Management in Acute Pancreatitis

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Acute pancreatitis

Definition
Acute pancreatitis - definition

• Inflammatory disease caused by activation, interstitial liberation and autodigestion of the pancreas by its own enzymes

• A group of reversible lesions characterised by inflammation of the pancreas

Acute pancreatitis

Anatomy

Physiology
Normal Anatomy & Physiology

- neutralize chyme
- digestive enzymes
- hormones
Exocrine Function

- common bile duct
- ampulla
- pancreatic duct
- pancreatic enzymes

Diagram showing the exocrine function of the pancreas with labeled parts: Head, Body, Tail, and Uncinate.
Enzyme Secretion

microscopic view of pancreatic acini
Enzyme Secretion

Hormonal
- CCK
- gastrin

Neural
- acetylcholine
- VIP
- GRP

Secretin (hormonal)

H₂O
bicarbonate
Digestive Enzymes in the Pancreatic Acinar Cell

PROTEOLYTIC ENZYMES
Trypsinogen
Chymotrypsinogen
Proelastase
Procarboxypeptidase A
Procarboxypeptidase B

AMYOLYTIC ENZYMES
Amylase

LIPOLYTIC ENZYMES
Lipase
Prophospholipase A2
Carboxylesterase lipase

NUCLEASES
Deoxyribonuclease (DNAse)
Ribonuclease (RNAse)

OTHERS
Procolipase
Trypsin inhibitor
Normal Enzyme Activation

duodenal lumen

enterokinase

trypsinogen

chymotrypsinogen
proelastase
prophospholipase
procarboxypeptidase

trypsin

chymotrypsin
elastase
phospholipase
carboxypeptidase
Exocrine Stimulation

- The more proximal the nutrient infusion…the greater the pancreatic stimulation (*dog studies*)
  - stomach – maximal stimulation
  - duodenum – intermediate stimulation
  - jejunum – minimal / negligible stimulation
- Elemental formulas tend to cause less stimulation than standard intact formulas
  - intact protein > oligopeptides > free amino acids
- Intravenous nutrients (even lipids) do not appear to stimulate the pancreas
Protective Measures

- **COMPARTMENTALIZATION** - digestive enzymes are contained within *zymogen granules* in acinar cells

- **REMOTE ACTIVATION** - digestive enzymes are secreted as *inactive proenzymes* within the pancreas

- **PROTEASE INHIBITORS** – *trypsin inhibitor* is secreted along with the proenzymes to *suppress* any premature enzyme activation

- **AUTO “SHUT-OFF”** – trypsin *destroys* trypsin in high concentrations
Acute pancreatitis

Pathogenesis
Pathogenesis

Trypsinogen → Trypsin → Systemic circulation

- Procolipase
- Proelastase
- Chymotrypsinogen
- Prophospholipase A2
- Xanthynedehydrogenase
- Trypsinogen
- Prokallycrein
- C3
- C5
- Plasminogen
- XII Factor

- Mesotrypsin
- Enzyme Y

- Alfa2-M
- Alfa2 + Trypsin

- RES
- Liver
- Spleen
- Bone marrow
- Nodes

- Clearance

- Colipase
- Elastase
- Chymotrypsin
- Phospholipase A2
- Xanthynedehydrogenase

- Kallycrein
- C3a
- C5a
- Plasminogen
- XIIa Factor

- Kininogens
- Kinins

Acute Pancreatitis
Pathogenesis

- premature enzyme activation
- autodigestion of pancreatic tissue
  - local vascular insufficiency
  - activation of white blood cells
  - release of enzymes into the circulation

- local complications
- distant organ failure
Pathophysiology

Oxidated Phospholipids

Activated Macrophages

TNF

PAF

IL-8

IL-6

A. gastrocuodenalis
A. pancreatica transr.
A. pancreatica dorsi.
A. mesenterica sup.
A. pancreatica duodenalis inf. ant. und post.
A. pancreatica duodenalis sup. ant. und post.
A. heptica comm.
Truncus coeliacus

Systemic Circulation

IL-8 PAF TNF

Tissue injury

Link between pankreatic inflammation and sytemic tissue damage

(from R.Stocker – “Acute pancreatitis nutritional symposium” 2000)
Relationship Between the Systemic and Cellular Immune Responses

- **Systemic immune response**
  - **Substrates**
    - Smooth bronchial muscle
    - Endothelium
    - Platelets
  - **Mediators**
    - Eicosanoids (PGE, LTB)
    - Cytokines (IL, TNF)
    - Nitric oxide (NO)

- **Cellular defense function**
  - Degranulation
  - Phagocytosis
  - Cytotoxicity
  - Lymphopoiesis
    - Polymorphonuclear neutrophil leucocytes
    - Makrophages
    - Lymphocytes
    - Cellproliferation

- **Systemic inflammatory response**
  - Smooth vascular muscle
  - Microcirculation
  - Ventilation
  - Permeability
  - Aggregation

**Gut I/R Injury or Systemic invasion of bacteria / toxins**

**Bi-phasic MODS**

**Fig.: 1**
Two mortality peaks of severe acute pancreatitis

Mortality

MOF

infection

1st – 2nd week

3rd – 4rd week
Pathophysiology

Ischaemia

Activation of enzymes

Intracellular activation of enzymes

Acinar cell injury

ACTIVATED ENZYMES

Interstitial inflammation oedema

Proteolysis (proteases)

Fat necrosis (lipase, phospholipase)

Haemorrhage (elastase)
Pathophysiology

Interstitial oedema → Impaired blood flow → Ischaemia

Release of intracellular proenzymes and lysosomal hydrolases → Activation of enzymes

Delivery of proenzymes to lysosomal compartment → Intracellular activation of enzymes

Acinar cell injury → ACTIVATED ENZYMES

Interstitial inflammation oedema → Proteolysis (proteases) → Fat necrosis (lipase, phospholipase) → Haemorrhage (elastase)
Pathophysiology

- Duct obstruction:
  - Gallstone
  - Chronic alcoholism
  - Interstitial oedema
  - Impaired blood flow
  - Ischaemia

- Acinar cell injury:
  - Alcohol, drugs, trauma, ischaemia, viruses
  - Release of intracellular proenzymes and lysosomal hydrolases
  - Activation of enzymes

- Defective intracellular transport:
  - Metabolic injury (experimental)
  - Alcohol, duct obstruction
  - Delivery of proenzymes to lysosomal compartment
  - Intracellular activation of enzymes

Acinar cell injury leads to activated enzymes:

- Interstitial inflammation oedema
- Proteolysis (proteases)
- Fat necrosis (lipase, phospholipase)
- Haemorrhage (elastase)
Acute pancreatitis

Etiology
Etiology

• Non-traumatic (75%)
  • Biliary tract disease
  • Alcohol
    • Viral infection (EBV, CMV, mumps)
    • Drugs (steroid, thiazide, furosemide)
    • Scorpion bites
    • Hyperlipidemia
    • Hyperparathyroidism

• Traumatic (5%)
  • Operative trauma
  • Blunt/penetrating trauma
  • Lab test ERCP/angiography

• Idiopathic (20%)
Etiology

Gallstones (35%-60%)
- Gallstone pancreatitis risk is highest among patients with small GS < 5mm and with microlithiasis
- GS pancreatitis risk is also increased in women > 60 yrs
Etiology

Alcohol (30-40%)

- Mechanism not fully understood

- Not all alcoholics get pancreatitis (only about 15%)

- This suggests a subset of the population predisposed to pancreatitis, with alcohol acting more as a co-precipitant
Etiology – Trauma

Blunt Trauma

– Automobile
– Bicycle handlebar injuries
– Abuse

Iatrogenic – ERCP (1-7%)

– Likely secondary to contrast but also very operator dependant
– Risk is also increased with Sphincter of Oddi manometry
Etiology - 1

Transabdominal ultrasound should be performed in all patients with acute pancreatitis **(strong recommendation, low quality of evidence)**

In the absence of gallstones and/or history of alcohol use serum triglyceride should be obtained and considered the etiology if > 1000 mg/dL **(conditional recommendation, moderate quality of evidence)**

In a patient older than 40 years, a pancreatic tumor should be considered as a possible cause of AP **(conditional recommendation, low quality of evidence)**
Etiology - 2

Endoscopic investigation in patients with acute idiopathic pancreatitis should be limited, as the risks and benefits of investigation in these patients are unclear (conditional recommendation, low quality of evidence)

Patients with idiopathic pancreatitis should be referred to centers of expertise (conditional recommendation, low quality of evidence)

Genetic testing may be considered in young patients (< 30 years old) if no cause is evident and a family history of pancreatic disease is present (conditional recommendation, low quality of evidence)
Acute Pancreatitis
Etiology

- EtOH: 35%
- Idiopathic: 10%
- Other: 10%
- Gallstones: 45%

Fagenholz H et al. AEP 2007;17: 491-49

Clinical Emergency Hospital of Bucharest, 2009
Incidence

Male:female ratio is
• 1:3— in those with gallstone and
• 6:1 in those with alcoholism
Famous people who have had pancreatitis

Alexander the Great

Ludwig von Beethoven

Dizzie Gillespie

Maximilian Schell

John Ashcroft
Acute pancreatitis

- Terminology
- Classification
- Epidemiology
Terminology of Acute Pancreatitis

Terms no longer used:
Hemorrhagic pancreatitis
Phlegmon

Acute Pancreatitis

INTERSTITIAL (edematous)

NECROTIZING

INFLAMMATORY MASS

STERILE NECROZIS

INFECTED NECROZIS

PSEUDOCYST

HEALING

PANCREATIC ABCCESS
Definitions of severity in acute pancreatitis: comparison of Atlanta and recent revision

<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild acute pancreatitis</td>
<td>Mild acute pancreatitis</td>
</tr>
<tr>
<td>Absence of organ failure</td>
<td>Absence of organ failure</td>
</tr>
<tr>
<td>Absence of local complications</td>
<td>Absence of local complications</td>
</tr>
<tr>
<td>Severe acute pancreatitis</td>
<td>Moderately severe acute pancreatitis</td>
</tr>
<tr>
<td>1. Local complications AND/OR</td>
<td>1. Local complications AND/OR</td>
</tr>
<tr>
<td>2. Organ failure</td>
<td>2. Transient organ failure (&lt;48h)</td>
</tr>
<tr>
<td>GI bleeding (&gt;500cc/24hr)</td>
<td>Persistent organ failure &gt;48h</td>
</tr>
<tr>
<td>Shock – SBP ≤90mm Hg</td>
<td></td>
</tr>
<tr>
<td>PaO₂ ≤60%</td>
<td></td>
</tr>
<tr>
<td>Creatinine ≥2mg/dl</td>
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</table>

Am J Gastroenterol 2013; 108:1400–1415; doi:10.1038/ajg.2013.218; published online 30 July 2013
Determinant-based Classification

Based on the factors that are causally associated with severity of acute pancreatitis

<table>
<thead>
<tr>
<th></th>
<th>Mild AP</th>
<th>Moderate AP</th>
<th>Severe AP</th>
<th>Critical AP</th>
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</thead>
<tbody>
<tr>
<td>(Peri)pancreatic necrosis</td>
<td>NO</td>
<td>Sterile</td>
<td>Infected</td>
<td>Infected</td>
</tr>
<tr>
<td></td>
<td>AND</td>
<td>AND/OR</td>
<td>OR</td>
<td>AND</td>
</tr>
<tr>
<td>Organ failure</td>
<td>NO</td>
<td>Transient</td>
<td>Persistent</td>
<td>Persistent</td>
</tr>
</tbody>
</table>

Determinant-Based Classification of Acute Pancreatitis Severity

An International Multidisciplinary Consultation
Determinant-based Classification

Based on the factors that are causally associated with severity of acute pancreatitis

**Local determinants**

**(Peri)pancreatic necrosis**
- Pancreatic, peripancreatic, both
- Solid, semisolid, without a radiologically wall

**Sterile (peri)pancreatic necrosis**
- Absence of proven infection in necrosis

**Infected (peri)pancreatic necrosis**
- Gas bubbles within (CT)
- Positive culture obtained
  - by image guided fine needle aspiration
  - During the first drainage or necrosectomy

**Systemic determinants**

**Organ failure**
- **Cardiovascular:** need for inotropic agent
- **Renal:** creatinine ≥ 171 μmol/L (≥2.0 mg/dL)
- **Respiratory:** PaO$_2$/FiO$_2$ ≤ 300 mmHg (≤40 kPa)

**Persistent organ failure**
For 48 hours or more

**Transient organ failure**
For less than 48 hours
Acute Pancreatitis – Epidemiology

Increases in total hospitalisation for acute pancreatitis and in the population rate of hospitalisation for acute pancreatitis during the study period (p for trend = 0.001 for both)

Acute pancreatitis

Diagnosis
Clinical Presentation

Pain (95%)
- Acute onset
  - Mid-abdominal or mid-epigastric
  - Radiates to the back (50%)
- Peak intensity in 30 minutes
  - Lasts for several hours

Nausea and vomiting (80%)

Abdominal distention (75%)

Abdominal guarding and tenderness (50%)

Restlessness and agitation

Differential Diagnosis
- Choleledocholithoasis
- Perforated ulcer
- Mesenteric ischemia
- Intestinal obstruction
- Ectopic pregnancy
Clinical signs

More severe cases

– Jaundice
– Ascites
– Pleural effusions – generally left-sided
– *Cullen’s sign* – bluish peri-umbilical discoloration
– *Grey Turner’s sign* – bluish discoloration of the flanks
Labs

Amylase

- Elevates within HOURS and can remain elevated for 4-5 days
- High specificity when using levels >3x normal
- Most specific = pancreatic isoamylase (fractionated amylase)
- Many false positives
Differential diagnosis – Amylase Elevation

Pancreatic Source

– Biliary obstruction
– Bowel obstruction
– Perforated ulcer
– Appendicitis
– Mesenteric ischemia
– Peritonitis

Salivary

– Parotitis
– DKA
– Anorexia
– Fallopian tube
– Malignancies

Unknown Source

– Renal failure
– Head trauma
– Burns
– Postoperative
Labs

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%
Lab Investigations

- Full blood count: neutrophil, *leucocytosis*
- Electrolyte abnormalities include *hypokaemia, hipocalcemia*
- Elevated LDH in biliary disease
- *Glycosuria* (10% of cases)
- Blood sugar: *hyperglycaemia* in severe cases
- Ultrasound look for stones diseases
Diagnosis

The diagnosis of AP is most often established by the presence of two of the three following criteria: (I) abdominal pain; (II) serum amylase and/or lipase greater than three times the upper limit of normal, and/or (III) characteristic findings from abdominal imaging (strong recommendation, moderate quality of evidence).

Contrast-enhanced CT and/or MRI of the pancreas should be reserved for patients in whom the diagnosis is unclear or who fail to improve clinically within the first 48-72 h after hospital admission (strong recommendation, low quality of evidence).
Diagnosis – Imaging

CT

– Excellent pancreas imaging

– Recommended in all patients with persisting organ failure, sepsis or deterioration in clinical status (6-10 days after admission)

– Search for necrosis – will be present at least 4 days after onset of symptoms; if ordered too early it will underestimate severity

– Follow-up months after presentation as clinically warranted for CT severity index of >3
CT Findings
Severe Pancreatitis

Tail Indistinct

Intraperitoneal fluid

Unenhancing Necrosis

Peripancreatic edema and inflammation
Balthazar's score

Severe = Score > 6 (CT Grade + Necrosis)

CT Grade

- Normal  A  0 points
- Focal or diffuse enlargement  B  1 point
- Intrinsic change or fat stranding  C  2 points
- Single ill-defined fluid collection  D  3 points
- Multiple collections of fluid or gas  E  4 points

Necrosis Score

- None  0 points
- 1/3 of pancreas  2 points
- 1/2 of pancreas  4 points
- > 1/2 of pancreas  6 points

## CT Severity Index

### Appearance

<table>
<thead>
<tr>
<th>Appearance</th>
<th>Normal</th>
<th>Enlarged</th>
<th>Inflamed</th>
<th>1 Fluid Collection</th>
<th>2 or More Collections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade</td>
<td>A</td>
<td>B</td>
<td>C</td>
<td>D</td>
<td>E</td>
</tr>
<tr>
<td>Score</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

### Necrosis

<table>
<thead>
<tr>
<th>Necrosis</th>
<th>None</th>
<th>&lt; 33%</th>
<th>33-50%</th>
<th>&gt; 50%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score</td>
<td>0</td>
<td>2</td>
<td>4</td>
<td>6</td>
</tr>
</tbody>
</table>

### Score vs. Morbidity and Mortality

<table>
<thead>
<tr>
<th>Score</th>
<th>Morbidity</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2</td>
<td>4%</td>
<td>0%</td>
</tr>
<tr>
<td>7-10</td>
<td>92%</td>
<td>17%</td>
</tr>
</tbody>
</table>

*Note: Balthazar et al. Radiology 1990,*
Acute pancreatitis

Predictors of Severity
Predictors of Severity

Why are they needed?

– appropriate patient triage & therapy
– compare results of studies of the impact of therapy

When are they needed?

– optimally, within first 24 hours (damage control must begin early)

Which is best?
Determining severity

• Clinical criteria
  • Early development/persistence of organ dysfunction
    – Ranson criteria
    – Atlanta criteria
    – POP score
    – BISAP

• Clinical assessment
  • Frequent VS, fluid status/UOP, pulse oximetry

• Radiographic criteria
  – CT severity index
    • Necrosis may not be evident until 48-72h
Ranson Criteria

At admission
1. Age > 55 years
2. WBC > 16,000/mm³
3. Glucose > 200 mg/dl
4. LDH > 350 UI/l
5. AST > 250 U/l

Within 48 Hours
1. Hct decrease of > 10 mg/dl
2. BUN increase of > 5 mg/dl
3. Base deficit > 4 mEq/l
4. Fluid sequestration > 6 L
5. Ca++ < 8 mg/dl
6. PaO2 < 60 mmHg

Number of Criteria
- < 2: 1%
- 3-4: 16%
- 5-6: 40%
- 7-8: 100%

Mortality
- 1%
- 16%
- 40%
- 100%

Directly related to fluid resuscitation
Independent predictors of mortality

Ranson JH et al. Surgery Gynecology and Obstetrics-1974; 139(1):69-84
Clinical findings associated with a severe course for initial risk assessment –
Intrinsic patient-related risk factors for developing of severe disease

### Patient characteristics
- Age >55 years (53,57)
- Obesity (BMI >30 kg/m²) (68)
- Altered mental status (69)
- Comorbid disease (53)

### The systemic inflammatory response syndrome (SIRS) (6,53,54,70,71)
Presence of >2 of the following criteria:
- pulse >90 beats/min
- respirations >20/min or PaCO₂ >32 mm Hg
- temperature >38°C or <36°C
- WBC count >12,000 or <4,000 cells/mm³ or >10% immature neutrophils (bands)

### Laboratory findings
- BUN >20 mg/dl (63)
- Rising BUN (63)
- HCT >44% (62)
- Rising HCT (62)
- Elevated creatinine (72)

### Radiology findings
- Pleural effusions (73)
- Pulmonary infiltrates (53)
- Multiple or extensive extrapancreatic collections (67)
Acute pancreatitis

Treatment
Initial assessment and risk stratification

Risk assessment should be performed to stratify patients in to higher and lower risk categories to assist triage, such as admission to ICU (conditional recommendation, moderate quality of evidence)

Patients with organ failure should be admitted to ICU or intermediary care setting whenever possible (strong recommendation, low quality of evidence)
When Do I Transfer to the Intensive Care?

- Severe pancreatitis

- Multi-organ failure
  - Pulmonary
  - Renal

- Consider it if you are placing the patient on antibiotics and/or ordering a CT to evaluate non-improvement
When Do I Transfer to the Intensive Care?

• Cardiovascular
  – Hypotension
  – ↑HR, ↑CO and ↓SVR

• Respiratory
  – Hypoxemia
  – Pleural effusion

• Renal
  – ATN
  – Oliguria

• Haematologic
  – DIC
  – Thrombocytosis

• Hepatic
  – Encephalopathy
  – ↑T bili (3mg/dl)
  – ↑AST/ALT 2x nl

• GI
  – Stress ulcer
  – Acalculous cholecystitis
Therapeutical goals

• Ventilatory support
• Fluid resuscitation
• Haemodynamic support (vasopresors, inotropes)
• Antibiotherapy
• Sedation
• Analgesia
• Early enteral nutrition
• Glycemic and triglycerides control
• Prokinetics
• Stress ulcer prophylaxis
• Thromboprophylaxis
**Fluids initial management**

Aggressive hydration, defined as 250-500 ml/h of isotonic crystalloid solution should be provided to all patients, unless cardiovascular and/or renal comorbidities exist. Early aggressive iv hydration is most beneficial the first 12-24 h, and may have little benefit beyond **(strong recommendation, moderate quality of evidence)**

In patients with severe volume depletion (hypotension and tachycardia), more rapid repletion (bolus) may be needed **(conditional recommendation, moderate quality of evidence)**

Lactated Ringer’s solution may be preferred **(conditional recommendation, moderate quality of evidence)**

Fluid requirements should be reassessed every 6h for the next 24-48 h. The goal of aggressive hydration should be to decrease the blood urea nitrogen **(strong recommendation, moderate quality of evidence)**
Fluid Resuscitation

- Fluid resuscitation volume should be carefully monitored to avoid over-resuscitation in patients at risk for IAH/ACS (Grade 1B)
- Hypertonic crystalloid and colloid-based resuscitation should be considered in patients with IAH to decrease the progression to secondary ACS (Grade 1C)

- Fluid resuscitation and “early goal-directed therapy” are cornerstones of critical care management
- Excessive fluid resuscitation is an independent predictor of IAH/ACS and should be avoided
- The use of goal-directed hemodynamic monitoring should be considered to achieve appropriate fluid resuscitation

How IAP Should Be Measured?

• If two or more risk factors for IAH / ACS are present, a baseline IAP measurement should be obtained (Grade 1B)

• If IAH is present, serial IAP measurements should be performed throughout the patient’s critical illness (Grade 1C)

• Physical examination is insensitive in detecting IAH

• IAP monitoring is a cost-effective, safe, and accurate tool for identifying the presence of IAH and guiding resuscitative therapy for ACS

• Serial IAP measurements are necessary to guide resuscitation of patients with IAH / ACS

Intra-Abdominal Pressure Monitoring Kit

- Kit contains everything you need
- Standardized measurement
- No reproducibility errors
- Ease & simplicity of use
- Time savings: 30 seconds to get data.
- Closed system
- No needles
- No contamination risks
When Do I Start Antibiotics?

- Acute pancreatitis - infection ~10%
  - 30-40% of those with necrosis get infection
- Prophylactic antibiotics
  - Controversial
  - No benefit in mild EtOH pancreatitis
  - Imipenem or meropenem in necrotizing pancreatitis
  - Selective gut decontamination may be beneficial?
  - Abx do not appear to promote fungal infection
- General recommendation for use:
  - Biliary pancreatitis with signs of cholangitis
  - >30% necrosis on CT scan
The role of antibiotics in acute pancreatitis - 1

Routine use of prophylactic antibiotics in patients with severe AP is not recommended (strong recommendation, moderate quality of evidence)

The use of antibiotics in patients with sterile necrosis to prevent the development of infected necrosis is not recommended (strong recommendation, moderate quality of evidence)

Infected necrosis should be considered in patients with pancreatic or extrapancreatic necrosis who deteriorate or fail to improve after 7-10 days of hospitalization. In these patients, either (I) initial CT-guided fine needle aspiration (FNA) for Gram stain and culture to guide use of appropriate antibiotics or (II) empiric use of antibiotics without CT FNA should be given (strong recommendation, low quality of evidence)
The role of antibiotics in acute pancreatitis - 2

In patients with infected necrosis, antibiotics known to penetrate pancreatic necrosis, such as carbapenems, quinolones, and metronidazole, may be useful (conditional recommendation, low quality of evidence)

Antibiotics should be given for an extrapancreatic infection, such as cholangitis, catheter-acquired infections, bacteremia, urinary tract infections, pneumonia (strong recommendation, high quality of evidence)

Routine administration of antifungal agents is not recommended (conditional recommendation, low quality of evidence)
Guidelines for managing pain

Follow guidelines for the administration of hourly opiates

On the wards

Mild
Pain score = 0-1
Hourly morphine as per guidelines
Paracetamol / N.S.A.I.D (if renal function satisfactory)
Once drinking – regular oral analgesia

Moderate
Pain score = 2-3
3 – 4 Morphine injections
Contact Pain Services Team/
On call anaesthetist to set up P.C.A

Pain continues to be severe
Pain scores = Greater than 3.
Not controlled with P.C.A.

Condition stable
MEWS score less than 5.
Contact Pain Services Team for assessment re Epidural

Condition deteriorating
MEWS score 5 or more.
Contact Outreach Team for assessment and Pain Services Team re Epidural
Epidural analgesia

- Thoracic trauma
  
  *(Bulger EM et al. Surgery 2004; 136:426-430)*

- Cardiac surgery
  

- Acute pancreatitis

- The effectiveness and safety of epidural analgesia has also been demonstrated in critically ill patients with severe acute pancreatitis

Epidural analgesia

• ↓ time to extubation
• ↓ ICU stay
• ↓ incidence of renal failure
• ↓ morphine consumption during the first 24 hours
• ↓ maximal glucose and cortisol blood concentrations
• improves forced vital capacity
  (Guay J. J Anesth 2006, 20:335-340)

• Gold standard - thoracic epidural analgesia (TEA) with a local anaesthetic/opioid infusion
Thoracic epidural analgesia

• ↓sympathetic activity and the stress response  
  (A segmental temporary sympathetic block)

• Improved mucosal capillary perfusion
  

• Accelerated recovery of intestinal function
  

• The faster resolution of postoperative ileus after major open surgery has been attributed to superior pain therapy, reduced opioid consumption, and sympathetic block
Epidural analgesia – adverse effects

Hypotension
• 3.0% to 10.2%
• Corelate with hypovolemia


Treatment failure
• 22% premature termination of postoperative epidural infusions
  – dislodgement (10%)
  – inadequate analgesia (3.5%)
  – sensory or motor deficit (2.2%)

(Ballantyne JC, McKenna JM & Ryder E. Acute Pain 2003;4: 89–97)

Neurological injury

Epidural abscess
Nutrition

Mild - moderate pancreatitis

– Calories from IVF (D5W) are sufficient
– No benefit from additional nutritional support
– Oral intake advancing to low fat diet once pain/anorexia resolve
– NGT decompression
  • If frequent emesis or evidence of ileus on plain films
  • Tube feed if anticipate NPO > 1 week

DO NOT follow amylase and lipase levels
Nutrition

Severe AP

*Enteral nutrition is preferred*

- Begin nutritional support as early as possible
  - NJ tube preferred
- however nasogastric feeds have been shown to be effective in 80% of cases
- NGTs should be used with caution in patients with ACS

*TPN only if*

- Can’t maintain adequate jejunal access
- Unable to meet caloric demands enterally for > 5 days
TPN + Glutamine in severe acute pancreatitis

double-blind study

Gln reduces the severity of acute-phase response

Gln supports lymphocyte proliferation

![Graph showing interleukin-8 levels on Day 4 and Day 7, with a significant difference indicated by an asterisk.](image)
Glutamine-TPN in acute pancreatitis

- reduced acute-phase response and better lymphocyte proliferation

  De Beaux, Nutrition 1998

- reduced length of TPN (10 vs 16 days, p< 0.05)
- reduced length of hospital stay (21 vs 25 days)

  Ockenga et al, Clin Nutr 2002
Glutamine-TPN in acute pancreatitis: other RCTs

- less infections and reinterventions
  
  Fuentes-Orozco et al, JPEN 2008

- less patients with complications
  

- lower incidence of complications, prevention of pancreatic infections
  
  He et al, Clin Nutr Suppl 2004
Nutrition in acute pancreatitis

In mild AP oral feeding can be started immediately if there is no nausea and vomiting and no abdominal pain (conditional recommendation, moderate quality of evidence). In mild AP initiation of feeding with a low-fat solid diet appears as safe as clear liquid diet (conditional recommendation, moderate quality of evidence).

In severe AP enteral nutrition is recommended to prevent infectious complications. Parenteral nutrition should be avoided unless the enteral route is not available, not tolerated or not meeting caloric requirement (strong recommendation, high quality of evidence).

Nasogastric and nasojejunal delivery of enteral feeding appear comparable (strong recommendation, moderate quality of evidence).
ERCP in acute pancreatitis

Patients with acute pancreatitis and concurrent acute cholangitis should undergo ERCP within 24 h of admission (strong recommendation, moderate quality of evidence).

ERCP is not needed in most patients with gallstone pancreatitis who lack laboratory or clinical evidence of ongoing biliary obstruction (strong recommendation, low quality of evidence).

In the absence of cholangitis and/or jaundice, MRCP or endoscopic ultrasound (EUS) rather than diagnostic ERCP should be used to screen for choledocholithiasis if highly suspected (conditional recommendation, low quality of evidence).

Pancreatic duct stents and/or postprocedure rectal nonsteroidal anti-inflammatory drug (NSAID) suppositories should be utilized to prevent severe post-ERCP pancreatitis in high-risk patients (conditional recommendation, moderate quality of evidence).
The role of surgery in acute pancreatitis - 1

In patients with mild AP, found to have gallstones in the gallbladder, a cholecystectomy should be performed before discharge to prevent a recurrence of AP (strong recommendation, moderate quality of evidence).

In a patient with necrotizing biliary AP, in order to prevent infection, cholecystectomy is to be deferred until active inflammation subsides and fluid collections resolve or stabilize (strong recommendation, moderate quality of evidence).

The presence of asymptomatic pseudocysts and pancreatic and / or extrapancreatic necrosis do not warrant intervention, regardless of size, location, and / or extension (strong recommendation, moderate quality of evidence).
The role of surgery in acute pancreatitis - 2

In stable patients with infected necrosis, surgical, radiologic, and/or endoscopic drainage should be delayed preferably for more than 4 weeks to allow liquefaction of the contents and the development of a fibrous wall around the necrosis (walled-off necrosis) (strong recommendation, low quality of evidence).

In symptomatic patients with infected necrosis, minimally invasive methods of necrosectomy are preferred to open necrosectomy (strong recommendation, low quality of evidence).
Conclusions

• Severe acute pancreatitis should be managed in ICU by a **multidisciplinary team** (surgeon, intensive care, gastroenterology, radiologist, nutritionist etc.)
• Infected necrosis carries a high mortality
• Antibiotics for suspected infected necrosis
• Tube feedings preferred, post ligament of Treiz
• Always look for the myriad of complications
• Guidelines are useful but not enough