Pancreas

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2 glands in 1:
- Exocrine: Acinar, ductal cells
- Endocrine: Islet cells

Neoplasms:
- Adenocarcinomas: Most common
- Pancreatic neuroendocrine neoplasms
- Acinar cell carcinoma: Rare
- Other

All pancreaticobiliary AdCAs look alike

FNA Bx of Pancreas

Primary indication:
- Chronic pancreatitis vs neoplasm

- Tissue biopsy:
  Complications—fistula, etc
  FN relatively high; FP up to 3%

- FNA biopsy:
  Safe and reliable
  At least as accurate as tissue Bx
  Much less morbidity/mortality

=> FNA Bx technique of choice

Normal Pancreas

Acinar

Ductal

Islet

2 Glands in 1

Acinar Cells: Exocrine

Normally predominate
- Serous acinic salivary gland
- Grape-like clusters
- Microacinar structures
- Pyramidal/polygonal cells
- Uniform nuclei, conspicuous nucleoli
- Granular (zymogen) cytoplasm

Ductal Cells

Normally present, but sparse
- Cohesive honeycomb sheets
- Uniform cells
  - cuboidal to columnar
- Smooth nuclei, fine chromatin,
  inconspicuous nucleoli
- Delicate cytoplasm,
  ± mucin, goblet cells
Reactive/Reparative Changes
WARD Cells: Worrisome Atypia in Reactive/Degenerative Cells

- Nuclear enlargement
- Prominent nucleoli
- Mitoses vs Order, cohesion
- Smooth nuclei
- Fine chromatin

Islet Cells: Endocrine
- Islets of Langerhans
  - <2% of cells, most in tail
- Islet cells
  - Neuroendocrine chromatin
  - Neurosecretory granules
  - Secrete ≥ 4 hormones
    - insulin
    - Gastrin
    - Somatostatin
    - Pancreatic polypeptide
- Rarely ID w/o special studies

Clues to GI Pickups vs Neoplasm
First diagnostic clue:
Neoplastic mucus is thick, sticky
“Spinnbarkeit”
The stringy, elastic character of cervical mucus time of ovulation

More Clues
- Chief Cells, Parietal Cells
- Gastric Cells
- Dense colloid-like mucus
- Degenerated cells
- Cyto-atypia
- Debris
- Striated Border
- “Neoplastic Mucus”

Summary: GI “Pick Ups”
- Intestinal cells: Starry sky
- Gastric cells: Mucin cup
- Neoplastic cells: Mucin column
- Neoplastic mucus: Thick, sticky, colloid-like;
  + cyto-atypia, inflam’n, degeneration, debris
- Pitfall: IPMNs ± intestinal or gastric cells
**Diseases of the Pancreas**

**Solid**
- Chronic pancreatitis
- Ductal adenocarcinoma
- Pancreatic neuroendocrine neoplasms
- Acinar cell carcinoma
- Pancreatoblastoma
- Solid pseudopapillary neoplasm
- Lymphoma
- Mesenchymal tumors
- Metastases

**Cystic**
- **Nonneoplastic**
  - Pseudocyst (most common)
  - Miscellaneous cysts
- **Neoplastic**
  - Serous cystadenoma
  - Mucinous cystic neoplasms
  - Intraductal papillary mucinous neoplasms
  - Cystic degeneration in a solid tumor

**Chronic Pancreatitis**

**Histology**
- Acinar atrophy
- Ductal metaplasia
- Chronic inflammation
- Fibrosis, calcification

**Autoimmune Pancreatitis**

M > F, 50s, ↑ serum IgG4
± Other autoimmune disease
- Stromal fragments with many:
  - Lymphocytes (T cells)
  - Plasma cells (IgG4 +)
- DDx: Adenocarcinoma

**Pseudocyst**

By far most common cyst
- Caused by pancreatitis
- Unilocular without septations
- No epithelial lining (pseudocyst)

Dx: Turbid brown fluid
  - ↑ amylase; no mucus
  - Histioctyes, inflam’t n, debris
  - Few/no epithelial cells
- DDx: WARD cells

**Lymphoepithelial Cysts**

Rare, mid-old age men
- Branchial cleft cysts
  - Squamous lining
  - Lymphoid stroma
  - Histioctyes
  - Cholesterol crystals
Neoplastic Pancreatic Cysts

10-25% of all cysts; ~5% all neoplasms
Two general types:
- Serous
- Mucinous
  - Mucinous cystic neoplasms
  - Intraductal papillary mucinous neoplasms
Dx: FNA biopsy plus—
  - clinical, radiology, fluid analysis
DDx: Cystic degeneration in solid tumors

Mucinous Cystic Neoplasm

Serous Cystadenoma

DDx Cystic Neoplasms

Pancreatic Cyst Fluid Analysis

Serous Cystadenoma

Mucinous Cystic Neoplasm

Intraductal Papillary Mucinous Neoplasm

### Pancreatic Cyst Fluid Analysis

<table>
<thead>
<tr>
<th></th>
<th>Viscosity</th>
<th>CEA</th>
<th>Amylase</th>
<th>Mucin</th>
<th>Cytology</th>
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</thead>
<tbody>
<tr>
<td>Pseudocyst</td>
<td>Low</td>
<td>Low</td>
<td>High</td>
<td>−</td>
<td>Inflammatory cells, debris</td>
</tr>
<tr>
<td>Serous</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>−</td>
<td>Cuboidal, glycogen rich cells, minimal atypia</td>
</tr>
<tr>
<td>Mucinous</td>
<td>High</td>
<td>High</td>
<td>Low</td>
<td>+</td>
<td>Columnar, mucinous cells, variable atypia</td>
</tr>
<tr>
<td>IPMN</td>
<td>High</td>
<td>High</td>
<td>High</td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>

### Serous Cystadenoma

Elderly, F > M, B,T > H
Spongy, stellate scar
Fluid:
- Thin, glycogen-rich
Low amylase & CEA

### Mucinous Cystic Neoplasm

Mid age, F >> M
tail, no duct con
↑ CEA, ↓ amylase
Thick sticky mucus
Cells: Bland to AdCA
Ovarian-like stroma

### Intraductal Papillary Mucinous Neoplasm

Elderly M > F
Head >> Tail
Duct can, ectasia
↑ CEA and amylase
Thick sticky mucus
Mucinous cells
Bland to malignant
Ductal Adenocarcinoma

By far most common pancreatic malignancy
FNA bx usually highly cellular, but can be limited by fibrosis
Dx: MD to PD carcinoma usually straightforward (Nuclear enlargement, pleomorphism, abnormal chromatin, nucleoli, etc)
WD can be subtle

Other Features

Variants of Pancreatic Carcinoma

Well-Differentiated Adenocarcinoma

1st clue: Too many [ductal] cells
Abnormal architecture (low power)
Too crowded (“tight wads”) Too loose (“drunken honeycombs”) Nuclear enlargement (≥2 x normal) Irregular nuclear membranes Increased mitoses Martian Popping Things (ie, rare, obviously malignant cells) + at least a few single atypical cells

Pitfall: WD Adenocarcinoma

3rd clue: Too many [glandular] cells/Abnormal architecture

Benign Malignant

Foamy Cell Carcinoma

Low grade adenocarcinoma
• Drunken honeycombs
• Irregular nuclear membranes
Abundant foamy cytoplasm => Low N/C ratios!
**Acinar Cell Carcinoma**
- Rare, mostly older, M>F
- ±Hypersecretory syndrome
  - Fat necrosis, polyarthralgia, eosinophilia
- Acinar cells only
- Clue: Crowded, atypia
- DDx: Benign pancreatic, PANS

**Oncocytic Neoplasms**
- Ductal, acinar, or neuroendocrine
- Special studies, eg, EM, immuno to determine nature of tumor

**Clear Cell Neoplasms**
- Ductal CA or Neuroendocrine neoplasms
- DDx: Metastatic clear cell tumors, particularly renal cell carcinoma

**Pancreatoblastoma**
- Very rare; bimodal: ~4 yrs + adults
- ↑ serum α-fetoprotein
- Dx: Small blue cell tumor, with:
  - Epithelial cells
  - Exocrine (acinar) cells
  - Endocrine (islet) cells
  - Mesenchymal (spindle) cells
- Pearl: Squamous pearls!

**Pancreatic Neuroendocrine Neoplasms**
- Unusual (~5%); most low-grade
- Mid age, F=M, body/tail > head
- Rare hormone syndromes aid dx
- Dx: ~ Carcinoid tumor
  - Monotonous tumor cells
  - Plasmacytoid ± endocrine atypia
  - "Salt- & pepper" chromat
  - Fine metachromatic NSGs
- DDx: Acinar CA–Zymogen granules
  - Adenocarcinoma–Mucin

**Pancreatic Neuroendocrine Neoplasms**

<table>
<thead>
<tr>
<th>Tumor grade</th>
<th>Equivalent</th>
</tr>
</thead>
<tbody>
<tr>
<td>grade 1</td>
<td>Typical carcinoid</td>
</tr>
<tr>
<td>grade 2</td>
<td>Atypical carcinoid</td>
</tr>
<tr>
<td>grade 3</td>
<td>Small cell NE carcinoma</td>
</tr>
<tr>
<td>Carcinoma</td>
<td>Large cell NE carcinoma</td>
</tr>
</tbody>
</table>
**Neuroendocrine Spectrum**

- PN Tumor, Grade 1
- Mitosis
- Necrosis
- PN Tumor, Grade 2
- PN CA: Small cell
- PN CA: Large cell

**Solid Pseudopapillary Neoplasm**

- Low-grade malignancy
- Mostly young females
- Dr. Pseudopapillae
- Bland nuclei w/ grooves
- Cytoplasmic processes
- α1AT+ β-catenin+, CK ±
- Pearl: hyaline globules!

**Other Rare Pancreatic Tumors**

- **Lymphoma**
  - Forms mass, can mimic pancreatic carcinoma
  - Most = large B cell type
- **Mesenchymal Tumors**
  - Benign, eg, angiomomas, lipomas, etc
  - Malignant, eg, leiomyosarcoma, "MFH," etc
- **Metastases**
  - Kidney, lung, breast, GI Tract, etc
  - Lymphoma, sarcoma, melanoma

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Thank you

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