Case 1

70 year old male came to the ER.

CC: 5 hours of right –sided abdominal pain that had awakened him from sleep ; also pain in the right shoulder and scapula.

Previous episodes mild right sided abdominal pain lasting 1-2 hours.
Case 1

Febrile with T 100.7 F, pulse 100, BP 150/90
Abdomen: RUQ and epigastric tenderness to light palpation, with inspiratory arrest and increased pain on deep palpation. (Murphy’s sign)

Labs: WBC 12,500; (normal bilirubin, Alk phos, AST, ALT).

Ultrasound shows normal liver, normal pancreas without duct dilatation and a distended thickened gallbladder with a stone in cystic duct.

DIAGNOSIS???
Acute Cholecystitis

Epigastric, RUQ pain
Radiate to shoulder
Fever, chills
Nausea, vomiting
Mild Jaundice
RUQ guarding, tenderness
Tender Mass (50%)

Acute Cholecystitis

Stone obstructs cystic duct
G.B. distended
Mucosa disrupted
Chemical Irritation: Conc. Bile
Bacterial Infection
  50 - 70% + culture: Lumen
  90 - 95% + culture: Wall
Bowel Organisms
  E. Coli, S. Fecalis
Culture **Normal** Biliary Tree:
   No Bacteria
Bacteria Normally **Cleared**

In G.B. with cholelithiasis
Bacteria cling to stones
If stone obstructs cystic duct orifice
   G.B. distended
   Mucosa Disrupted
Bacteria invade G.B. Wall
Gallstones (Cholelithiasis)

- 10 - 20% Adults
- 35% Autopsy: Over 65

- Over 20 Million
- 600,000 Cholecystectomies
- #2 reason for abdominal operations

Cholesterol/mixed stones
Gallstones
(Cholelithiasis)

- Two major types- classified by composition
  - Cholesterol (mixed) and pigment stones
  - Mixed stones - cholesterol with (bilirubin, calcium salts, protein, bile acids, fatty acids)
- Western nations: 90% stones are cholesterol/mixed stones; 10% pigment stones
- Mixed stones – associated with high cholesterol
- Pigment stones – associated with hemolysis, biliary tract infections
**Cholelithiasis**

- **50 - 70% Asymptomatic**
- **Pain:**
  - Biliary colic
  - Epigastric, RUQ
  - Abrupt, may last hours
  - Sudden obstruction:
    - Cystic Duct, CBD
  - Pain relieved
  - Stone back into G.B. or passes thru CBD
- **Fatty Food Intolerance:**
  - Indigestion, N. and V.
**Choledocholithiasis**  
*(Stones in the common bile duct)*

5 - 25% of pts. with G.B. stones  
**Pain:** Epigastric, RUQ  
Stones may be passed  
**Obstructive Jaundice**  
May be intermittent  
**Ascending Cholangitis**  
Infection: to liver  
20%: No pain; 25% no jaundice

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**Chronic Cholecystitis**

- Associated with calculi in 95% of cases.  
- Multiples episodes of inflammation cause GB thickening with chronic inflammation/ fibrosis and muscular hypertrophy.  
- Rokitansky - Aschoff Sinuses (mucosa herniates through the muscularis mucosae)  
- With longstanding inflammation GB becomes fibrotic and calcified “porcelain GB”
Chronic cholecystitis
Chronic Cholecystitis

- Fibrosis
- Chronic Inflammation
- Rokitansky - Aschoff Sinuses
- Hypertrophy: Muscularis
Cholesterolosis

Focal accumulation of cholesterol-laden macrophages in lamina propria of gallbladder (incidental finding).

Adenomyoma of Gall Bladder
Carcinoma: Gall Bladder

Uncommon: 5,000 cases / year
Fewer than 1% resected G.B.
Sx: same as with stones
5 yr. survival: Less than 5%
(survival relates to stage)

90%: Stones
Long Hx: symptomatic stones
Stones: predispose to CA., but uncommon complication
Gallbladder carcinoma

Case 2

56 year old woman presents to ER in shock, following rapid onset of severe upper abdominal pain, developing over the previous day.

Hx: heavy alcohol use.

LABs: Elevated serum amylase and elevated peritoneal fluid lipase
Case 2- clinical course

Patient developed rapid onset of respiratory failure necessitating intubation and mechanical ventilation.

Over 48 hours, she was increasingly unstable, with evolution to multi-organ failure, and she expired 82 hours after admission.

An autopsy was performed.

Acute pancreatitis
Elastase destruction of blood vessels – with hemorrhage
Acute Pancreatitis

- Edema, congestion
- Advanced hemorrhagic pancreatitis, fat necrosis
- Necrotic abscess, gangrene

Pathophysiology of acute pancreatitis

<table>
<thead>
<tr>
<th>Severity</th>
<th>Stage 1. Pancreatic injury</th>
<th>Stage 2. Local (peripancreatic) effects</th>
<th>Stage 3. Systemic complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Edema, inflammation, fat necrosis, variable necrosis of pancreatic secretory cells</td>
<td>Retroperitoneal edema, extensive fat necrosis, ileus with “third-spacing” of fluid and electrolytes</td>
<td>Hypotension/shock, metabolic disturbances, organ failure, sepsis</td>
</tr>
<tr>
<td>Severe</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Acute Pancreatitis

US: 45% of cases have gallstones and choledocholithiasis; 35% associated with heavy alcohol ingestion

Pathology: Enzyme release is triggered with digestion of pancreas, necrosis of fat and lobules, hemorrhage from damaged blood vessels.

Variable severity: may lead to liquefactive necrosis, hemorrhage. Mild cases – may have local complications: abscess, pseudocyst.

ETIOLOGIES
- Obstructive
- Toxins/drugs
- Metabolic
- Infection
- Vascular
- Trauma
- Idiopathic
Protection against autodigestion

- Duct lumen
- Pressure gradient favoring unidirectional flow out of gland into duodenum
- Presence of trypsin inhibitors in pancreatic tissue and secretions
- Secretion of most enzymes as inactive precursors (zymogens)
- Packaging of enzymes in membrane-bound zymogen (secretory) granules

Possible role of secretory block in genesis of pancreatitis

- Intracellular activation of trypsinogen due to:
  - Lysosomal enzymes?
  - Autoactivation related to change in zymogen granule pH or redox state?
- Block in enzyme secretion due to:
  - Gallstone impacted at duodenal papilla
  - Excessive alcohol use
  - Metabolic disturbance (e.g., ↑ Ca²⁺, ↑ triglyceride)
  - Drugs (Azathioprine, dDi)
Chronic Pancreatitis

Continuing inflammation with irreversible changes in architecture, structure and function.

Fibrosis of parenchyma with distortion of duct architecture, loss of exocrine secretory function.

Changes may be focal or widespread.
Chronic pancreatitis with Stones
Chronic pancreatitis
Complications of Chronic Pancreatitis

Chronic abdominal pain, severe and unremitting, radiating to back

Malabsorption due to reduced enzyme secretion. (After 90% of pancreas is fibrotic, reduced lipase and trypsin secretion lead to steatorrhea).

Pancreatic diabetes associated with decreased islets.

Pancreatic pseudocysts with extension or rupture in adjacent organs.

Risk factor for development of carcinoma of pancreas.

Case 3

67 year old woman with recent onset painless jaundice.

History of 15lb weight loss over last 3 months.

She smoked 1 pack per day x 35 years.

Physical exam: palpable GB

ERCP was performed with Endoscopic Ultrasound (EUS) evidence of a large mass in the head of the pancreas.

An endoscopic FNA was performed.
Normal pancreas
ductal epithelium

Patient’s FNA
Dx: Adenocarcinoma

Carcinoma of Pancreas

Weight loss: 70%
Pain: Abdominal 50%
Back 25%
Persistent jaundice
Anorexia
Loose stools
Nausea, vomiting
Courvoisier’s Sign: Dilated palpable GB often reflects tumor obstructing the common bile duct
Carcinoma of Pancreas

- Enlarged, palpable G.B.: 50%
- Mass in upper abdomen
- Enlarged, nodular liver
- Ascites
- Jaundice
- Migratory thrombophlebitis
  (Trousseau’s sign)

Adenocarcinoma: Pancreas

- 60 - 70% Head
- 20 - 30% Body
- 5 - 10% Tail
Pancreatic adenocarcinoma – Lymph node metastases

Pancreatic adenocarcinoma – perineural invasion
**Prognosis:**
**Adenocarcinoma: Pancreas**

100 Patients
- 90 - 95 unresectable tumor
- 5 - 10 resection
- 1 - 2% 5 year survival
Most pts. die: 6 - 12 months

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**Pancreas Cancer Genetics**

5-10% of cases are familial, some with defined genetic syndromes

Hereditary Pancreatitis: germline mutations in trypsinogen gene on 7q35 with 40% lifetime risk of developing pancreatic cancer.

Pancreatic cancers described in BRCA2 mutations in familial breast cancer kindreds.

Associated with germline p16 mutations, and HNPCC.

Role of oncogenes: KRAS-90%, p16-95%, p53-75%
In-situ progression to Cancer

Pancreatic Cystic Lesions

- Pseudocyst (benign – NOT a NEOPLASM)
- Serous cystadenoma (benign)
- Mucinuous cystic neoplasm (benign, borderline or malignant)
- Intraductal papillary mucinuous neoplasm (benign, borderline or malignant)
Pancreatic Pseudocyst

NOT NEOPLASTIC - RESULT OF ACUTE PANCREATITIS

Pancreatic serous cystadenoma

BENIGN
Mucinous cystic neoplasm

Not associated with the pancreatic duct
Clinical spectrum: benign to malignant

Intraductal mucinous neoplasm

Associated with the pancreatic duct
Clinical spectrum: benign to malignant
Pancreatic Endocrine Neoplasms

- 5% of pancreatic neoplasms
- “Islet cell Tumors” – inaccurate; arise from pluripotential ductal cells that differentiate along neuroendocrine lines.
- All have malignant potential except microadenomas (<5mm); No definite criteria to distinguish between benign and malignant (except for mets)
Pancreatic Endocrine Tumors
Pancreatic Endocrine Neoplasms

Functional - recognizable syndrome; detect hormone in serum.
  • Insulinoma (most common); hypoglycemia; 10% malignant
    • 10% assoc with MEN1
  • Gastrinoma; duodenal ulcers; 75% malignant
    • 25% assoc with MEN1

Nonfunctional - no syndrome; normal serum hormone levels (except Pancreatic Polypeptide).
  • Incidental; Obstructive Sx- head of pancreas; 50 – 90% malignant.

Pancreatic Endocrine Neoplasms

  • Usually occur in body/tail
  • Hypervascular, circumscribed
  • Highlighted with Octreotide Scan (somatostatin receptors)
  • Usually slow growing, mets to LNs, liver, bone
    (recommend resection of mets)
Pancreatic Endocrine Neoplasms

Classification:

Neuroendocrine neoplasm, well differentiated
- Low grade: 0-1 mit/50HPF; no necrosis
- Intermediate grade: >2mit/50 HPF; +/- necrosis

Neuroendocrine carcinoma, high grade

Small cell carcinoma / large cell neuroendocrine
- High grade: >10mit/10 HPF; widespread necrosis