FINE NEEDLE ASPIRATION BIOPSY OF THE PANCREAS
METHODS OF SAMPLING

- Endoscopic retrograde cholangiopancreatography (ERCP):
  - **Brush cytology**
    - Biliary duct
    - Pancreatic duct
- Percutaneous transhepatic cholangiography (PTC)
  - < performed because of their interventional capabilities
    - < stenting of the ductal system
- Percutaneous FNA under image guidance
  - < Transabdominal ultrasound (US)
  - < Computed tomography (CT)

ENDOSCOPIC ULTRASOUND-FINE NEEDLE ASPIRATION (EUS-FNA)
Brush cytology (ERCP)
ERCP PERFORMANCE

• Sensitivities for the diagnosis of pancreatic neoplasia between 45% and 70%

• Sampling improvement

• Diagnosis improvement
  – Thin layer slides
# Differential Diagnosis

<table>
<thead>
<tr>
<th></th>
<th>ERCP</th>
<th>FNAB</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Benign Pathologies</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pancreatitides</td>
<td>Pancreatitides</td>
<td>Pancreatitides</td>
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<tr>
<td>Cholangitis</td>
<td>Cholangitis</td>
<td>Pseudocyst</td>
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<tr>
<td>IPMN</td>
<td>IPMN</td>
<td>Abcess</td>
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<td></td>
<td></td>
<td>Cystadenoma</td>
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<tr>
<td></td>
<td></td>
<td>Endocrine Hyperplasia</td>
</tr>
<tr>
<td><strong>Malignant Pathologies</strong></td>
<td>Cholangiocarcinoma</td>
<td>Ductal pancreatic Adenocarcinoma</td>
</tr>
<tr>
<td></td>
<td>Ductal pancreatic Adenocarcinoma</td>
<td>IPMN</td>
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<tr>
<td></td>
<td></td>
<td>Ductal pancreatic Adenocarcinoma</td>
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<tr>
<td></td>
<td></td>
<td>Endocrine Tumour</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cystadenocarcinoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lymphoma</td>
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<tr>
<td></td>
<td></td>
<td>Metastasis</td>
</tr>
</tbody>
</table>
Percutaneous aspiration ➔ Ct

Sensitivities for the diagnosis of pancreatic neoplasia
85 to 95%

< EUS-FNAB
75 to 95%
<table>
<thead>
<tr>
<th>Percutaneous aspiration 3%</th>
<th>EUS-FNA 0-2%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Major Complications</strong></td>
<td><strong>Major Complications</strong></td>
</tr>
<tr>
<td>Haemorrhage</td>
<td>Perforation</td>
</tr>
<tr>
<td>Acute Pancreatitis</td>
<td>Haemorrhage</td>
</tr>
<tr>
<td>Sepsis &lt; cystic lesion</td>
<td>Sepsis &lt; cystic lesion</td>
</tr>
<tr>
<td></td>
<td>Acute Pancreatitis</td>
</tr>
<tr>
<td><strong>TUMOR SEEDING ALONG NEEDLE TRACT &lt;1%</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Minor Complications</strong></td>
<td><strong>Minor Complications</strong></td>
</tr>
<tr>
<td>Abdominal discomfort</td>
<td>Abdominal discomfort</td>
</tr>
<tr>
<td>Hematoma</td>
<td>Hematoma</td>
</tr>
<tr>
<td>Vasovagal reaction</td>
<td>Vasovagal reaction</td>
</tr>
</tbody>
</table>
PANCREATIC EUS-FNA

• Part of a routine algorithm
  – Small lesions < 5mm
  – Proximity of the lesion
    • dissemination
  – During staging
  – No complications 0-2%

• Sensitivity: 76 - 94%
• Specificity: 100%
• False positive cases: rare
• False negative cases: 9% (4-14)
  – < Percutaneous biopsies: 20%
  – < ERCP: 30%

→ Suspicious cases: 5.4 - 12%

Eloubeidi MA et al, Cancer Cytopathol 2003
Lin F et al, Cancer Cytopathol 2003
Larghi A et al, Gastrointest Endoscopy 2004
Raut CP et al, J Gastrointest Surg 2003
CONTRAINDICATIONS

- Contraindications for upper endoscopy

  - Absolute contraindications
    - Patient instability to cooperate
    - Severe shock
    - Respiratory distress

  - Relative contraindication
    - Coagulopathies
SAMPLE PREPARATION

⇒ ADEQUATE SAMPLES

⇒ CORRECT INTERPRETATION
CAUSES OF FALSE-NEGATIVE DIAGNOSIS

• Sampling errors
  – Small lesions
  – Difficult anatomic location
    • Isthmus, uncinate processus
  – Extensive fibrosis
  – Extensive necrosis
  – Excessive bleeding
  – Operator’s inexperience
CAUSES OF FALSE-NEGATIVE DIAGNOSIS

• Obscuring factors
  – Excessive air drying
  – Obscuring inflammation
  – Obscuring necrotic debris
  – Contamination by benign gastrointestinal epithelium
CAUSES OF FALSE-NEGATIVE DIAGNOSIS

• Interpretative errors
  – Under diagnosis of well-differentiated or low grade neoplasms
  – Non specific cyst fluid findings
ASSESSMENT OF SPECIMEN ADEQUACY

• « Even trained endosonographers were not able to provide a reliable assessment of pancreatic-mass FNA adequacy by using gross visual inspection of the specimen on a slide. »

• « Rapid on-site cytopathology reduced the number of passes, ensured specimen adequacy, provide definitive diagnosis and should be used if possible. »

• ↑ 7 à 10% diagnostic value

• Number of passes
  – ➔ 10-50

Binmoeller et al, Gastrointest Endosc 2002,56:suppl S86-91
Chang et al, Gastrointest Endosc 2002,56:suppl S28-34
Klapman et al, Am J Gastroenterol 2003,98(6);1289-94
Savoy AD et al, Gastrointest Endosc. 2007
Nguyen YP et al, Gastrointest Endosc. 2009
SAMPLE PREPARATION

1. **Air dried smears**
   - Diff-Quik stain
   - **Onsite assessment**
     - specimen adequacy
       » ↓ numbers of required passes
       » ↓ risk and unpleasantness for the patient
     - Preliminary diagnosis
       » Need for additional material for ancillary studies
SAMPLE PREPARATION

• 2. Sample rinsed in alcohol-based solution
  – Thin layer slides
  – Papanicolaou stain
  – Lost of background material
<table>
<thead>
<tr>
<th></th>
<th><strong>Diff Quick</strong></th>
<th><strong>PAPANICOLAOU</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Technical dependence</strong></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Air dried</strong></td>
<td>No artefact</td>
<td>Artefacts</td>
</tr>
<tr>
<td><strong>Liquid-based preparation</strong></td>
<td>Artefacts</td>
<td>No artefact</td>
</tr>
<tr>
<td><strong>Cellular size</strong></td>
<td>Increased</td>
<td>Same as histology</td>
</tr>
<tr>
<td><strong>Cytoplasm</strong></td>
<td>Well seen</td>
<td>Less well seen</td>
</tr>
<tr>
<td><strong>Nuclei</strong></td>
<td>Not always seen</td>
<td>Well seen</td>
</tr>
<tr>
<td><strong>Nucleoli</strong></td>
<td>Well seen</td>
<td>Well seen</td>
</tr>
<tr>
<td><strong>Stroma</strong></td>
<td>Well seen</td>
<td>Well seen</td>
</tr>
</tbody>
</table>
SAMPLE PREPARATION

• **3. Cell block** < clotted bloody material
  – Alcohol based solution
  – 10% neutral buffered formalin
  
  – Information about cellular architecture
  – Immunocytochemistry
CYTOBLOC

1. Fixation
2. Centrifugation
3. Polymerisation
4. Inclusion in paraffine

- Histologic slides
- HE stain
- Special stains
- Immunohistochemistry
PANCREATIC CYTOPATHOLOGY
CYTOLOGY OF NORMAL PANCREAS

• **Acinar cells = predominant cell type**
  – Small to medium-sized cohesive groups
  – Some single cells
  – Pyramidal or triangular shape
  – Abundant granular cytoplasm
  – Round, eccentric or central nuclei
  – Fine chromatin
  – Often distinct nucleoli

• **Papanicolaou stain**
  – Blue-green

• **Air dried Diff quik stain**
  – Enhance abundance and granularity of the cytoplasm
CYTOLOGY OF NORMAL Pancreas

• Ductal cells < larger interlobular ducts
  – Two-dimensional flat sheets with « honeycomb » appearance
  – Cuboidal to columnar shape
  – Basally located nuclei
  – Scant pale cytoplasm
  – Round to oval nuclei
  – Occasional goblet cells

• Papanicolaou stain
  – Blue

• Papanicolaou stain
  – Purple
CYTOLOGY OF NORMAL PANCREAS

• Islet cells
  – Rarely identified
  – Tail of the pancreas
CONTAMINANTS < EUS-FNA

• **Duodenal mucosa**
  
  • *Trans duodenal* lesion in the head and uncinate
    – Two-dimensional flat sheet
    – Variable single cells
    – Round nuclei
    – Pale cytoplasm with well-defined borders
    – Intermixed goblet cells
    – Thin extra cellular mucus
CONTAMINANTS < EUS-FNA

• **Gastric mucosa**
  - < transgastric < lesions of the pancreatic body or tail
  - Two-dimensional flat sheet
  - Variable single cells
  - Round nuclei
  - Pale cytoplasm with well-defined borders
    • Frequently admixed with mucus
CONTAMINANTS < PERCUTANEOUS ASPIRATION

• **Mesothelial cells**
  – Mistaken for ductal epithelium
    • Two-dimensional flat sheet
    • Round to oval nuclei
    • Moderate amount of pale cytoplasm
    • Intercellular windows

• **Hepatocytes**
  – Polygonal cells Abundant well defined granular cytoplasm
  – Round to oval nuclei
  – Prominent nucleoli
GENERAL APPROACH OF PANCREATIC CYTOPATHOLOGY

• Clinical and imaging data are essential to provide diagnosis

• Starting point: solid or cystic lesion
  – Quite different differential diagnosis

• Trans duodenal or gastric EUS-FNA

• Presence of chronic pancreatitis
REPORTING TERMINOLOGY

• Critical for the clinical management

• **Solid lesions**
  – No neoplasm seen
  – Atypical/indefinite diagnosis
  – Definitive diagnosis of neoplasm

• **Cystic lesions**
  – Non-specific cyst
  – Descriptive/qualified diagnosis
  – Definitive diagnosis of neoplasm
I Solid lesions

PANCREATIC DUCTAL ADENOCARCINOMA

CHRONIC PANCREATITIS
PANCREATIC DUCTAL ADENOCARCINOMA

• Most common cytological neoplastic diagnosis

• 85 to 90% of all pancreatic cancers

• Location
  – 50% < head
  – 15% < body
  – 5% < tail

• Imaging technique = solid mass
PANCREATIC DUCTAL ADENOCARCINOMA

- Cytological features

- High cellularity

- Background
  - Clean
  - Inflammatory
  - Mucinous
  - Necrotic

- Predominantly ductal cells
PANCREATIC DUCTAL ADENOCARCINOMA

• Cytological features

• Cell groups with overcrowding and/or disorderedly arrangement

• Isolated atypical cells
  – Often few in number
  – Extremely helpful for making the diagnosis

• Nuclear atypia
  – Nuclear enlargement (at least 2X the size of red blood cells)
  – Irregular nuclear contours
  – Coarse chromatin
  – Macro nucleoli
  – Bi- and multinucleation
  – Mitotic figures
VARIANTS OF PANCREATIC DUCTAL CARCINOMA

• Adenosquamous carcinoma (5%)

• Anaplastic carcinoma
  – DD: melanoma, lymphoma, sarcoma

• Osteoclastic giant cell carcinoma

• Signet ring cell carcinoma (1%)

• Foamy gland adenocarcinoma

• Small cell undifferentiated carcinoma
  – DD: metastatic small cell carcinoma
Adenosquamous carcinoma

CK5/6
Anaplastic carcinoma
SIGNET RING CELL CARCINOMA
DIFFERENTIAL DIAGNOSIS OF PANCREATIC DUCTAL ADENOCARCINOMA

• Chronic pancreatitis

• Acinar cell carcinoma

• Endocrine tumour

• Metastases
CHRONIC PANCREATITIS

• Cellularity
  – variable, scant to cellular depending on fibrosis

• Presentation
  – Monolayer cohesive honeycomb pattern tissue fragments
  – Rare single cells
  – Rare focal and mild peripheric crowding

• Type of cells
  – Mixed cellular elements: ducts, acini, inflammatory cells, fibrosis

• Necrosis
  – Rare
<table>
<thead>
<tr>
<th>Chronic pancreatitis</th>
<th>Well differentiated adenocarcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Various cellular elements</td>
<td>Ducts</td>
</tr>
<tr>
<td>Ducts</td>
<td></td>
</tr>
<tr>
<td>Acini</td>
<td></td>
</tr>
<tr>
<td>Ilets</td>
<td></td>
</tr>
<tr>
<td>Inflammatory cells</td>
<td></td>
</tr>
<tr>
<td>Flat monolayered sheets with uniformly spaced nuclei</td>
<td>Flat, monolayered sheets with noticeable nuclear crowding and overlapping</td>
</tr>
<tr>
<td>Round to ovale nuclei</td>
<td>Abnormally shaped nuclei: pyramidal, carrot-shaped</td>
</tr>
<tr>
<td>Normal chromatin distribution</td>
<td>Frequent chromatin clearing</td>
</tr>
<tr>
<td>Few small nucleoli</td>
<td>Many prominent nucleoli</td>
</tr>
<tr>
<td>Rare to no intact single epithelial cells</td>
<td>Few to many intact epithelial cells</td>
</tr>
<tr>
<td>Rare to no mitosis</td>
<td>Rare to no mitosis</td>
</tr>
<tr>
<td>No necrosis</td>
<td>Generally no necrosis</td>
</tr>
</tbody>
</table>
WELL-DIFFERENTIATED DUCTAL ADENOCARCINOMA
CHRONIC PANCREATITIS
DIAGNOSTIC PITFALLS

• Nature of the lesion
  – Localisation
  – Prominent fibrosis

• Chronic pancreatitis
  – Reactive architectural and/or cytological atypia = PanIN

• Well-differentiated ductal adenocarcinoma
  – Lack of obvious cytological features of malignancy

• Conservative attitude of the cytopathologists
MAJOR AND MINOR CRITERIA FOR DIAGNOSIS OF ADENOCARCINOMA

• Major
  – Nuclear crowding or overlapping
  – Irregular nuclear membrane
  – Irregular chromatin

• Minor
  – Nuclear enlargement
  – Single epithelial cells
  – Necrosis
  – Mitoses

Minimum 2 major criteria
or
1 major criteria and 3 minor criteria

100% de diagnostics

Robins DB et al, Acta Cytol, 1995
APPROPRIATE DIAGNOSTIC CRITERIA

- Major and minor Robin’s criteria
  - Nuclear membrane irregularity (M)
  - Nuclear crowding and overlapping (M)
  - Nuclear enlargement (m)

None of these criteria, when present alone is enough to diagnose malignancy

Inspection of all epithelial sheets

Eloubeidi MA et al, Cancer Cytopathol 2003
Lin F et al, Cancer Cytopathol 2003
Robins DB, Acta Cytol 1995
APPROPRIATE DIAGNOSTIC CRITERIA

- Minimal number of cells necessary to diagnose malignancy
  - Subject of debates

- More than six groups of atypical cells showing not all cytological criteria of malignancy
  or

- All cytological criteria of malignancy present in less than six epithelial groups

Considered as suspicious for adenocarcinoma

# Diagnostic Criteria

## Ancillary Testing

<table>
<thead>
<tr>
<th>Biomarkers</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>P53</td>
<td>48%</td>
<td>97%</td>
</tr>
<tr>
<td>DPC4</td>
<td>21%</td>
<td>100%</td>
</tr>
<tr>
<td>P16</td>
<td>82%</td>
<td>73%</td>
</tr>
<tr>
<td>MUC1</td>
<td>96%</td>
<td>94%</td>
</tr>
<tr>
<td>Mesothelin</td>
<td>68-100%</td>
<td>91-95%</td>
</tr>
<tr>
<td>PSCA</td>
<td>84%</td>
<td>91%</td>
</tr>
</tbody>
</table>

Chhieng DC, Stelow EB. Pancreatic Cytopathology
Essential in Cytopathology
Series Editor
Rosenthal DL
Springer 2007
Malignant transformation of ductal cells is associated with a modification of MUC1 expression, characterised by strong cytoplasmic positivity and sometimes focal apical staining, whereas normal expression is limited to the apical/luminal pole of the ductal or acinar cells, which can be used as internal control.
Malignant transformation of ductal cells is associated with a modification of MUC1 expression, characterised by strong cytoplasmic positivity and sometimes focal apical staining, whereas normal expression is limited to the apical/luminal pole of the ductal or acinar cells, which can be used as internal control.
AUTOIMMUNE PANCREATITIS

- «The diagnosis should be suggested with chronic pancreatitis without any apparent risk factors for chronic pancreatitis»

- High degree of clinical suspicion for ductal adenocarcinoma

- IgG4
  - Immunocytochemistry
  - Serum assay
ACINAR CELL CARCINOMA

- Rare primary pancreatic neoplasm
- Affects older individuals
- Men > woman
- Better overall survival rate
ACINAR CELL CARCINOMA

- Cytological features
  - Cellular aspirate
    - Single cells
    - Loose clusters with formation of acini
  - Background
    - No necrosis and debris
    - Naked nuclei
ACINAR CELL CARCINOMA

- Cytological features
  Neoplastic cells
  - Abundant granular cytoplasm with indistinct cell borders
  - Atypical central or eccentric nuclei with prominent nucleoli
ACINAR CELL CARCINOMA

• Differential diagnosis
  
  – Pancreatic endocrine tumour
    • Rosette formation
    • Smaller cells with scant cytoplasm
    • « plasmacytoid appearance »
    • Salt and pepper chromatin

  – Solid-pseudo papillary neoplasm
    • Cytoplasmic hyaline globules, PASD+
    • Branching papillary clusters
    • Myxoid stroma

  – Pancreatoblastoma
    • Two cell population
      – Primitive epithelial cells
      – Stromal cells

  – Normal pancreatic parenchyma
    • Mixture of acini and ductal elements
    • Acini in small grapelike clusters

  – Ductal adenocarcinoma (undifferentiated variety)
ACINAR CELL CARCINOMA

Ancillary testing

- **Reactive**
  - Pancytokeratin
  - Chymotrypsin
  - Alpha-1-antichymotrypsin
  - Alpha-1-antitrypsin
  - Lipase
  - Trypsin

- **Non reactive**
  - CD56
  - Synaptophysin
  - Chromogranin A
  - Vimentin
PANCREATOBLASTOMA

• 0.5% of epithelial tumours

• Children ≤ 10 years of age

• Slight male predominance
PANCREATOBLASTOMA

• Cytological features
  – Cellular aspirate
  – Biphasic population
    • Epithelial cells
      – Tree-dimensional syncitial groups of pleomorphic cells
      – Acinar structures with abundant cytoplasm and prominent nucleoli
      – Squamoid corpuscles
PANCREATOBLASTOMA

• Cytological features
  – Biphasic population
    • Stromal component
      – Primitive spindle-shaped cells
      – Heterologous stroma (cartilage)
PANCREATOBLASTOMA

• Differential diagnosis

  – Primary pancreatic neoplasms
    • Pancreatic ductal carcinoma
    • Solid pseudopapillary neoplasm
    • Pancreatic endocrine tumour
    • Acinar cell carcinoma

  – Childhood malignancies
    • Wilms tumor
    • Neuroblastoma
    • Malignant lymphoma
    • Other
PANCREATOBLASTOMA

• Ancillary testing

  – Diffusely positive
  • CAM5.2
  • Lipase
  • Trypsin
  • Chymotrypsin
  • Alpha-1-antitrypsin

  – Sometimes positive
  • αFP
  • CEA
  • Ca19-9

  – Scattered cells positive
  • Chromogranin A
  • Synaptophysin
SOLID-PSEUDOPAPILLARY NEOPLASM

• Solid-cystic tumour

• 1% of all exocrine pancreatic neoplasms

• Predominant in adolescent girls and young women

• Low malignant potential
SOLID-PSEUDOPAPILLARY NEOPLASM

• Cytological features
  – Highly cellular aspirate showing relative uniform cell population
  – Single cells
  – Loose clusters
  – Branching papillary tissue with central capillary
SOLID-PSEUDOPAPILLARY NEOPLASM

• Cytological features
  – Monotonous bland cells
  – Scant ill-defined, vacuolated amphophilic cytoplasm
    • Occasionally PAS+
    • Granules or vacuolisation
  – Round to oval nuclei
    • Clefted nuclei or nuclear grooves
  – Myxoid and metachromatic stroma and background
  – Rare necrotic debris (areas of cystic degeneration)
SOLID-PSEUDOPAPILLARY NEOPLASM

- **Differential diagnosis**
  - **Uniform cells**
    - Pancreatic endocrine tumour
    - Acinar cell carcinoma
    - Pancreatoblastoma
  - **Cystic lesion with papillae**
    - Intraductal papillary mucinous neoplasm
SOLID-PSEUDOPAPILLARY NEOPLASM
Ancillary testing

- Reactive
  - Vimentin
  - NSE
  - Progesterone receptor
  - B-catenin
  - Alpha-1-antitrypsin
  - Alpha-1-antichymotrypsin
  - CD10
  - CD3

- No reactive
  - Cytokeratin
  - Chromogranin A
  - CEA
  - Ca19-9
  - Synaptophysin
  - Trypsin
  - Chymotrypsin
  - Amylase
  - Estrogen receptor
PANCREATIC ENDOCRINE TUMORS

• Diagnosed in 1/100000 people

• 2% of pancreatic neoplasms

• 2 major types
  – 60-85% functioning tumour: with clinical syndrome directly related to a hormone, secreted by the tumour
  – 20-40% non functioning tumour: incidentaloma or pancreatic mass

• Any age (more common in older adults)

• No sex predilection

• Tail>>>>> head

• 20% are calcified

• Association with
  – MENI
  – Von Hippel Lindau syndrome
PANCREATIC ENDOCRINE TUMORS

- cytological features
  - Cellular aspirate
  - Monotonous extremely dyshesive cell population
  - Loosely cohesive cell groups
  - Rosette or pseudo rosette formation
PANCREATIC ENDOCRINE TUMORS

cytological features

– Relative uniform round to polygonal cells
– Plasmacytoid cells
– Delicate, granular amphophilic or basophilic cytoplasm
– Round to oval nuclei, eccentrically located
– Salt and pepper chromatin
– Small inconspicuous nucleoli
PANCREATIC ENDOCRINE TUMORS

CHROMOGGRANIN A
PANCREATIC ENDOCRINE TUMORS
PANCREATIC ENDOCRINE TUMORS

• Ancillary testing

• For diagnosis
  – Chromogranin A
  – Synaptophysin
  – Mib 1

• For differential diagnoses
  – Cytokeratin
  – MUC 1
  – CD 45…
PANCREATIC ENDOCRINE TUMORS

• Less frequent cytological features
  – Predominantly single cells
  – Diff-quick: Fine red cytoplasmic granules
  – Bi and multinucleation ≠ malignancy
  – Nuclear pleomorphism ≠ malignancy
  – Mitotic figures = suggests aggressive course
  – Naked nuclei
  – Necrotic debris = suggests aggressive course
  – Calcification
  – Amyloid deposition
  – Thin capillaries
II CYSTIC LESIONS OF THE PANCREAS

PSEUDOCYST

↕

CYSTIC MUCUS-PRODUCING NEOPLASIA
CYSTIC LESIONS OF THE PANCREAS

• Congenital cyst
  – Simple or solitary true cyst
  – Polycystic diseases
  – Cystic fibrosis
  – Enteric duplication cysts
  – Biliary and pancreatic duct anomalies
  – Dermoid cyst
  – Lympho epithelial cysts

• Retention cyst
  – Post obstructive
    • < pancreatic cancer
    • < pancreatic lithiasis
    • < cholelithiasis, cholecystitis
    • < parasitic infections
      – < amebic, clonorchis sinensis, Ascaris lumbricoides

• Miscellaneous cyst
  – Nutritional (tropical) fibrocalcic pancreatitis
  – Extra pancreatic cysts

• Infectious cyst
  – Secondary pancreatic infection
  – Hydatid cyst
  – Giardia
CYSTIC LESIONS OF THE PANCREAS

- Pseudocyst
  - Postinflammatory
  - Post-traumatic
  - Postchirurgical
  - Congenital

- Cystic neoplasms
  - Serous
    - Serous cystadenoma
  - Mucinous
    - Mucinous cystadenoma
    - Mucinous cystadenocarcinoma
    - Intraductal papillary mucinous neoplasm
  - Vascular
    - Lymphangioma
    - Hemangioma
  - Solid pseudopapillary tumour
  - Cystic pancreatic endocrine tumour
  - Ductal carcinoma with cystic degeneration
  - Acinar cell cystadenoma carcinoma
PRAGMATIC APPROACH

• Imaging data

• Identification of mucus < right clinical context

• Chemical analysis of pancreatic cyst fluid
  
  – Amylase <250U/L
    • Serous cystadenoma and mucinous neoplasm
  
  – CEA< 250ng/mL
    • Serous cystadenoma and pseudocyst

  – CEA>800ng/mL
    • Mucinous neoplasm

  – Ca19-9<36U/mL
    • Serous cystadenoma and pseudocyst
PSEUDOCYST

• Most common cystic lesion (75-90%)

• Cavities
  – < lysis tissue after leakage of pancreatic enzyme
  – DD retention cyst < dilatation of the pancreatic duct system

• Often known histories of chronic pancreatitis
  – < alcoholism
  – < biliary lithiasis

• Intra-extrapancreatic

• Unique/multiple

• Unilocular
  – May connect with the pancreatic duct

• Cyst fluid
  – CEA< 250ng/mL
  – Ca19-9<36U/mL
PSEUDOCYST

• Cytological features
  – Red brown fluid
  – Variable inflammatory cells
  – Hemosiderin-laden macrophages
  – Background
    • Blood, granular debris
    • Occasionally bile pigment
  – No cyst lining-epithelium
  – Normal pancreatic components and fibroblasts
PSEUDOCYST

• Epithelial cells
  – < Chronic pancreatitis
  – < Contaminant

Mucinous epithelium ≠ contaminant
Background mucin
Mucin-containing histiocytes

Excludes the diagnosis
CYSTIC MUCUS-PRODUCING NEOPLASIA

• Diagnostic approach

  – 10% EUS-FNA < 10% cystic lesion of the pancreas < 1% malignancy

  – Presence of thick, extracellular mucus strongly favour the diagnosis
    • < gelatinous and sticky material often difficult to smear
    • Mucus < mucus producing neoplasia thicker < gastrointestinal epithelium

  – Amylase < 250 U/L
  – CEA > 800ng/mL

  – The accurate sub classification may not be always possible

⇒ Descriptive interpretation
CYSTIC MUCUS-PRODUCING NEOPLASIA

• MUCUS
  – < gelatinous and sticky material often difficult to smear
  – Mucus < mucus producing neoplasia thicker < gastrointestinal epithelium
  – **Diff-Quick**: purple or metachromatic
  – Papanicolaou: more variable from greenish-blue to orangophilic
INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS

• Both sexes

• Elderly patients < main duct type
  – Younger < branch duct type

• History of recurrent acute pancreatitis
• History of chronic obstructive pancreatitis

• Clear connection between the cyst and the pancreatic duct system

• Throughout the pancreas
  – Mostly head < main duct type
  – Uncinate process < branch duct type

• FNA ⇔ Smaller lesions < branch duct type
• FNA < Sendai consensus guidelines
INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS

• Cytological features
  – "As varied as the histological findings"
  – Overlapping mucinous cystic neoplasm
INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS

• Cytological features

  – Extracellular material
    • Thick, viscous mucus
    • Entrapped inflammatory cells
    • Necrotic debris (higher grade lesion)

  – Cellularity
    • Variable raised in high grade and invasive lesions

  – Variable degrees of cytological atypia
    • Sheets of epithelium < low grade lesions
    • Three-dimensional clusters < high grade lesions

  – Papillary groups

  – Gastric or pancreatobiliary differentiation < low grade lesions

  – Intestinal differentiation < high grade lesions
INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS

• Ancillary
MUCINOUS CYSTIC NEOPLASMS

- Less common than IPMN
- Middle-aged woman
- Body and tail of the pancreas
- Multioculated cysts
- No connection with the pancreatic duct system
- Ovarian-type stroma
MUCINOUS CYSTIC NEOPLASMS

• Cytological features

  – Extracellular material
    • Thick, viscous mucus
    • Entrapped inflammatory cells
    • Necrotic debris (higher grade lesion)

  – Cellularity
    • Variable raised in high grade and invasive lesions

  – Variable degrees of cytological atypia
    • Sheets of epithelium < low grade lesions
    • Three-dimensional clusters < high grade lesions
DIFFERENTIAL DIAGNOSIS AND PITFALLS

• MCN-IPMN

• Mucus
  – Thick
  – Metachromatic
  – Entrapped inflammatory cells
  – Necrotic debris
  – Individual or groups of tumour cells

• BENIGN GASTRIC AND INTESTINAL CONTAMINANT

• Mucus
  – Thin
  – Few inflammatory cells
  – Occasional entrapped groups of benign gastric or intestinal epithelium

• Cytomorphology
  – « honeycomb » pattern
SEROUS CYSTADENOMA

- Almost universally benign
- Tail

- Micro or macrocystic
  - < according the size of their cysts
  - Similar cytological findings

- Woman > man

- Classic radiologic features
  - Central scar
  - Multiloculated cyst

- Cyst fluid
  - Amylase <250U/L
  - CEA< 250ng/mL
  - Ca19-9<36U/mL
SEROUS CYSTADENOMA

• Cytological features
  – Scant cellularity
    • Non diagnostic interpretation
  – Watery fluid
  – Proteinaceous or bloody background
  – Monolayered sheets
  – Small, flat clusters
  – Homogeneous, bland, round nuclei
  – Clear cytoplasm with well-defined borders
  – Cytoplasmic glycogen (PAS-PASD)
SEROUS CYSTADENOMA

• Differential diagnosis
  – Benign pancreatic ductal and acinar epithelium
  – Mesothelial cells
  – Cystic pancreatic endocrine tumour
  – Endothelium neoplasm (hemangioma)
  – Mucinous cystic neoplasm