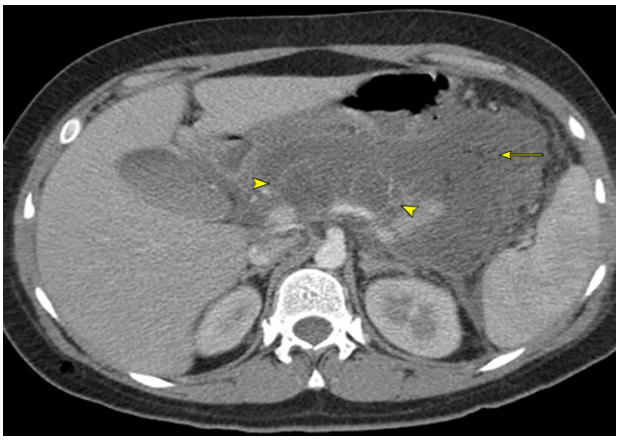
- Fluid collection in peri-pancreatic tissue
- Well-defined wall
- Contains no solid material
- High fluid amylase
- Disruption of main pancreatic duct or intra-pancreatic branch can lead to leakage of pancreatic fluid with a persistent localized fluid collection
- Usually can only be diagnosed 4 weeks after acute pancreatitis (takes time for wall to from)
- Rare in acute pancreatitis (more common in chronic).



Computed tomographic scan showing a massive pancreatic pseudocyst compressing the stomach and obliterating the pancreas.

3. **Acute necrotic collection**

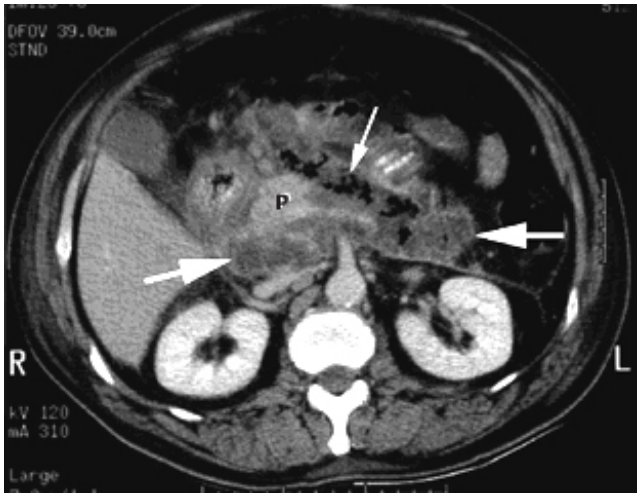
- During the first 4 weeks identifiable as collection containing variable amounts of fluid and necrotic tissue
- Can involve pancreatic parenchyma or peri-pancreatic tissue
- Varying amounts of solid necrotic material and fluid, may be multiple, may appear loculated
- Difficult to distinguish from acute fluid collection on imaging in first week.



The axial CT image shows pancreatic necrosis with a nonenhancing region in the neck and the body of the pancreas (between arrowheads). In the surrounding anterior pararenal space, there is a large fluid accumulation that contains islands of necrosis (arrow).

4. Infected pancreatic necrosis (Walled off necrosis)

- No correlation exists between the extent of necrosis and the risk of infection and duration of symptoms
- Infected necrosis is rare during the first week
- Important to diagnose – determines the need for antibiotics and active intervention
- The diagnosis is assumed when
    - There is extraluminal gas in pancreatic/peri-pancreatic tissue on CT
    - Percutaneous image-guided FNA is + for bacteria/fungi on MCS
- Associated with increased morbidity and mortality



Computed tomography (CT) scan reveals gas bubbles (arrow) within an area of pancreatic necrosis. Leaving only a small residual pancreatic head (P). The presence of gas bubbles is a pathognomonic sign of infection of the necrosis

5. Walled-off necrosis

- Necrotic tissue contained within enhancing wall of reactive tissue
- Mature encapsulated collection of pancreatic/peri-pancreatic necrosis and has a well-defined inflammatory wall
- Usually diagnosed 4 weeks/more after the onset of necrotizing pancreatitis
- May be infected, multiple and may be present at sites distant from the pancreas
- CT scan may not readily distinguish solid from liquid content and may misdiagnose walled off necrosis as a pseudocyst
- MRI, transabdominal ultrasound or endoscopic ultrasound may be required for this distinction.

Other local complications:

- Gastric outlet obstruction
- Splenic/portal vein thrombosis
- Colonic necrosis

Systemic complications:

Exacerbation of a pre-existing comorbidity such as COPD, coronary artery disease or CCF precipitated by acute pancreatitis (not new onset organ failure)

Organ dysfunction:

Modified Marshall Scoring System used to classify organ dysfunction (not the SOFA score as the SOFA score is validated for critically ill patients)

- The score can be repeated frequently to assess for worsening or improvement
- A score of 0 – 4 is given for each organ system
- A score of 2/more equals organ dysfunction
- The APACHE 2 score can also be used to assess the severity of acute pancreatitis – it is the most widely validated scoring system

Modified Marshall scoring system for organ dysfunction:

Organ system	**Score**				
	0	**1**	**2**	**3**	**4**
Respiratory (PaO2/FiO2)	>400	301-400	201-300	101-200	≤101
Renal*					
(Serum creatinine, micromole/L)	≤134	134-169	170-310	311-439	>439
Cardiovascular (systolic blood pressure, mmHg)•	>90	<90, fluid responsive	<90, not fluid responsive	<90, pH <7.3	<90, pH <7.2
For nonventilated patients, the FiO2 can be estimated from below:					
Supplemental oxygen (L/min)	**FiO2 (percent)**				
Room air	21				
2	25				
4	30				
6-8	40				

9-10	50

A score of 2 or more in any system defines the presence of organ failure.* A score for patients with pre-existing chronic renal failure depends on the extent of further deterioration of baseline renal function. No formal correction exists for a baseline serum creatinine ≥134 micromole/L. • Off inotropic support.

Role of imaging

CT scan

- Disadvantages in first 5 – 7 days after onset:
    - Cannot distinguish necrosis from severe interstitial edema
    - Progressive – edema/necrosis still evolving – cannot evaluate full extent
- Best use of an early-stage CT scan is to confirm the diagnosis when the clinical situation is unclear.
- Best use of a CT scan after the first 5 to 7 days is to evaluate the presence of local complications in patients with moderately severe or severe pancreatitis to guide ongoing care (sterile or infected necrosis).

MRI

- MRI can be helpful in distinguishing a pseudocyst from walled off necrosis
- MRCP
    - Useful to identify retained CBD stones
    - Can decrease the use of ERCP with attendant complications

Endoscopic ultrasound

- Sensitive in detecting cholelithiasis and choledocholithiasis
- Useful for imaging guided FNA or interventions like cystgastrostomy and endoscopic necrosectomy
- Contrast-enhanced endoscopic ultrasound can accurately differentiate a pseudocyst or walled-off necrosis from a cystic neoplasm of the pancreas.

Management of acute pancreatitis

Initial resuscitation and management

- Begins in the emergency department – confirm the diagnosis, risk stratification according to the Revised Atlanta Criteria, pain control and fluid resuscitation
- Reassess for response to fluids before leaving the emergency department (End points of resuscitation)

Early fluid resuscitation

- Aggressive volume resuscitation
    - Under-resuscitation – increased risk of pancreatic necrosis and mortality
    - Over-resuscitation – complications such as pulmonary edema
- Suggested regimen
    - Resuscitate using Ringer's Lactate
    - Fluid bolus of 20ml/kg
    - Then a continuous infusion of 3ml/kg/hour
    - Reassess every 6 – 8 hours.
    - Arterial blood gas: Base deficit is probably a better endpoint – aim for less than 4 – as it is readily available, quick to respond to adequate resuscitation/under-resuscitation and quick to measure.
    - Cardiac output monitoring likely to most sensitive to assess fluid response/status
    - Urine output as endpoint hampered by possible underlying renal dysfunction or organ dysfunction associated with acute pancreatitis (especially if patients present late)
- Ringer's lactate contains calcium – use with caution in patients with hypercalcemia

Blood tests: ABG (pH, Po2, pCO2, BE, Lactate, Bicarb, electrolytes) U&E (dehydration- check renal status, replace electrolytes. FBC (WCC high- immune response- no sepsis) LFT (check associated cholangitis- especially if worsening LFTs. Check ALT/AST for possible biliary pancreatitis, INR, CRP (very high in obese patients and its sign of poor prognosis if trend going up in general). GGT/ALP might be elevated due to edema in the HOP causing obstruction in the distal CBD.

Indications for ICU admission

- Respiratory failure
- Hypotension not responding to fluids
- MODS
- Persistent SIRS
- Increased urea/creatinine/ hematocrit
- Underlying cardiac/ pulmonary illness

Indications for transfer to specialist unit

- Failure to respond to initial resuscitation

Analgesia

- Effective analgesia is a priority.
- PCA pump containing opioids or intermittent opioid boluses (no evidence regarding which opioid is best – any opioid based analgesia can be used).
- Monitor saturation if repeated boluses of opioids given.

Nutrition

- Mild acute pancreatitis can have early enteral feeding, the patient will commence eating when they feel hungry. This typically occurs a few days after the onset of their symptoms.
- In severe acute pancreatitis enteral nutrition is initiated early (within 24 to 48 hours) in all patients to decrease the risk of major infection (decrease bacterial translocation in the gut). If they do not tolerate enteral feeding they must be converted to total parenteral nutrition.

Antibiotics

- Routine use of antibiotics is **not** recommended in patients with acute pancreatitis, regardless of the type (interstitial or necrotizing) or disease severity (mild, moderately severe, or severe)

Specific indication: In patients with confirmed sepsis: gas seen in pancreatic necrosis on CT scan, FNA positive culture, or clinical deterioration (spiking temperatures).

Treatment of local complications

Acute peripancreatic fluid collection

- Usually remain asymptomatic, and resolve spontaneously without the need for drainage

Pancreatic pseudocyst

- Treated only if symptomatic
- Endoscopic cyst-gastrostomy

Infected necrosis

- The occurrence of pancreatic infection is a leading cause of morbidity and mortality in acute necrotizing pancreatitis.
- The majority of infections (approximately 75 percent) are monomicrobial with gut-derived organisms (eg, *Escherichia coli, Pseudomonas, Klebsiella,* and *Enterococcus)*.
- If empiric antibiotics are initiated, antibiotics known to penetrate pancreatic necrosis (e.g. carbapenems or quinolones and metronidazole) should be used.
- Necrosectomy should be accomplished initially by a minimally invasive approach (endoscopic or percutaneous radiologic guided). **Step up approach**.
- In a randomized controlled trial, PANTER trial, compared with open necrosectomy, a minimally invasive step-up approach consisting of percutaneous drainage followed, if necessary, by open necrosectomy, reduced the rate of the composite end point of major complications or death among patients with necrotizing pancreatitis and infected necrosis
    - Percutaneous drainage catheters and treatment with antibiotics
    - Catheter irrigated and upsized as needed
    - If no improvement in 72 hours – minimally invasive retroperitoneal approach
    - Decreased complications and death by 29%.

- Open surgical necrosectomy should only be used if minimally invasive methods are not possible or fail

Sterile necrosis

- If the aspirated material on CT-guided FNA is sterile, one should discontinue antibiotics and continue conservative treatment for 4 – 6 weeks.
- The use of antibiotics in patients with sterile necrosis to prevent the development of infected necrosis is not recommended.
- Sterile necrosis does not require therapy.

- **Indications for intervention** (radiological, endoscopic, or surgical) in a patient with sterile necrosis with no signs of an infection include:
    - Ongoing gastric outlet, intestinal, or biliary obstruction due to mass effect 4 – 8 weeks after onset of acute pancreatitis.
    - Persistent symptoms (eg, abdominal pain, nausea, vomiting, anorexia or weight loss) >8 weeks after the onset of acute pancreatitis.
    - Disconnected duct syndrome (full transection of the pancreatic duct) with persisting symptomatic collections with necrosis (eg, pain, obstruction) >8 weeks after the onset of acute pancreatitis.

Indications for EUS/MRCP prior to ERCP

- Persistent elevation of liver function tests and/or dilation of common bile duct without overt cholangitis
- Pregnant patients
- Altered anatomy that would make an ERCP technically challenging

Cholecystectomy

- Cholecystectomy should be performed after recovery in all patients with gallstone pancreatitis including those who have undergone an endoscopic sphincterotomy (ERCP) to prevent a recurrent acute pancreatitis.
- In patients who have had mild pancreatitis, cholecystectomy can usually be performed safely within seven days after recovery and/ or in the same index hospitalization.
- In patients who have had severe necrotizing pancreatitis, cholecystectomy should be delayed until active inflammation subsides and fluid collections resolve or stabilize.

Conclusion

Know the Revised Atlanta Criteria to diagnose and stage the acute pancreatitis

All patients with moderate or severe acute pancreatitis must be referred to a tertiary center of an HPB surgeon

Routine antibiotics are not required early in the course of acute pancreatitis, including severe acute pancreatitis. Only prescribe antibiotics with infected pancreatic necrosis, which typically occurs after the second week of the disease.

Encourage enteral feeding early, if this fails then consider total parenteral nutrition

Recommended reading

Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus.

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