Cholecystitis
- acute
- chronic

Gallbladder tumors
- Adenomyoma (benign)
- Adenocarcinoma

Pancreatitis
- acute
- chronic

Pancreatic tumors

Intro to Gallbladder & Pancreas Pathology

Helen Remotti M.D.

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%)

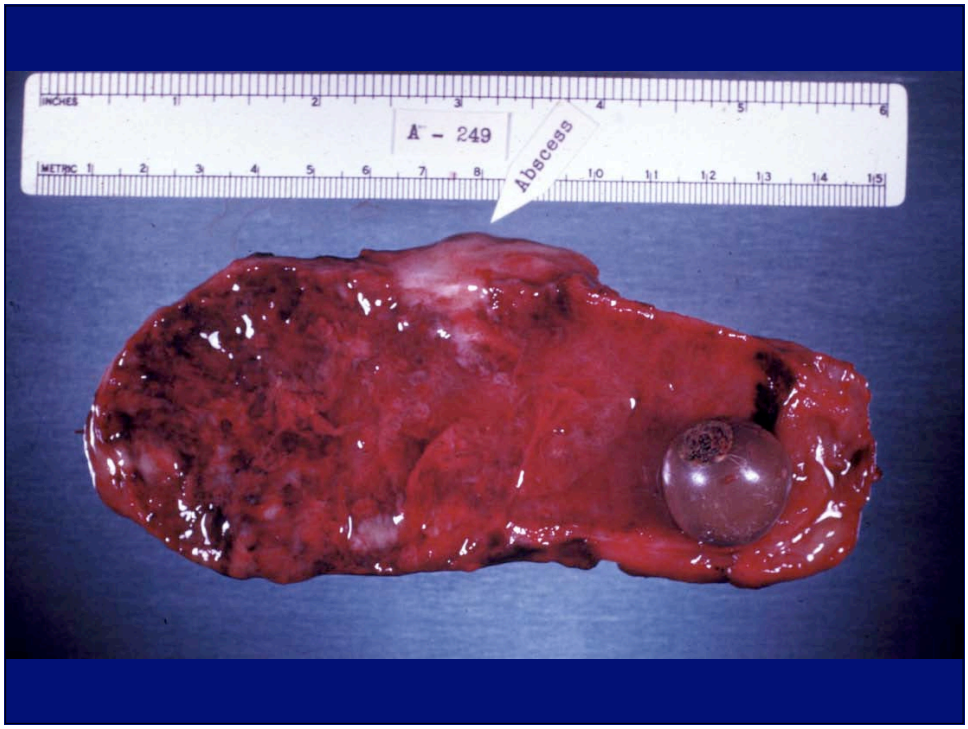
Acute Cholecystitis

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)

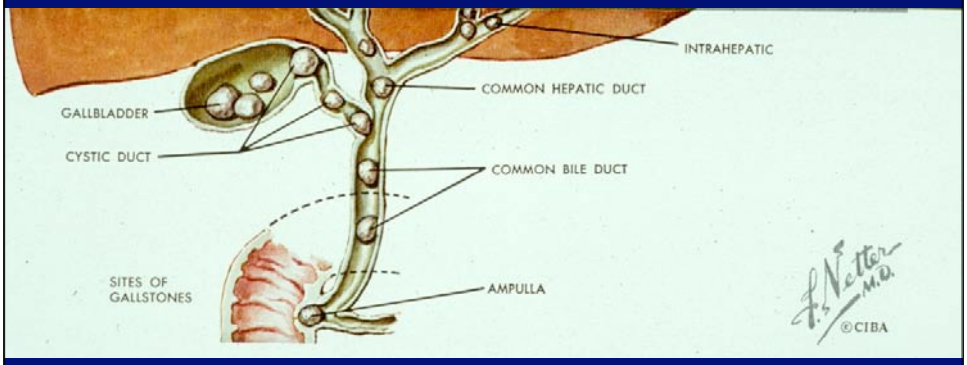
- 10 - 20% Adults
- 35% Autopsy: Over 65

- 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

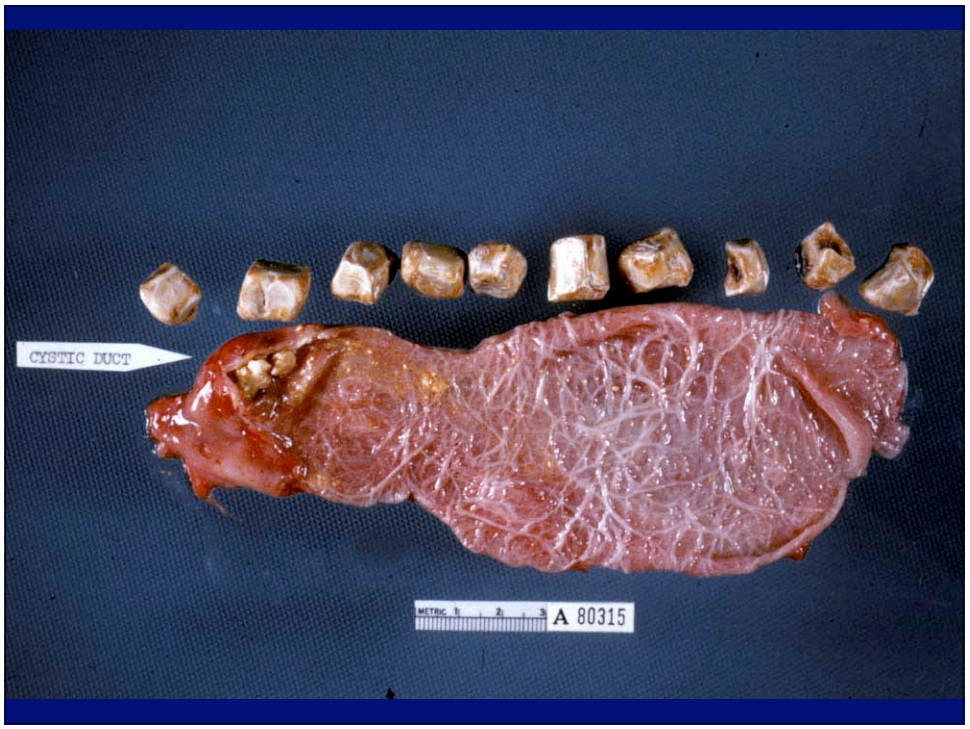
Ascending Cholangitis

Infection: to liver

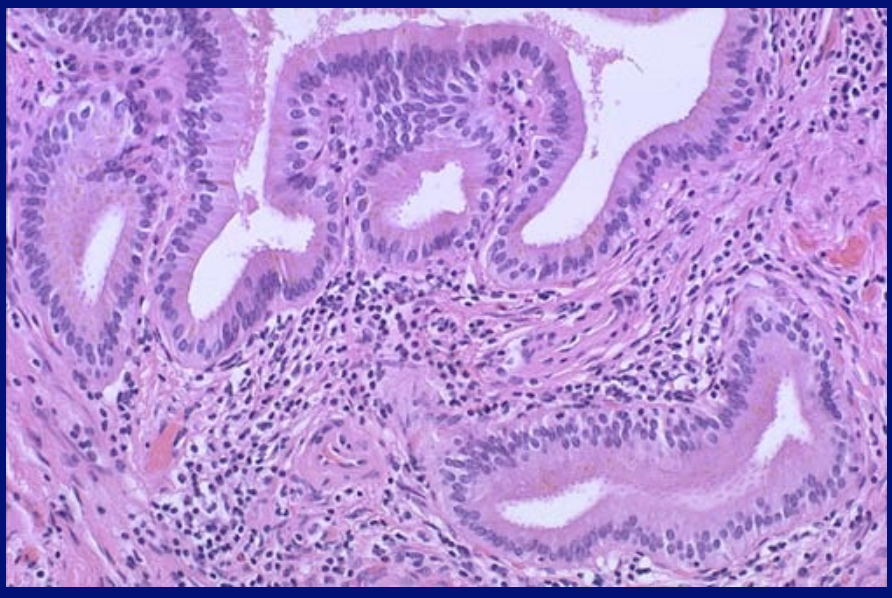
20%: No pain; 25% no jaundice

Chronic Cholecystitis

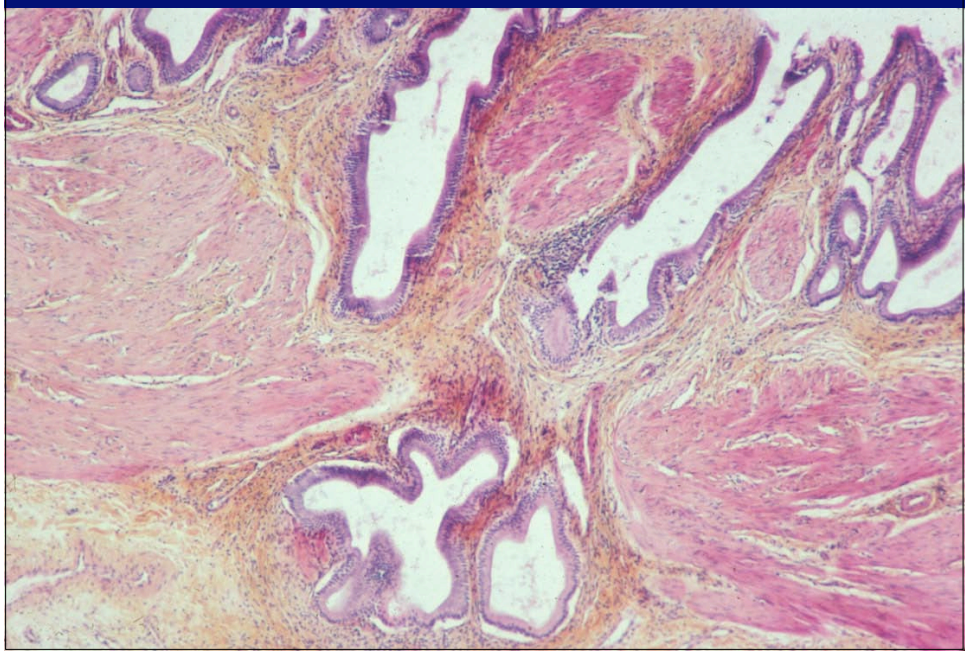
- Associated with calculi in 95% of cases.
- Multiples episodes of inflammation cause GB thickening with chronic inflammation/ fibrosis and muscular hypertrophy.
- Rokitansky - Aschoff Sinuses (mucosa herniates through the muscularis mucosae)
- With longstanding inflammation GB becomes fibrotic and calcified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



Chronic cholecystitis



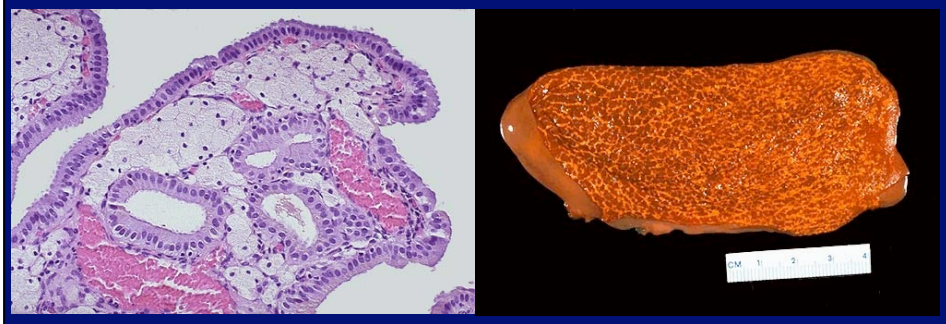
Rokitansky-Aschoff sinuses



Chronic Cholecystitis

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

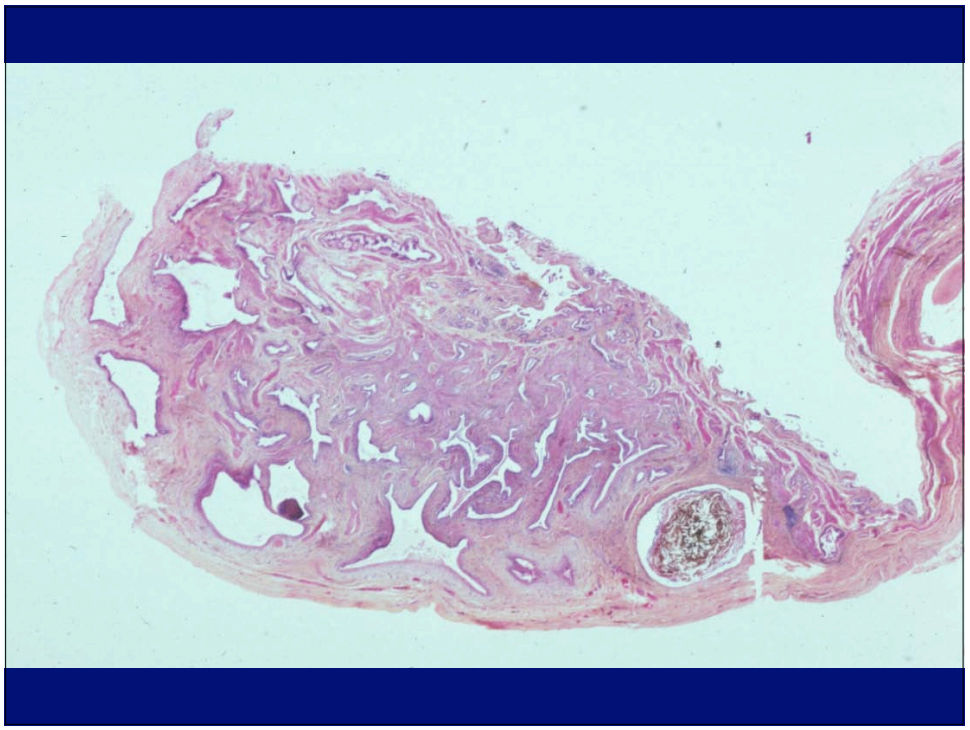
Cholesterolosis

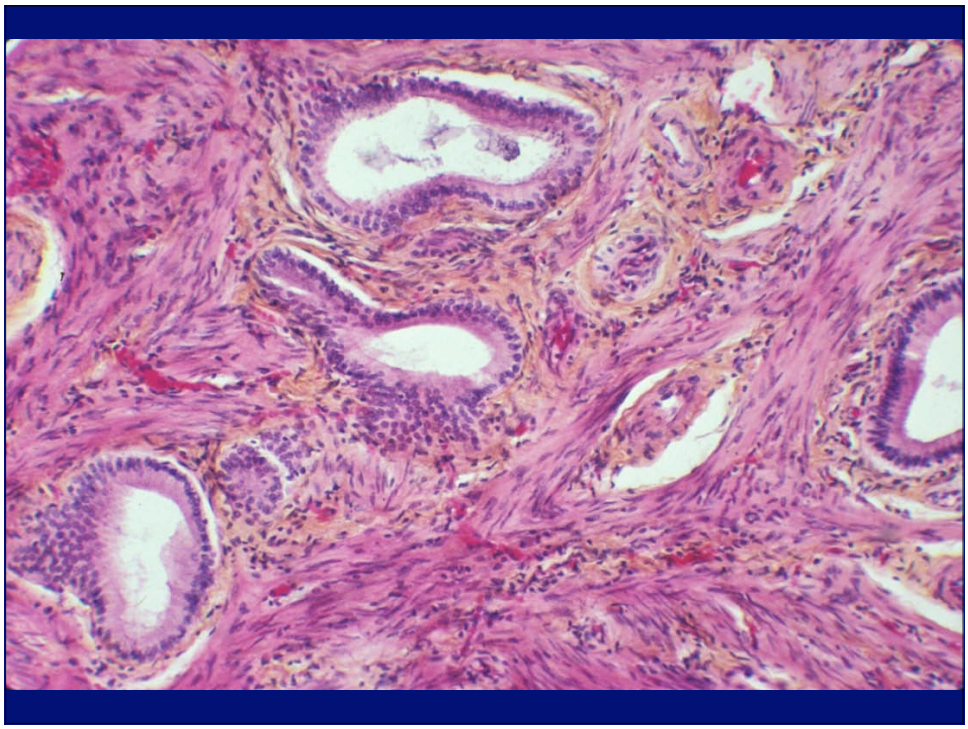


Focal accumulation of cholesterol-laden macrophages in lamina propria of gallbladder (incidental finding).

Adenomyoma of Gall Bladder


Fundus
Cystic Duc
A-56792
METRIC 1 2 3 4 5





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)

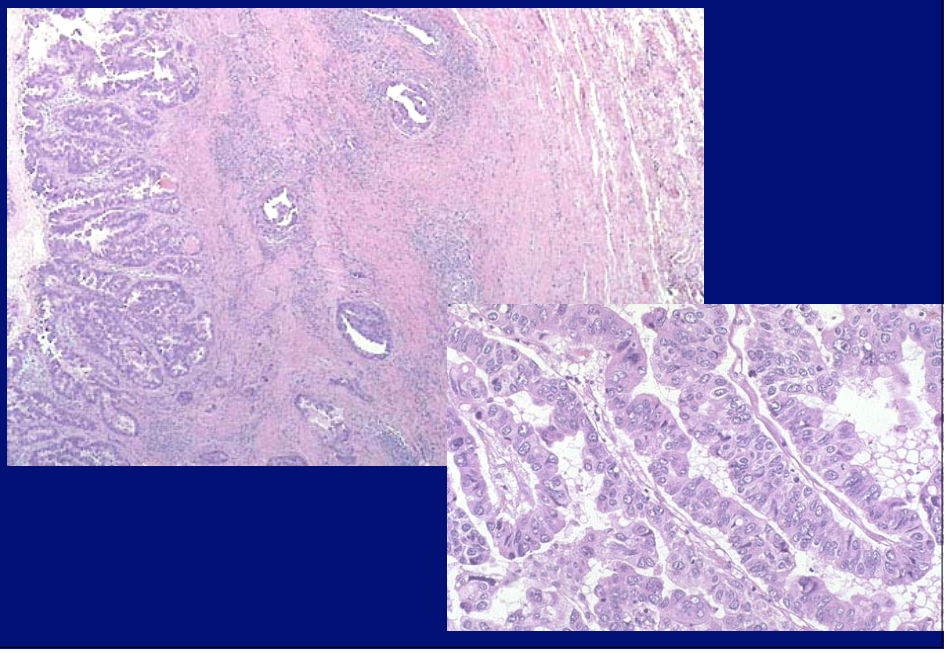
90%: Stones

Long Hx: symptomatic stones

Stones: predispose to CA., but uncommon complication


METRIC 1 2 3 4
A-50786

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.

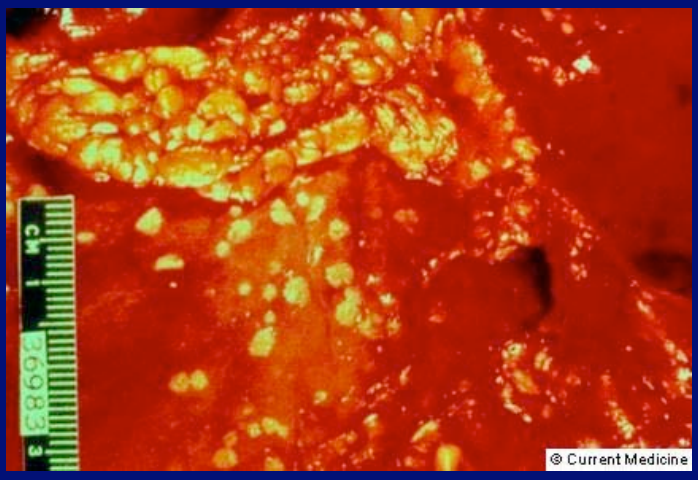
LABs: Elevated serum amylase and elevated peritoneal fluid lipase

Case 2- clinical course

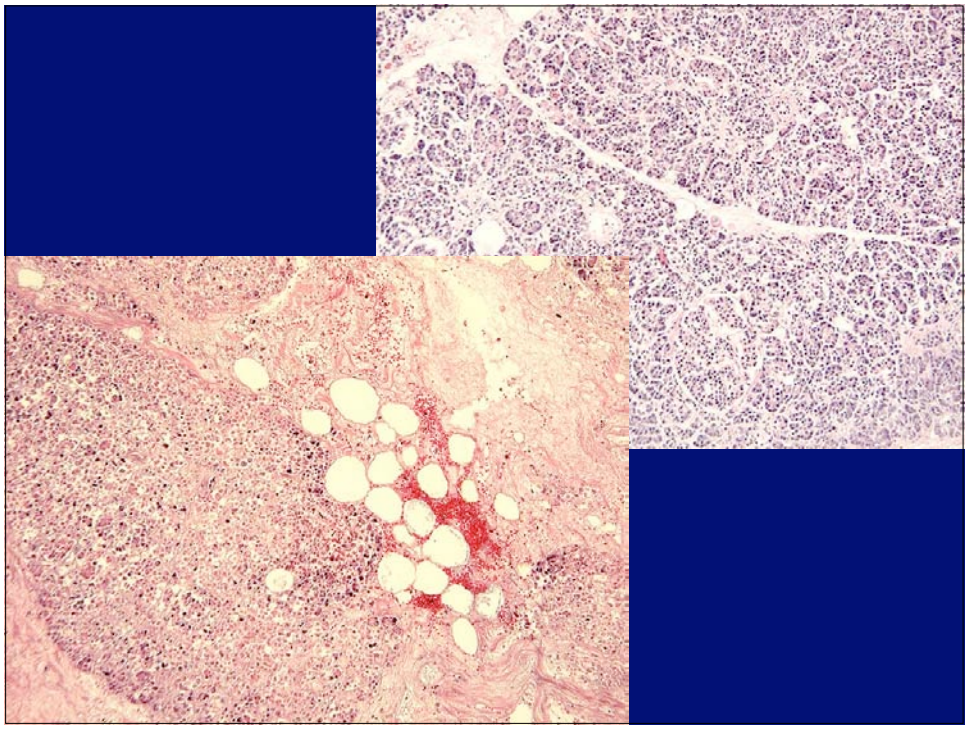
Patient developed rapid onset of respiratory failure necessitating intubation and mechanical ventilation.

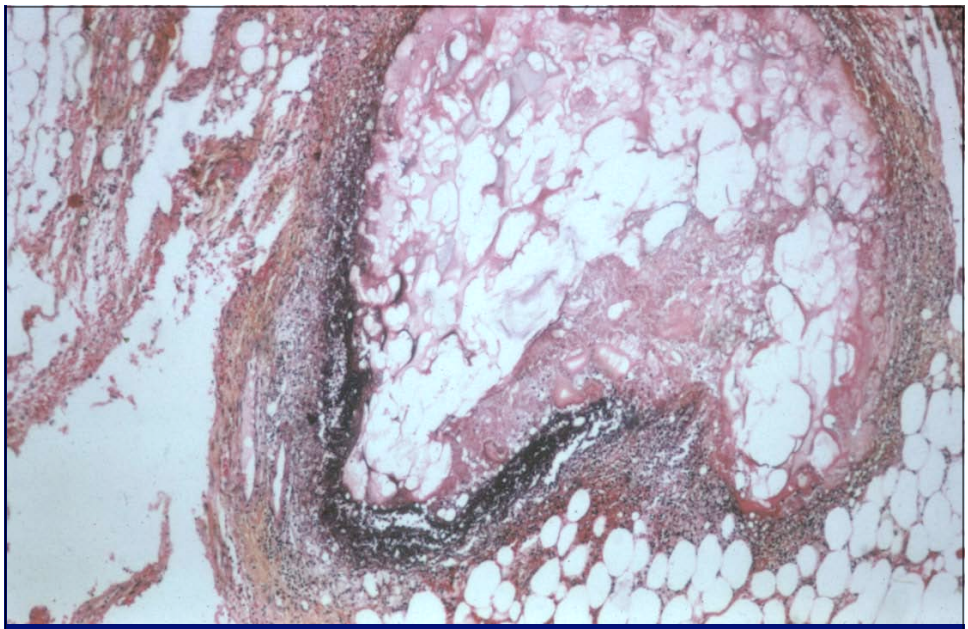
Over 48 hours, she was increasingly unstable, with evolution to multi-organ failure, and she expired 82 hours after admission.

An autopsy was performed.

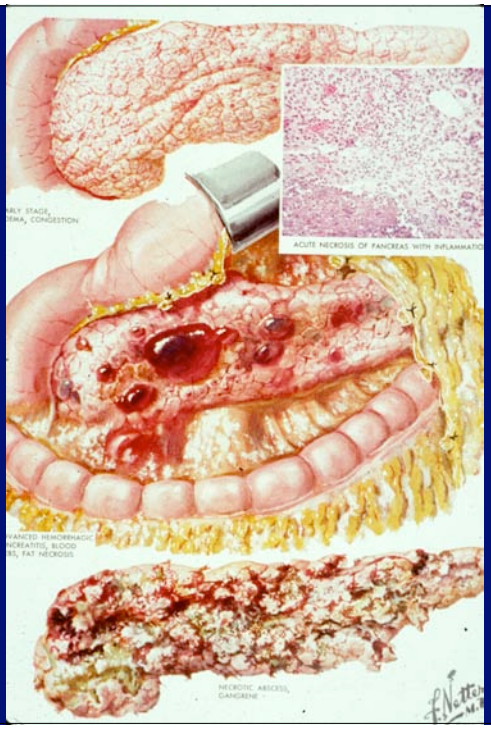


Acute pancreatitis





Elastase destruction of blood vessels – with hemorrhage



Acute Pancreatitis

Edema, congestion

Advanced hemorrhagic pancreatitis, fat necrosis

Necrotic abscess, gangrene

Pathophysiology of acute pancreatitis

Severity

Mild

Severe

Stage 1. Pancreatic injury
Edema, inflammation, fat necrosis, variable necrosis of pancreatic secretory cells

Stage 2. Local (peripancreatic) effects
Retroperitoneal edema, extensive fat necrosis, ileus with "third-spacing" of fluid and electrolytes

Stage 3. Systemic complications
Hypotension/shock, metabolic disturbances, organ failure, sepsis

Acute Pancreatitis

US: 45% of cases have gallstones and choledocholithiasis;

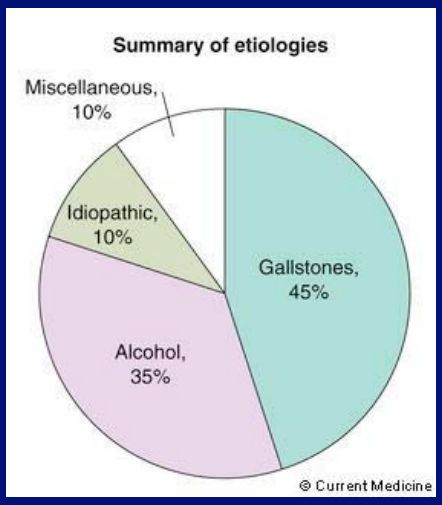
35% associated with heavy alcohol ingestion

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.

Acute Pancreatitis



ETIOLOGIES

Obstructive

Toxins/drugs

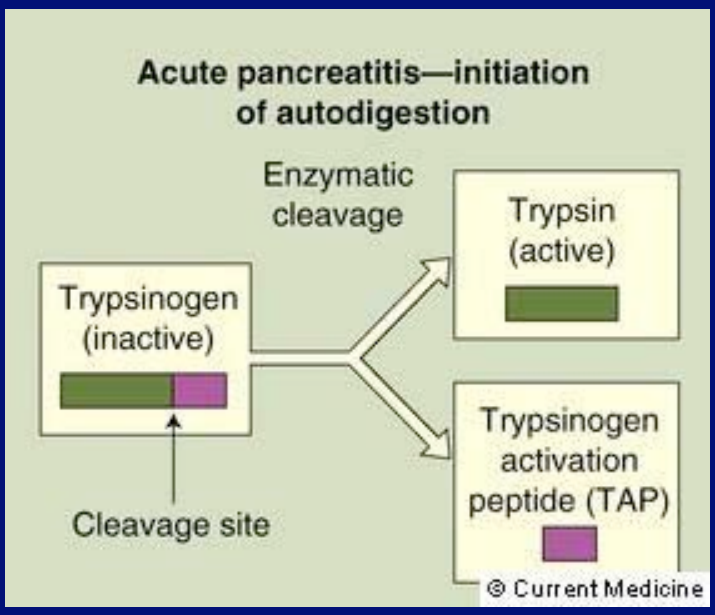
Metabolic

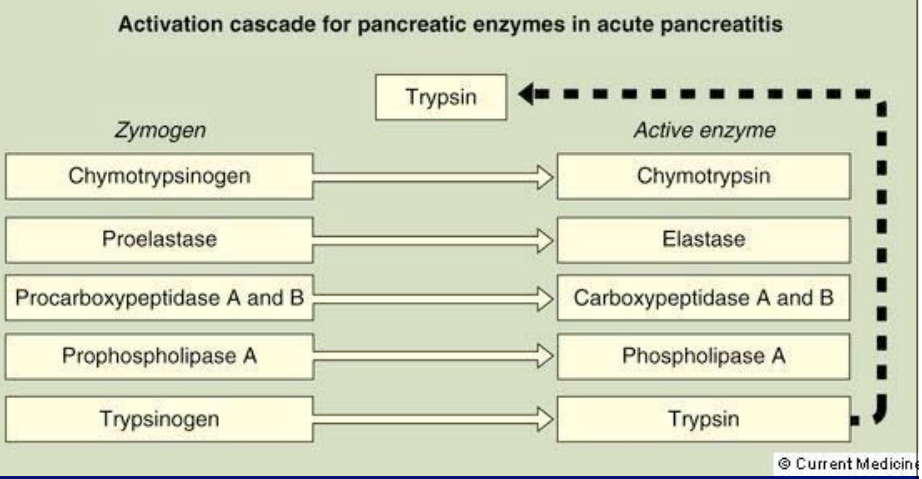
Infection

Vascular

Trauma

Idiopathic


Acute pancreatitis—initiation of autodigestion
Enzymatic cleavage
Trypsin (active)
Trypsinogen (inactive)
Trypsinogen activation peptide (TAP)
Cleavage site
© Current Medicine


Activation cascade for pancreatic enzymes in acute pancreatitis
Trypsin
Zymogen
Active enzyme
Chymotrypsinogen
Chymotrypsin
Proelastase
Elastase
Procarboxypeptidase A and B
Carboxypeptidase A and B
Prophospholipase A
Phospholipase A
Trypsinogen
Trypsin
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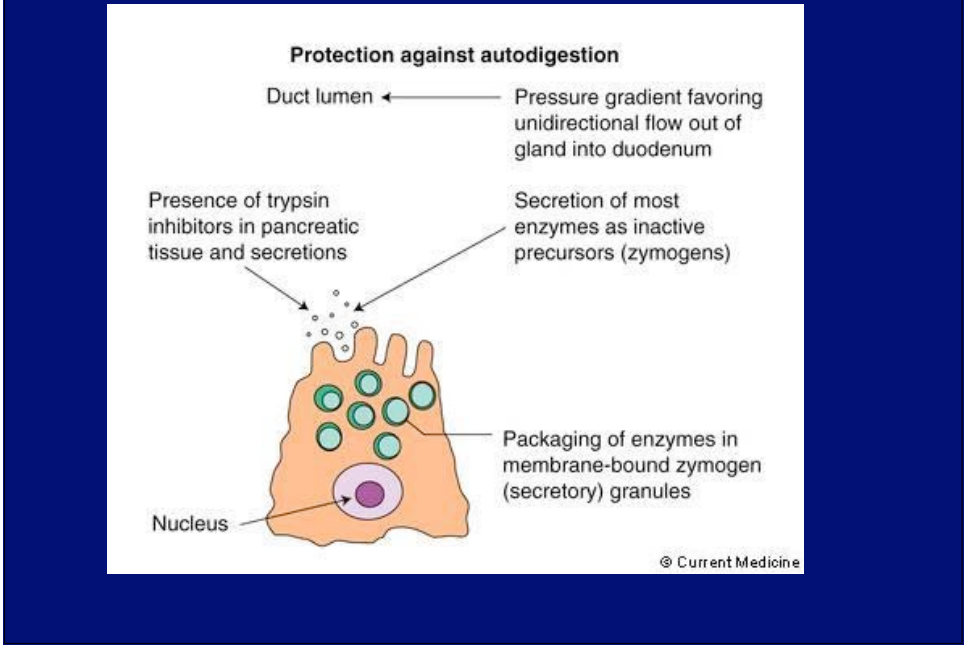
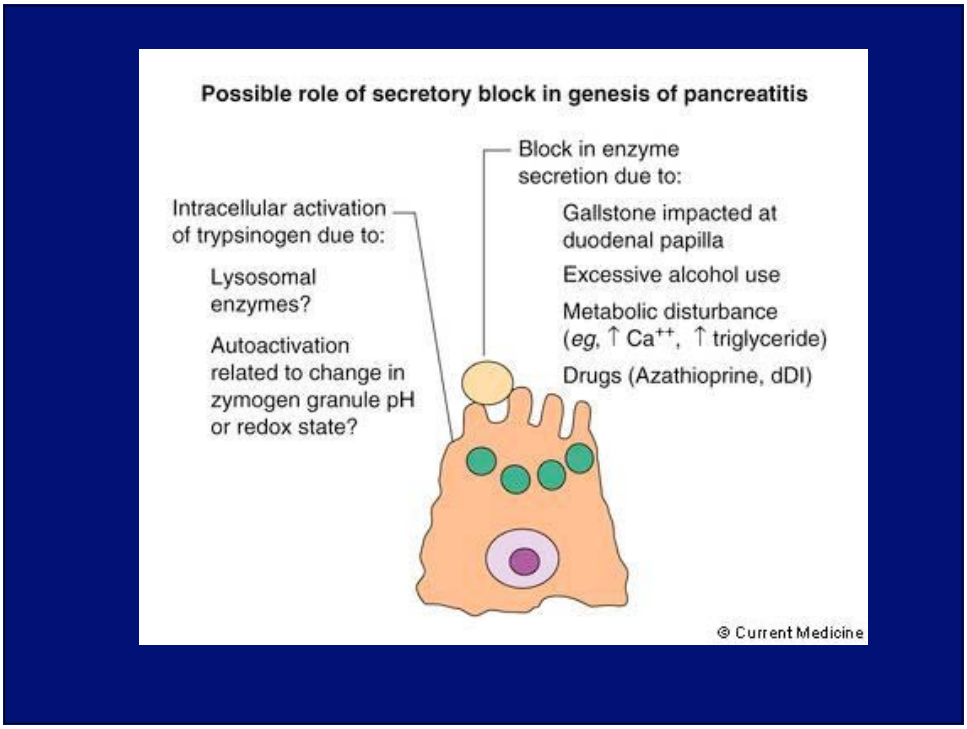

Protection against autodigestion
Duct lumen
Pressure gradient favoring unidirectional flow out of gland into duodenum
Presence of trypsin inhibitors in pancreatic tissue and secretions
Secretion of most enzymes as inactive precursors (zymogens)
Packaging of enzymes in membrane-bound zymogen (secretory)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


Possible role of secretory block in genesis of pancreatitis
Block in enzyme secretion due to:
Gallstone impacted at duodenal papilla
Excessive alcohol use
Metabolic disturbance (eg, ↑ Ca++, ↑ triglyceride)
Drugs (Azathioprine, dDI)
Intracellular activation of trypsinogen due to:
Lysosomal enzymes?
Autoactivation related to change in zymogen granule pH or redox state?
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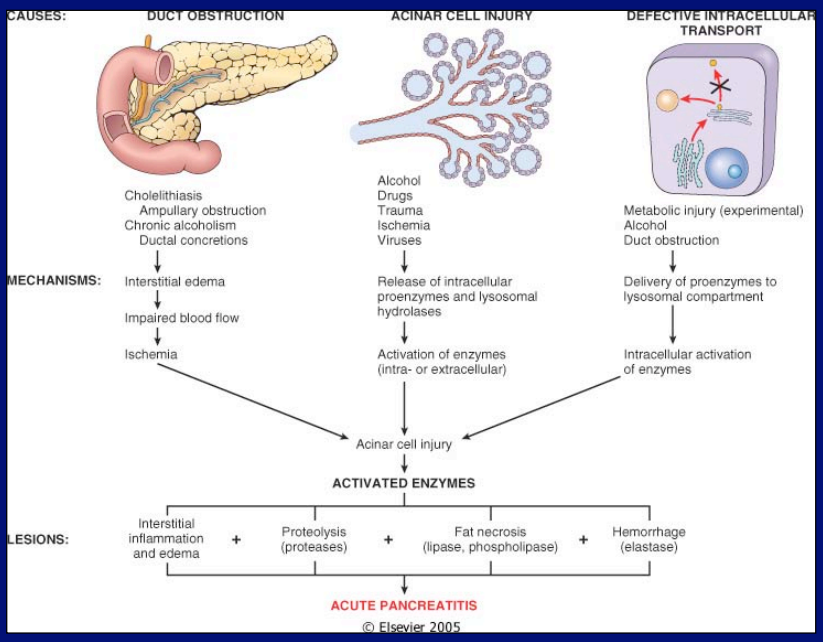


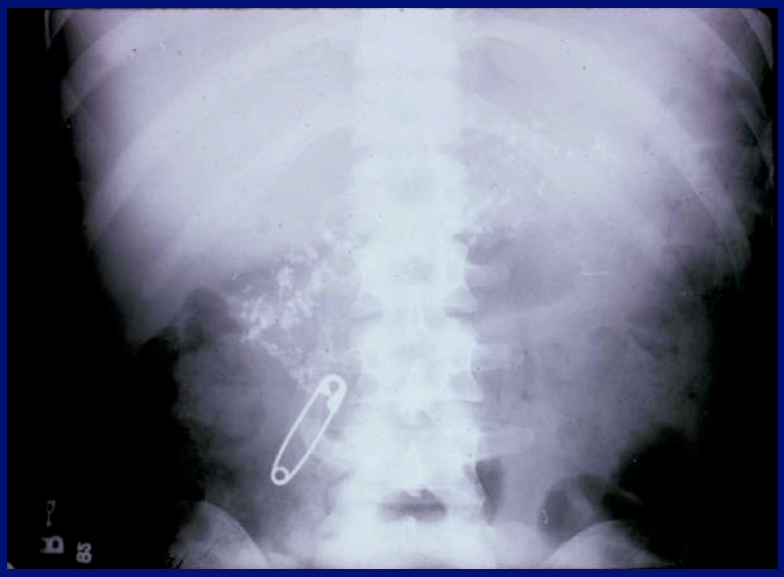
Chronic Pancreatitis

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

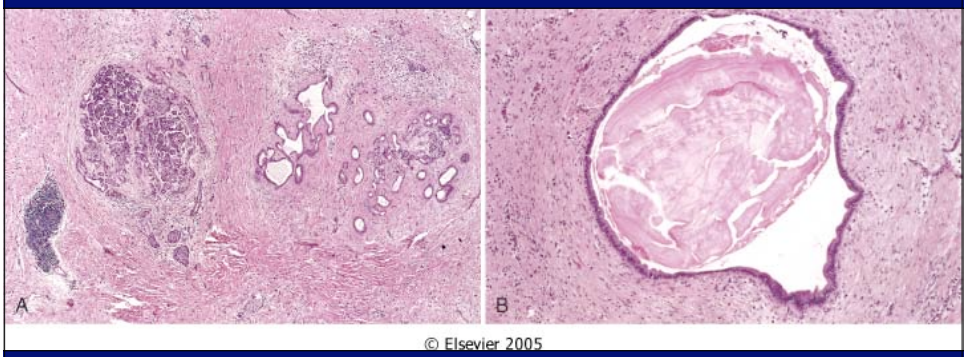
Fibrosis of parenchyma with distortion of duct architecture, loss of exocrine secretory function.

Changes may be focal or widespread.

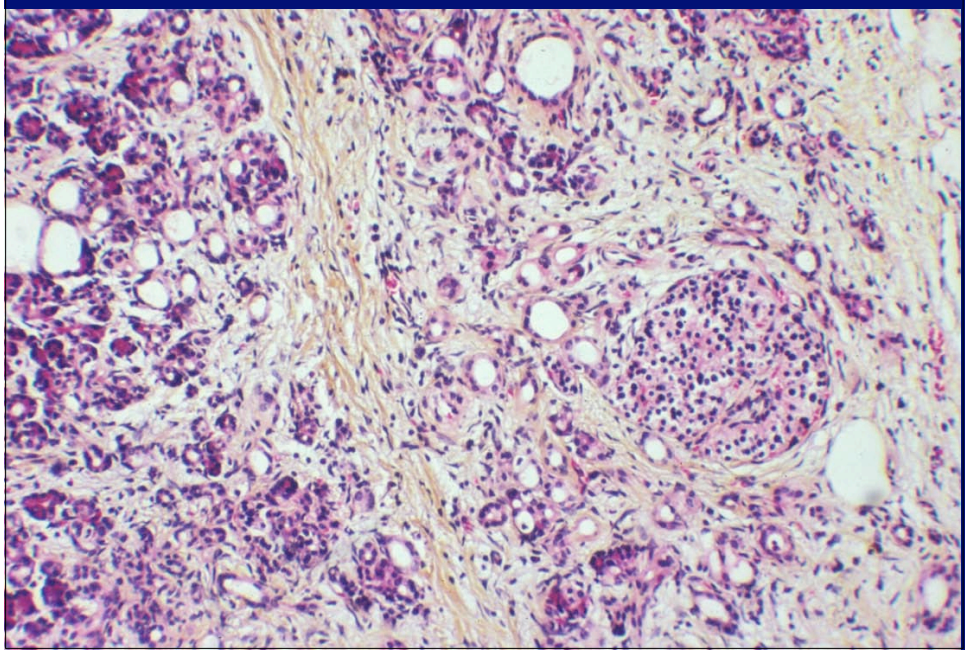
Chronic pancreatitis with Stones



Chronic pancreatitis



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

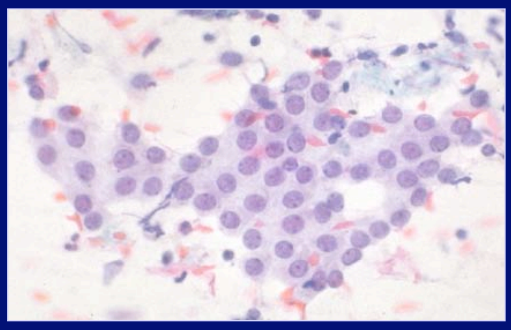
67 year old woman with recent onset painless jaundice.

History of 15lb weight loss over last 3 months.

She smoked 1 pack per day x 35 years.
Physical exam: palpable GB

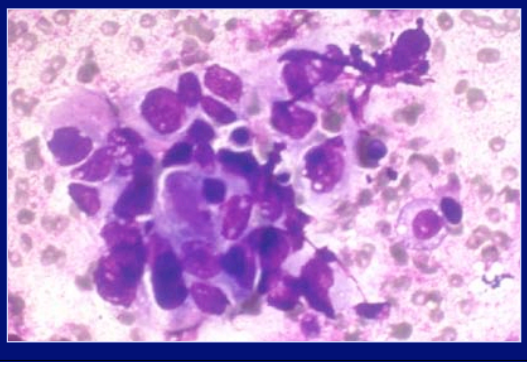
ERCP was performed with Endoscopic Ultrasound (EUS) evidence of a large mass in the head of the pancreas.

An endoscopic FNA was performed.



Normal pancreas

ductal epithelium



Patient's FNA

Dx: Adenocarcinoma

Carcinoma of Pancreas

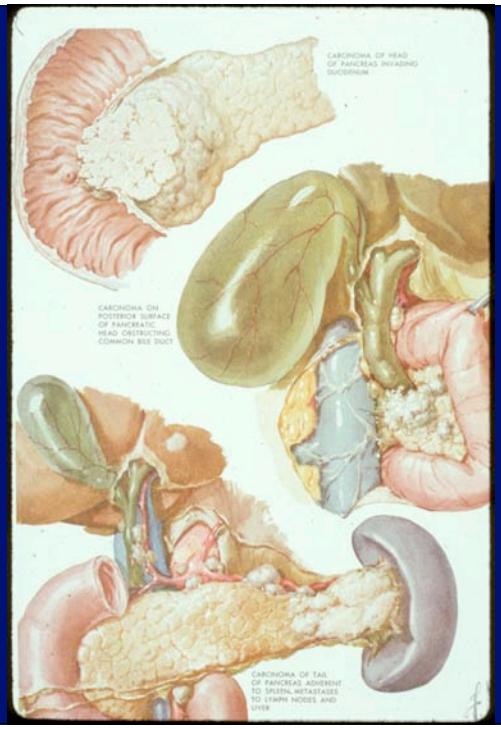
Weight loss:		70%
Pain:	Abdominal	50%
	Back	25%

Persistent jaundice

Anorexia

Loose stools

Nausea, vomiting



Courvoisier's Sign: Dilated palpable GB often reflects tumor obstructing the common bile duct

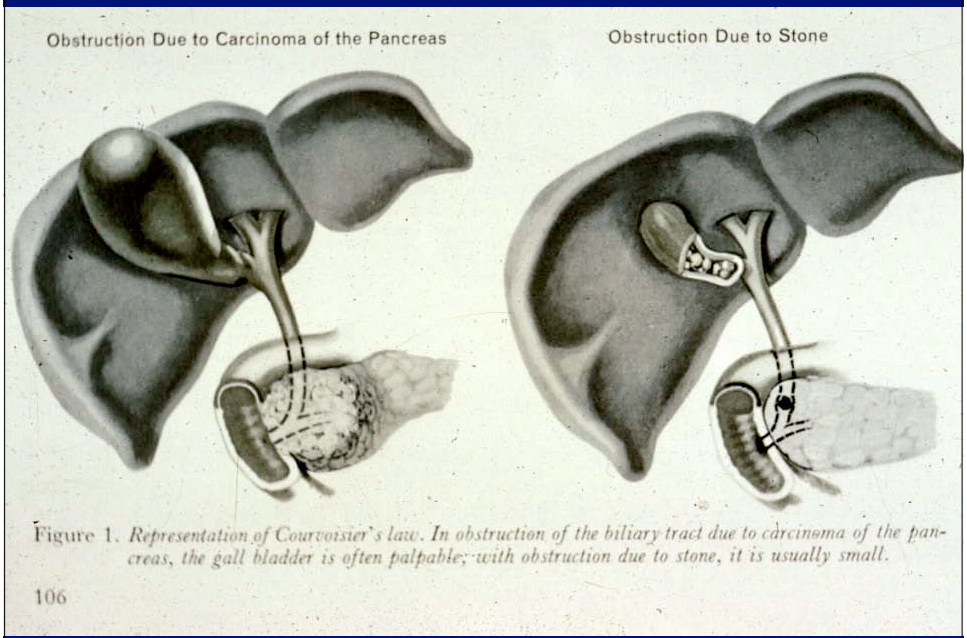


Figure 1. *Representation of Courvoisier's law. In obstruction of the biliary tract due to carcinoma of the pancreas, the gall bladder is often palpable; with obstruction due to stone, it is usually small.*

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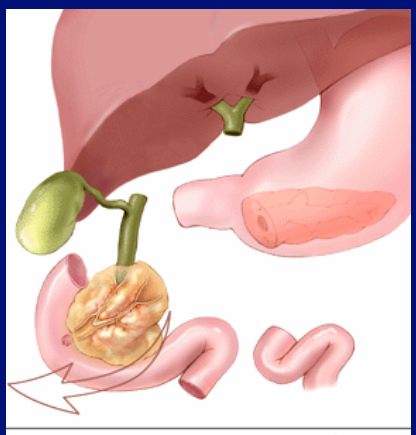
Carcinoma of Pancreas

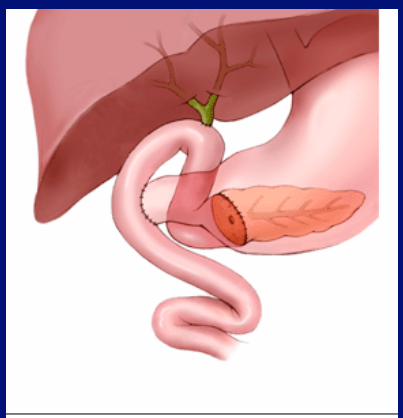
Enlarged, palpable G.B.: 50%
Mass in upper abdomen
Enlarged, nodular liver
Ascites
Jaundice
Migratory thrombophlebitis
(Trousseau's sign)

Adenocarcinoma: Pancreas

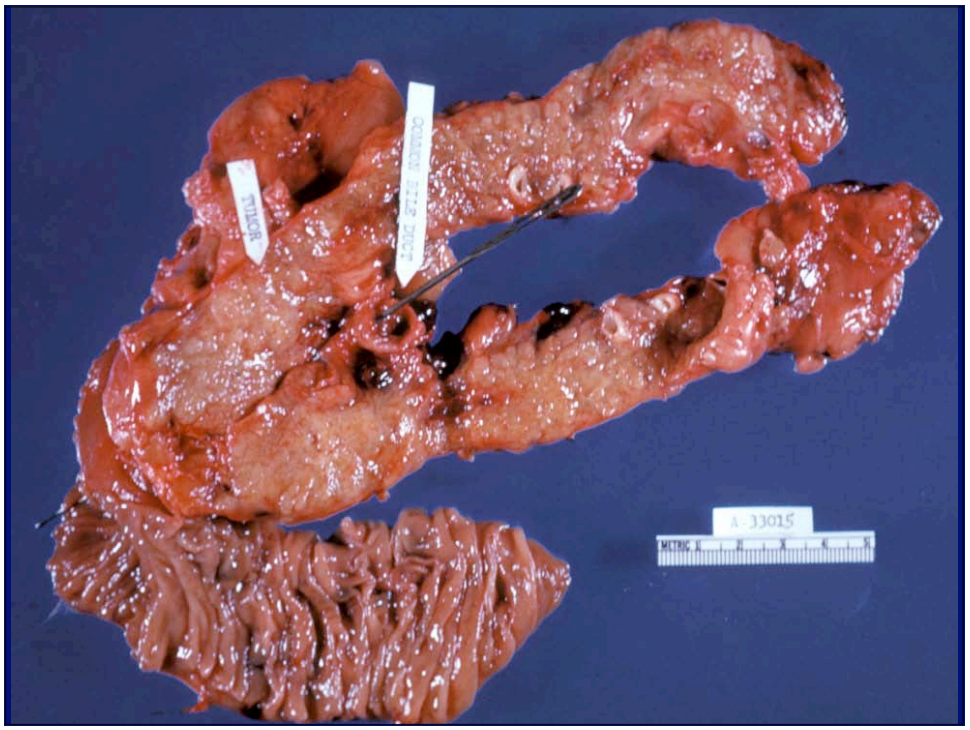
60 - 70% Head
20 - 30% Body
5 - 10% Tail

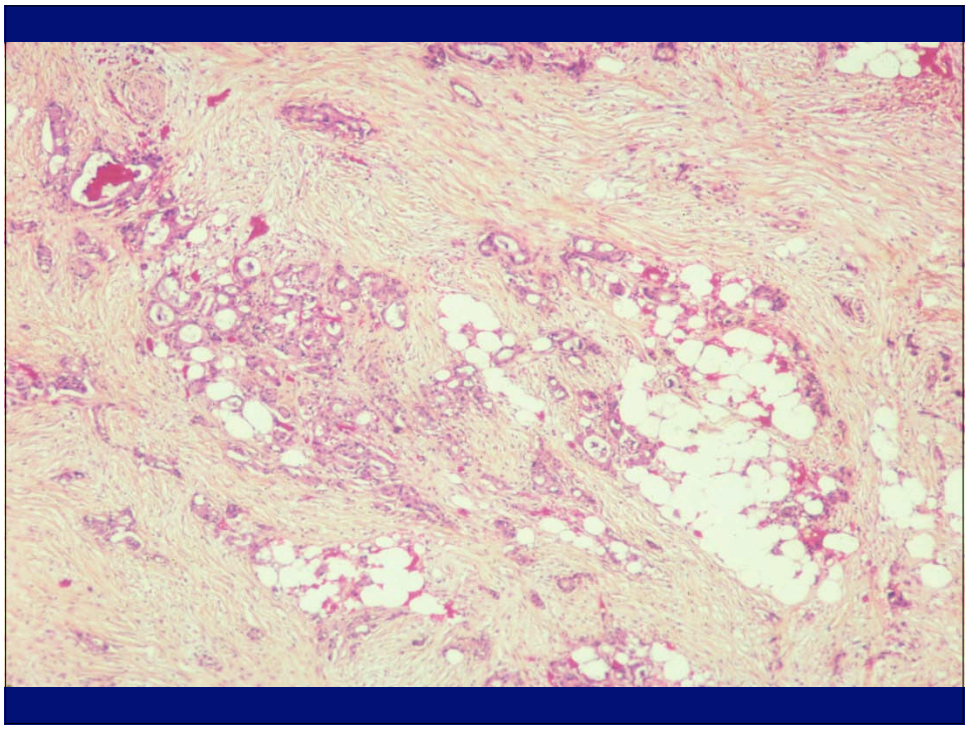


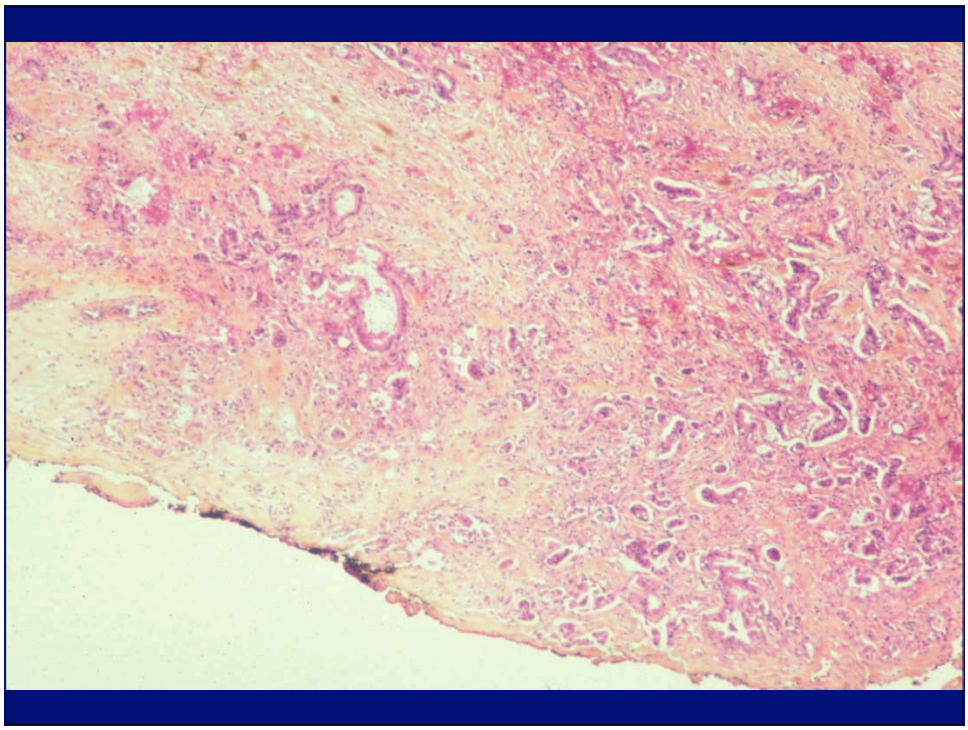
Organs removed during a Whipple



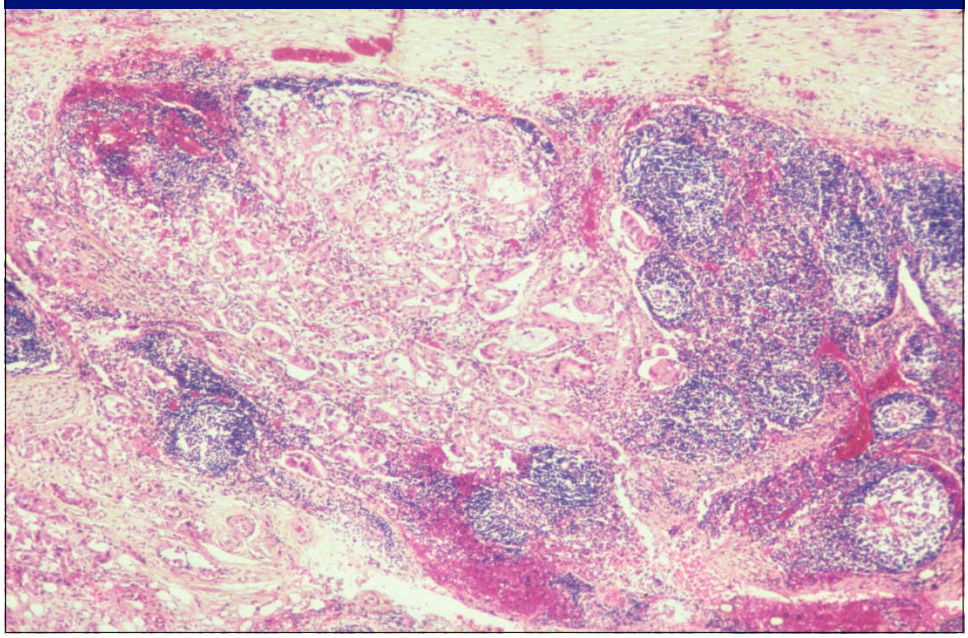
Most common anatomy after Whipple



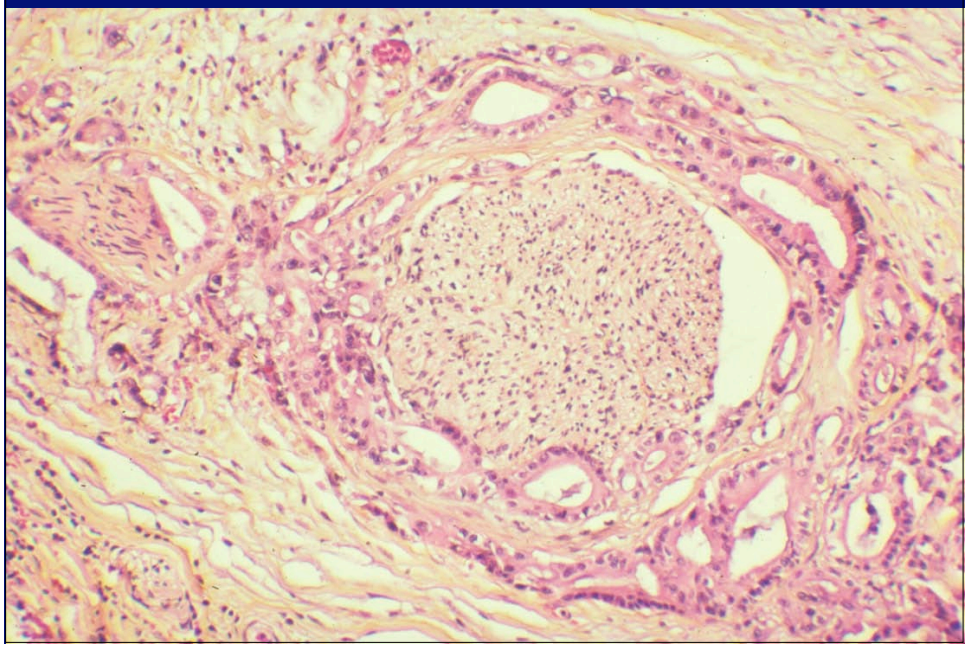




Pancreatic adenocarcinoma – Lymph node metastases



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

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.

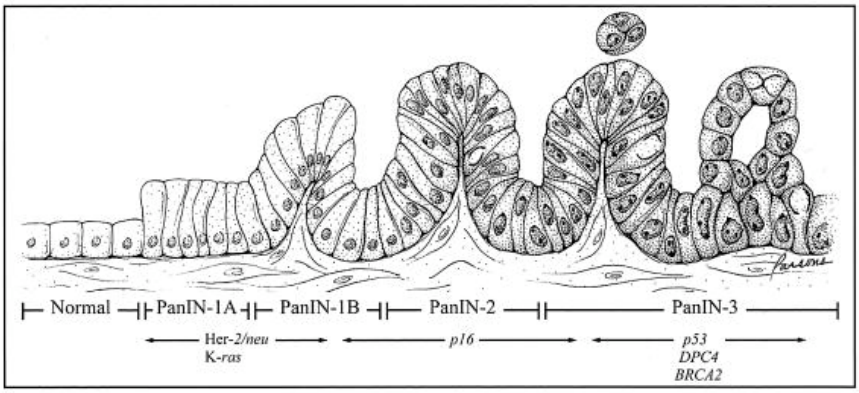
Pancreatic cancers described in BRCA2 mutations in familial breast cancer kindreds.

Associated with germline p16 mutations, and HNPCC.

Role of oncogenes: KRAS-90%, p16-95%, p53-75%

In-situ progression to Cancer

Takaori and Hruban *Pancreas* 2004 28:256-262.

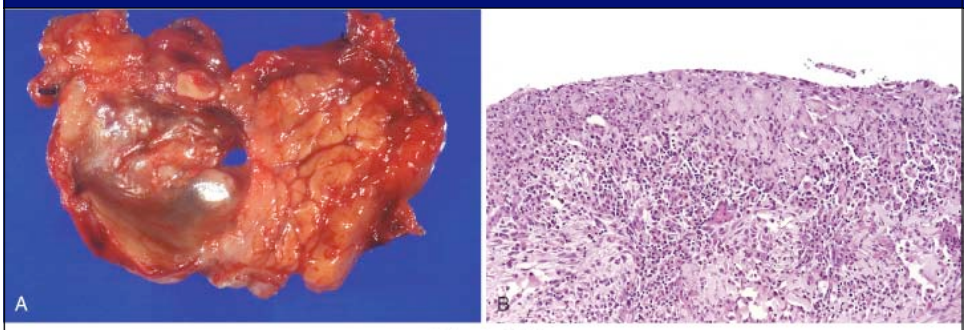


Pancreatic Cystic Lesions

- Pseudocyst (benign – NOT a NEOPLASM)
- Serous cystadenoma (benign)

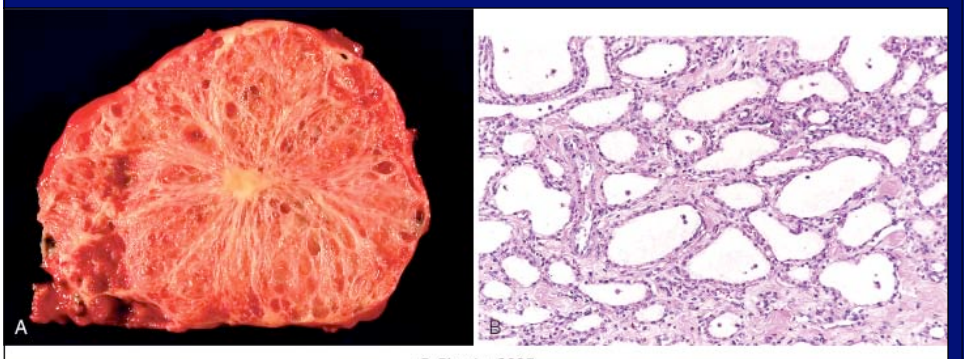
- Mucinous cystic neoplasm (benign, borderline or malignant)
- Intraductal papillary mucinous neoplasm (benign, borderline or malignant)

Pancreatic Pseudocyst



NOT NEOPLASTIC - RESULT OF ACUTE PANCREATITIS

Pancreatic serous cystadenoma



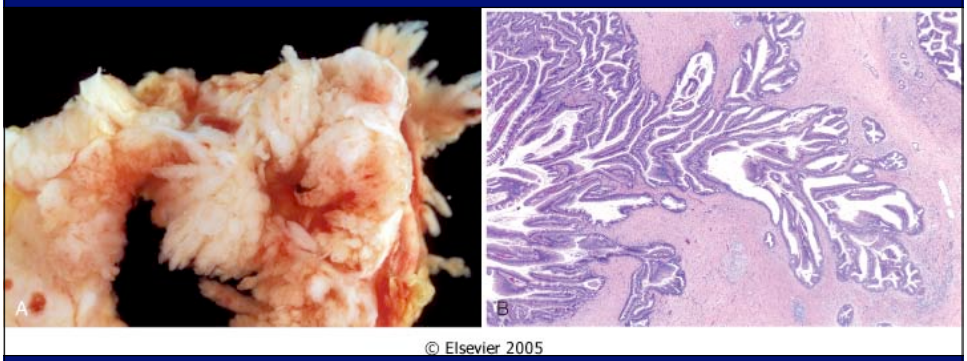
BENIGN

Mucinous cystic neoplasm

Not associated with the pancreatic duct

Clinical spectrum: benign to malignant

Intraductal mucinous neoplasm

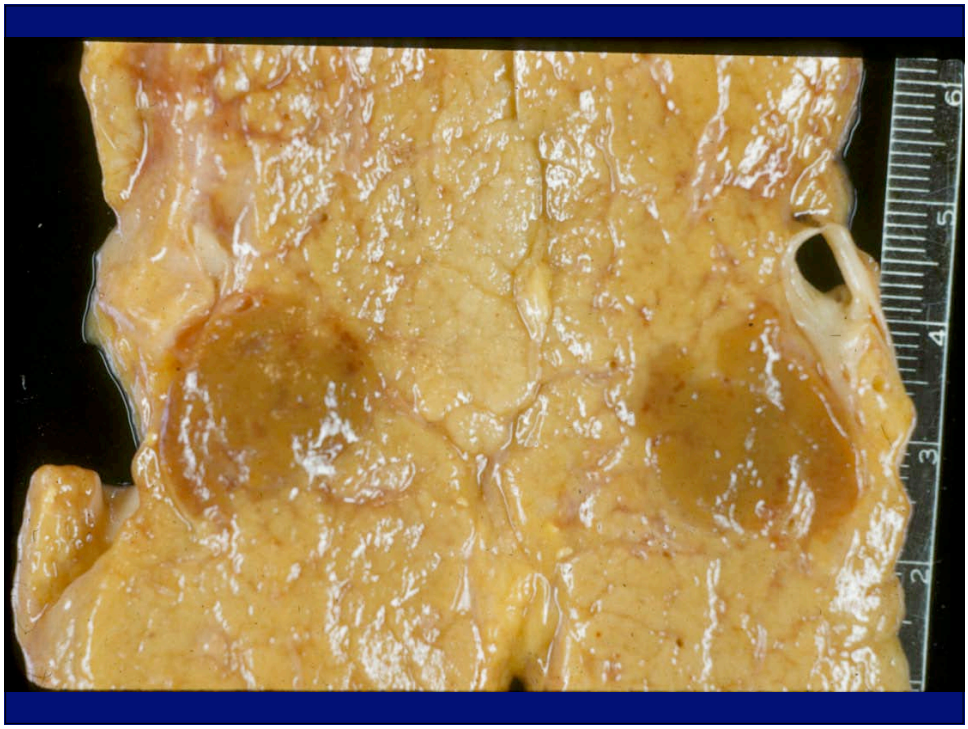


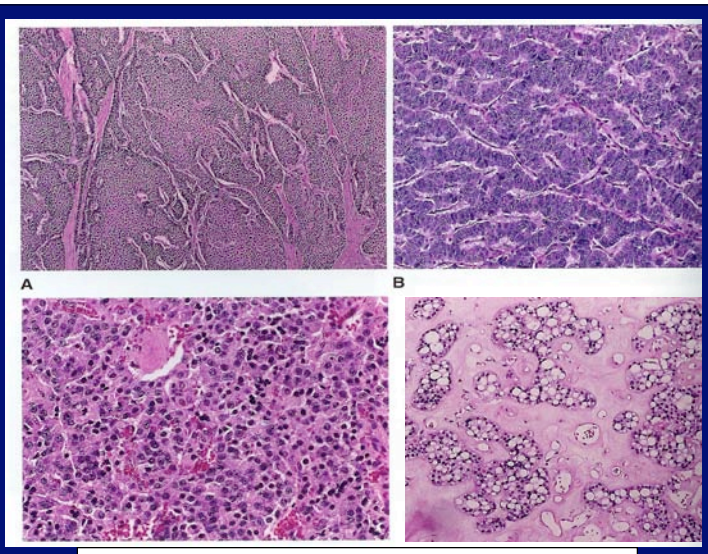
Associated with the pancreatic duct

Clinical spectrum: benign to malignant

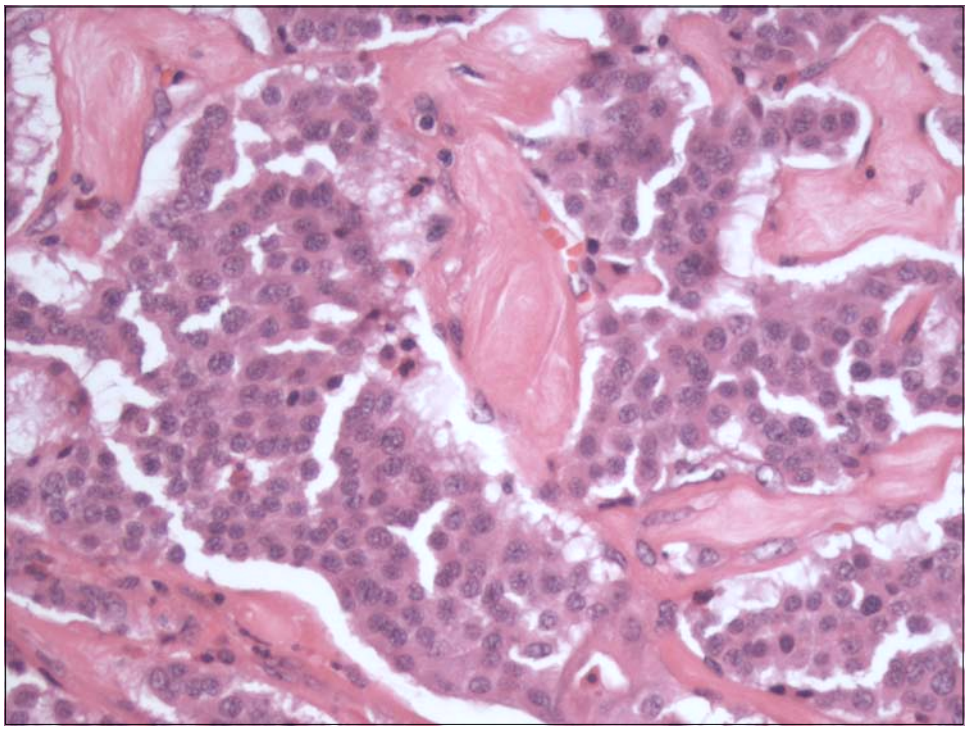
Pancreatic Endocrine Neoplasms

- 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