Pancreatic Cytopathology: The Hopkins Experience

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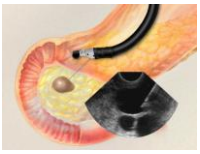
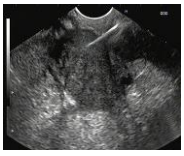
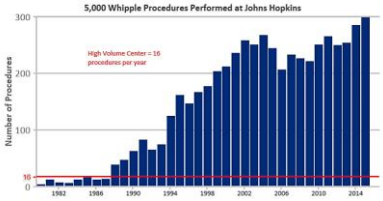
Fine Needle Aspiration of the Pancreas

- 60-80% of FNA diagnoses are MALIGNANT
  - 85-90% are ACA

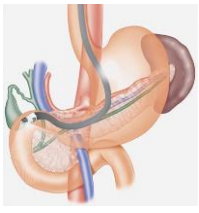



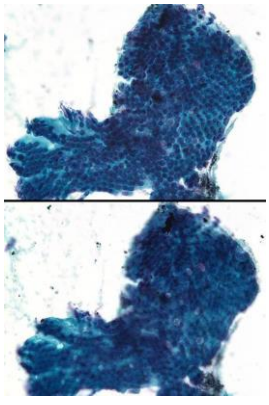
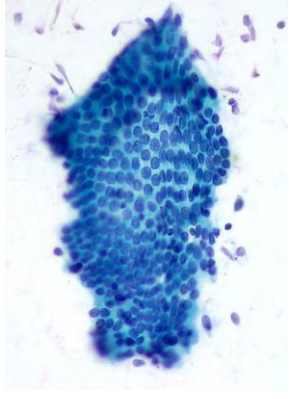
- 2015 – 960 Pancreatic FNAs
- Pancreas Multidisciplinary Cancer Clinic
- Pancreas Cyst Clinic


Diagnostic Pitfalls

❖ 3rd most common organ where misinterpretation of normal cellular elements lead to an erroneous "neoplasm" diagnosis#

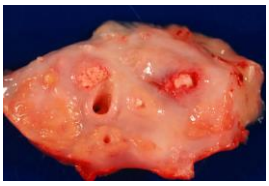
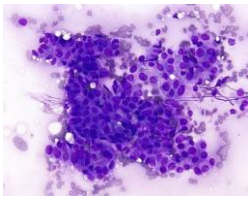
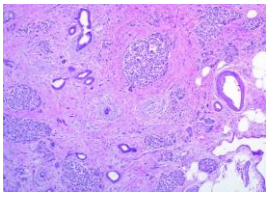
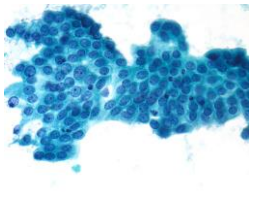


#Young NA, et al. Arch Pathol Lab Med 2002

Pancreatic Cytopathology The "Fear Factor"

- ~ 10% of Whipple surgeries performed for presumed malignancy (clinical and/or FNA findings) reveal benign disease on histopathology
- ~ 25% of these have autoimmune pancreatitis (AIP) or lymphoplasmacytic sclerosing pancreatitis (LSP)

Chronic Pancreatitis - a diagnosis of exclusion

Papanicolaou Society of Cytopathology – Proposed Terminology Scheme for Pancreatobiliary Cytology

I. Nondiagnostic
- Insufficient cellular material for diagnosis

II. Negative
- Pancreatitis-acute, chronic, autoimmune
- Pseudocyst
- Lymphoepithelial cyst
- Spenule/accessory spleen

III. Atypical
- Mild-moderate cellular atypia, NOS
- Ductal epithelium with mucinous metaplasia and mild-moderate nuclear atypia

IV. Neoplastic

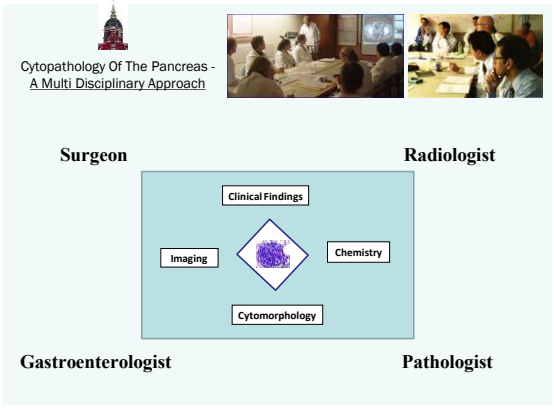
Benign
- Serous cystadenoma
- Mature teratoma
- Schwannoma

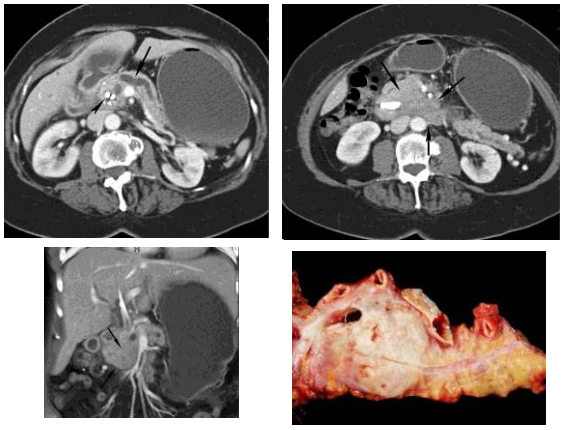
Other
- Pancreatic neuroendocrine tumor
- Solid-pseudopapillary neoplasm
- Mucinous cyst (IPMN or MCN), NOS, e.g. only thick, colloid-like mucin or elevated CEA or +*KRAS* mutation
- Mucinous cyst (IPMN or MCN) with low-grade mucinous epithelium/dysplasia
- Mucinous cyst (IPMN or MCN) with high-grade dysplasia
- GIST

V. Suspicious
- Severe cellular atypia, suspicious for invasive ductal carcinoma or other high-grade malignant neoplasm

VI. Positive/Malignant
- Adenocarcinoma of the pancreatobiliary ducts and variants
- Acinar cell carcinoma
- High-grade neuroendocrine carcinoma (small and large cell type)
- Pancreatoblastoma
- Lymphoma(s)
- Sarcoma (s)
- Metastases

Pitman MB, et al. Diagn Cytopathol 2014



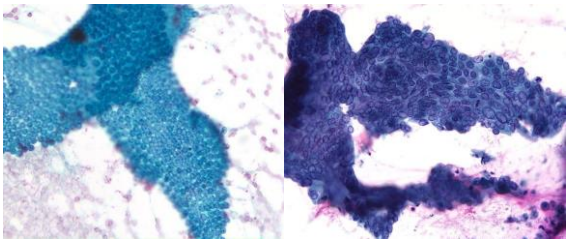


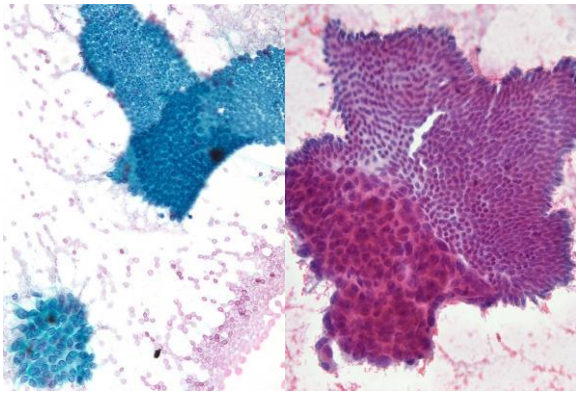
Solid Neoplasms Of The Pancreas

[Exocrine Pancreas]

- Ductal Adenocarcinoma
- Variants
- Acinar Cell Carcinoma
- Pancreatoblastoma

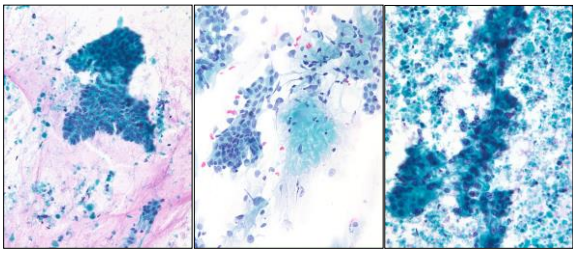
Ductal Adenocarcinoma





ACA – Cytologic Grading

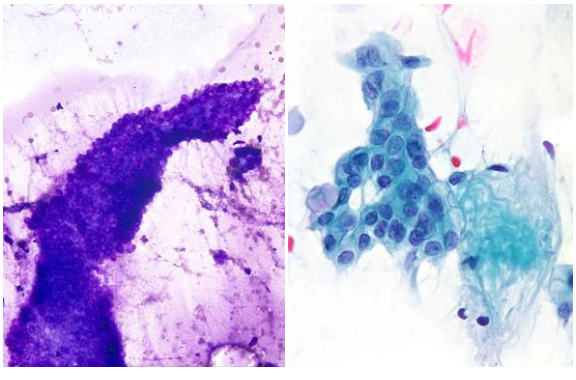
Well -	Moderate -	Poor -
Flat Sheets	→	More crowded 3-D
Tissue fragments	→	More single cells
Pleomorphism (Focal)	→	Pleomorphism (Extensive)
Hypochromatic Micronucleoli	→	Hyperchromatic Macronucleoli

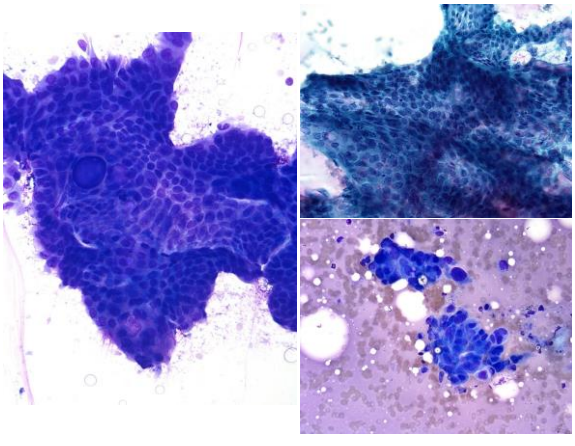


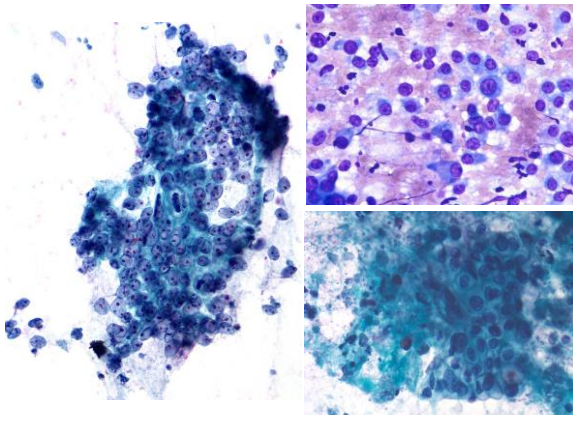
Why do we grade?

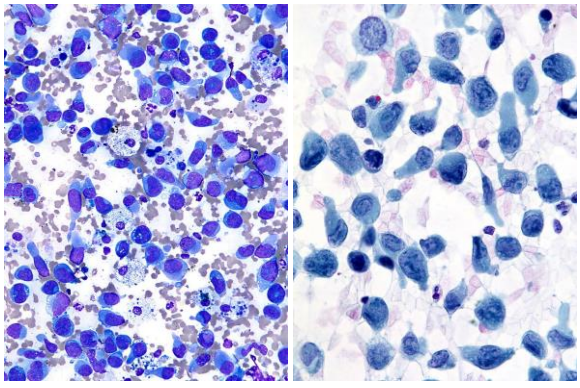
- Fine-tune our diagnosis and differential diagnoses
- Optimize cancer therapy
- Prognostication (indicator of poor outcome in resectable disease)

- Grading should preferably be two tiered (not five)





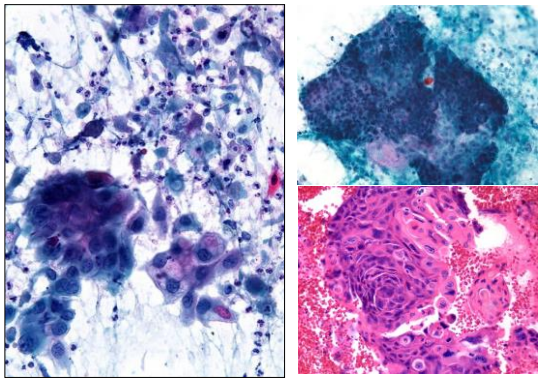


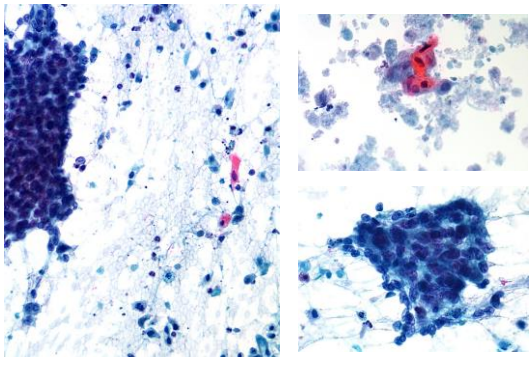


Ductal CA - Variants

- Mucinous Non-cystic Adenocarcinoma (Colloid)
- Signet-ring Cell Carcinoma
- Medullary Carcinoma
- Adenosquamous Carcinoma
- Undifferentiated Carcinoma With Osteoclast-like Giant Cells
- Anaplastic (Undifferentiated) Carcinoma

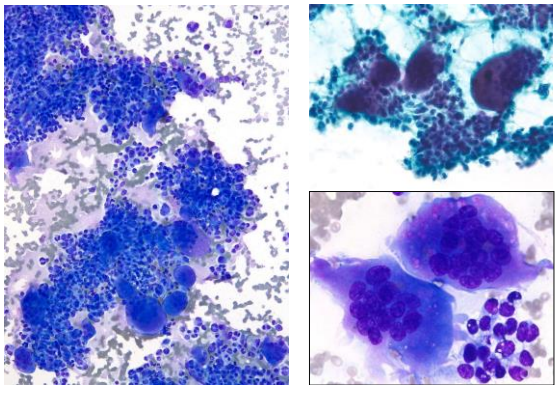
Adenosquamous Cell Carcinoma

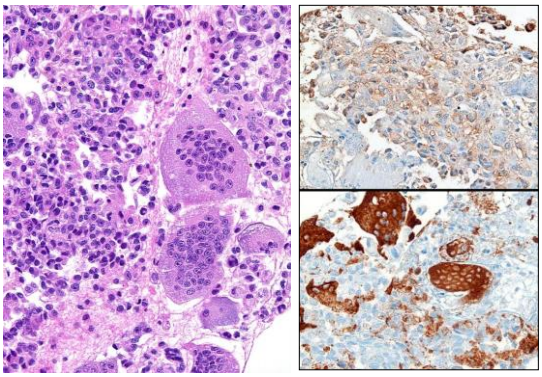




- Poorer Prognosis - median overall survival – 10 mo
- The proportion of squamous differentiation is often not associated with median overall survival (< 30% versus > or = 30%)

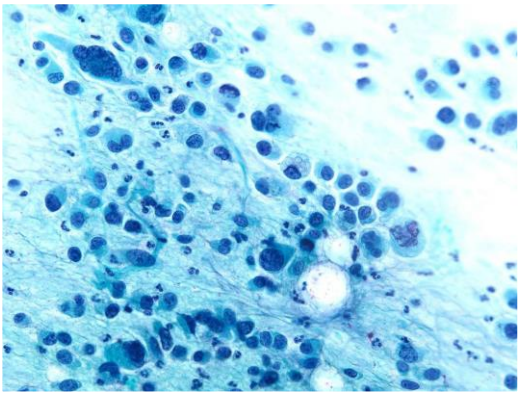
Undifferentiated Carcinoma with Osteoclast-like Giant Cells

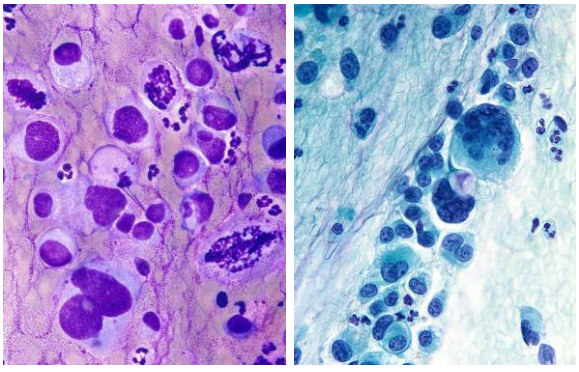




- Often a component of an in-situ or invasive ACA
- Poor prognosis (< one year)

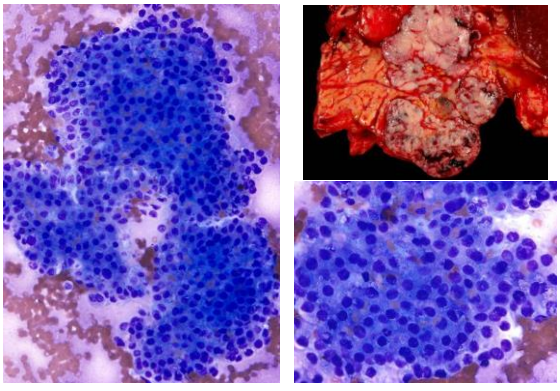
Anaplastic (undifferentiated) Carcinoma

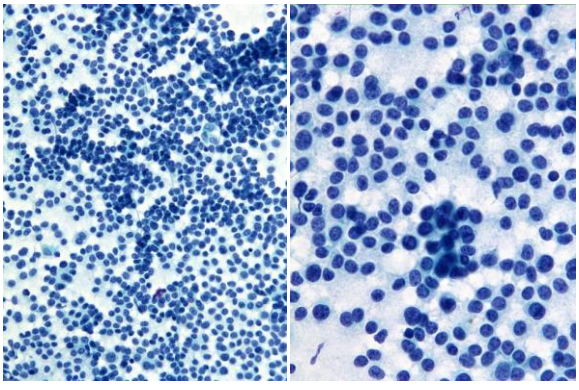


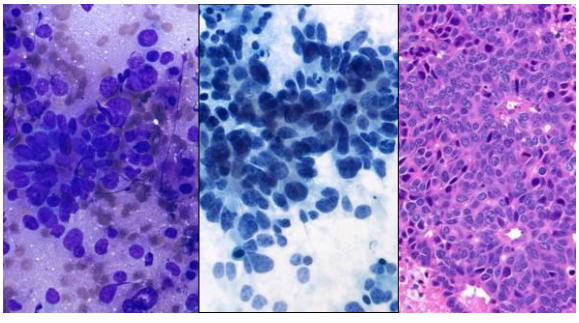


- Extremely bad prognosis
- Rule out metastasis to the pancreas (melanoma)

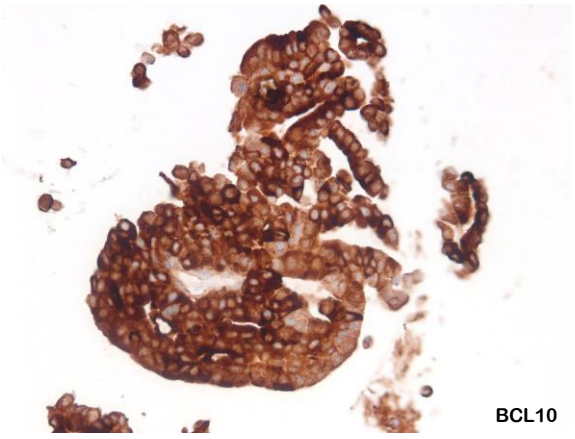
Acinar Cell Carcinoma







- Trypsin/chymotrypsin (90%), BCL-10 (85%)
- Focal neuroendocrine marker immunoexpression (up to 43%)
- Alterations in the *KRAS* oncogene and in the *SMAD4* (*DPC4*) and *p53* tumor suppressor genes are usually not seen
- Overall median survival 19-57 months (age, size and stage)

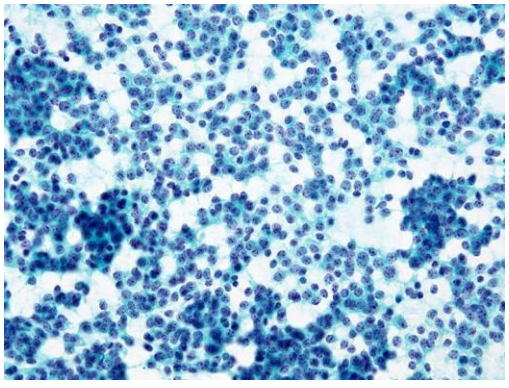


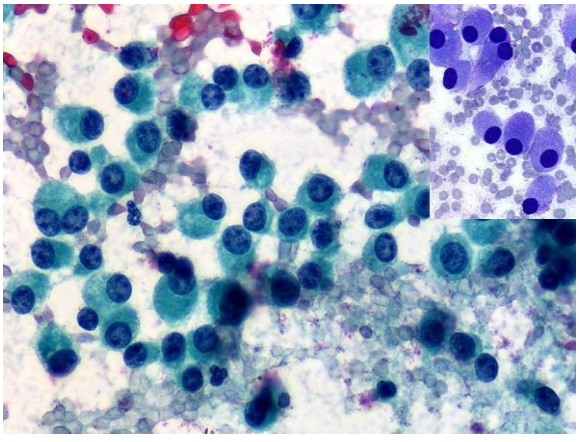
BCL10

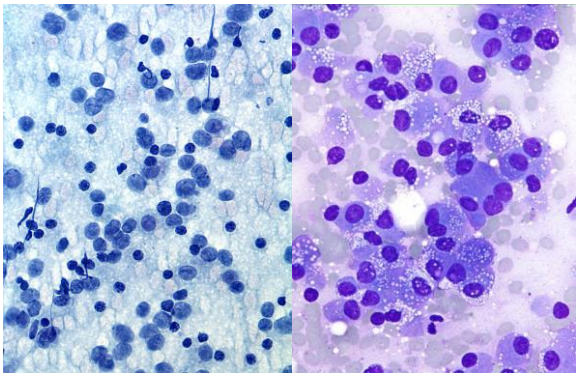
Endocrine Pancreas

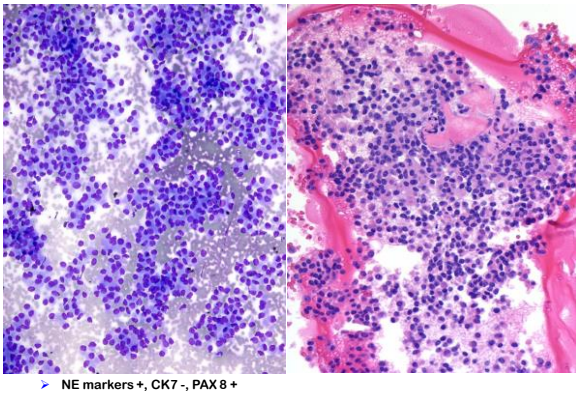
- Pancreatic Neuroendocrine Tumor (PanNet)
- High-grade NE Carcinoma
  - Small cell type
  - Large cell type

Pancreatic Neuroendocrine Tumor (PanNet)

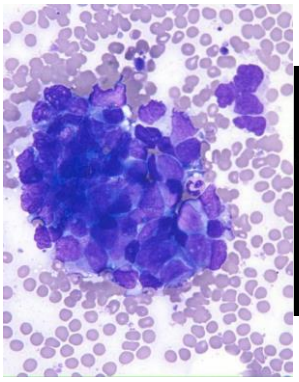


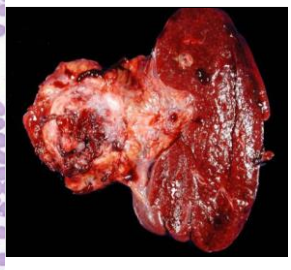


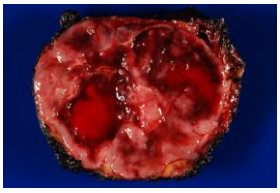


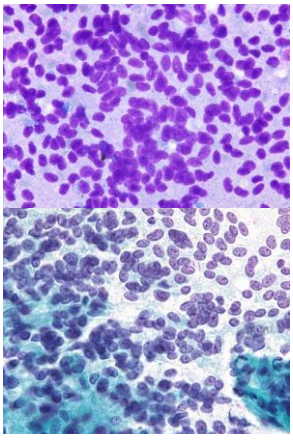


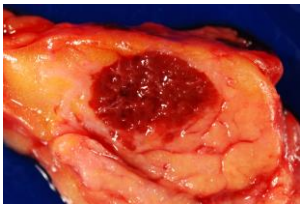
- NE markers +, CK7 -, PAX 8 +
- Size (>0.5cm are malignant)
- Grading with Ki-67 % (G1 0-2%, G2 3-20%, G3->20% or NE Carcinoma)

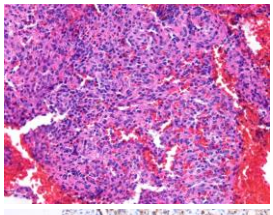


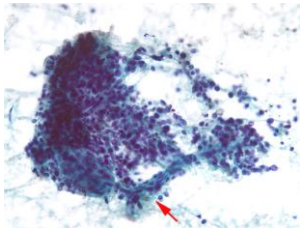


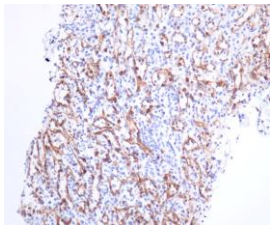






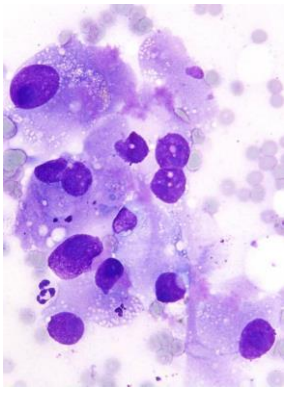


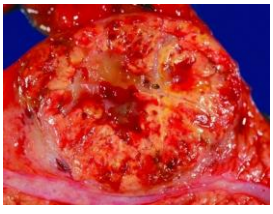


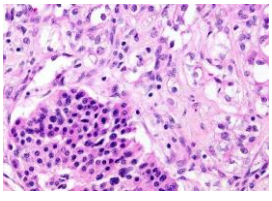


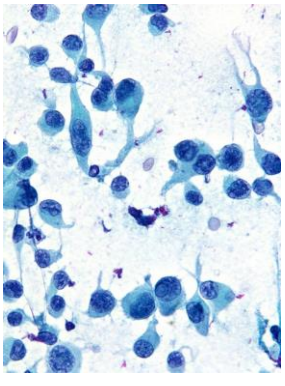
Metastatic Tumors

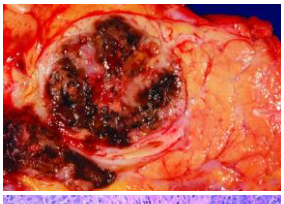
- Adenocarcinomas
  - Lung, Stomach, Colon, Breast
  - Renal Cell Carcinoma
- Hepatocellular Carcinoma
- Malignant Melanoma
- Sarcomas
  - Leiomyosarcoma
  - MFH
  - MPNST

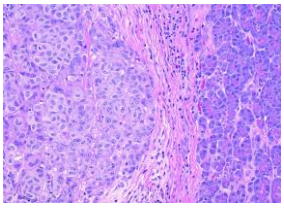








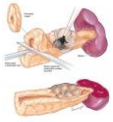




Cystic Neoplasms Of The Pancreas

[Exocrine Pancreas]

- Serous Cystic Neoplasm
- Mucinous Cystic Neoplasm
- Intraductal Papillary Mucinous Neoplasm (IPMN)
- Solid-pseudopapillary Neoplasm

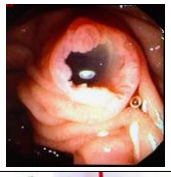


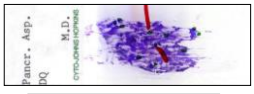
Cystic Lesions Of The Pancreas

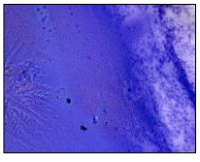
[Practical Issues]

- Morphologic Interpretation
- Radiologic Imaging
- Cyst Fluid analysis
  - CEA, Amylase, CA 19-9, kras
- Terminology

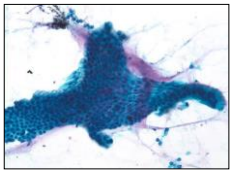
	Mucinous Cystic Neoplasm	Intraductal papillary Mucinous Neoplasm	Solid-pseudopapillary Neoplasm	Serous Cystic Neoplasm
Gender (F:M)	20:1	1:1.5	10:1	7:3
Head/Tail	Tail	Head	Tail=Head	Tail=Head
Relation to Duct	None	Always	None	None
Central Scar	None	None	None	Often
Cyst Contents	Mucinous	Mucinous	Necrotic/ Hemorrhagic	Serous

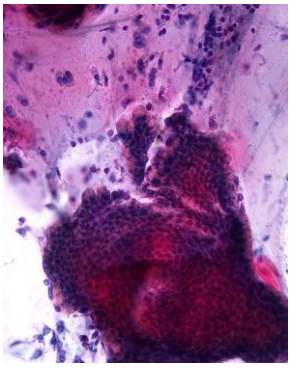


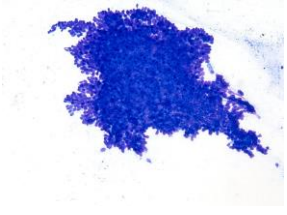


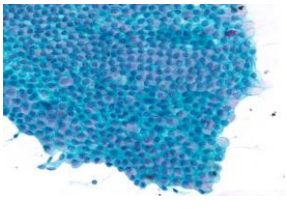


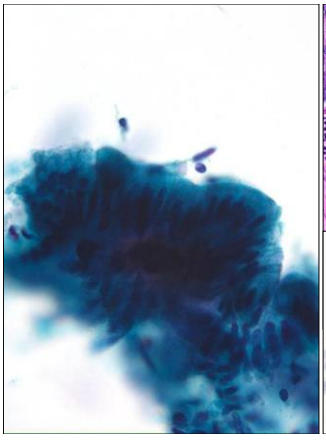
- Cyst Fluid CEA of >190ng/ml
- Ductal Communication

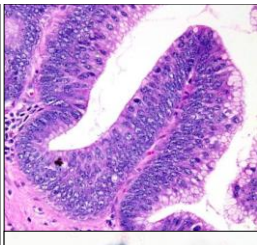


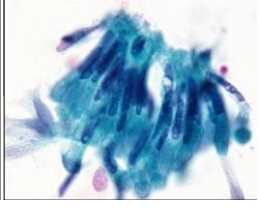


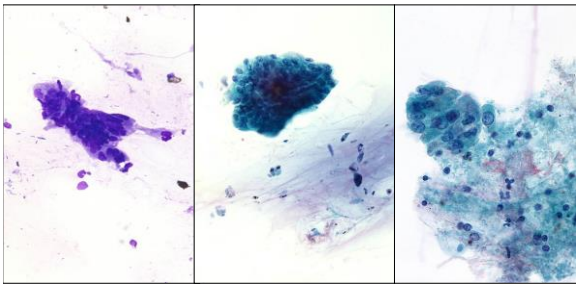


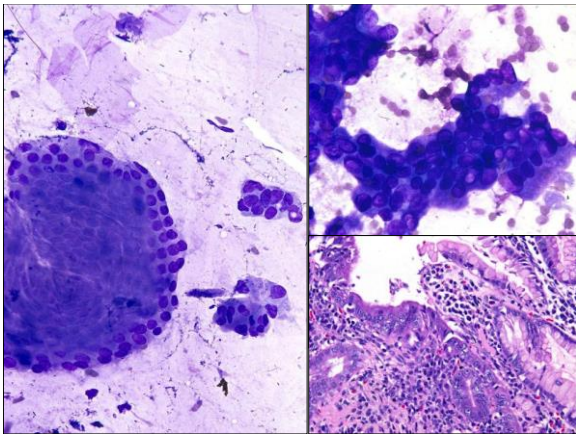






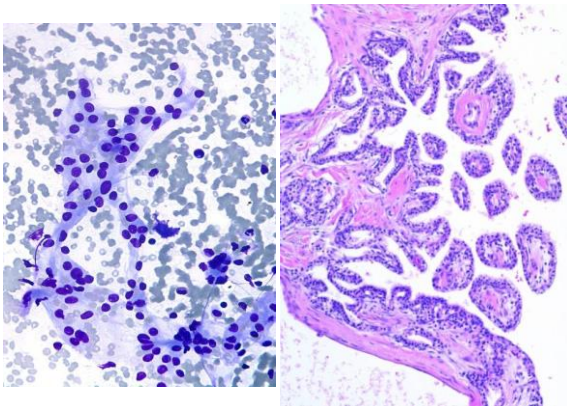




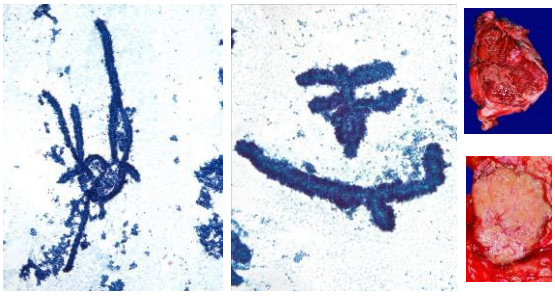


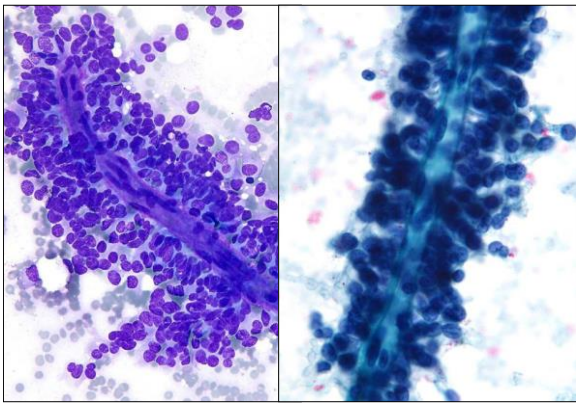
FNA Reporting Terminology

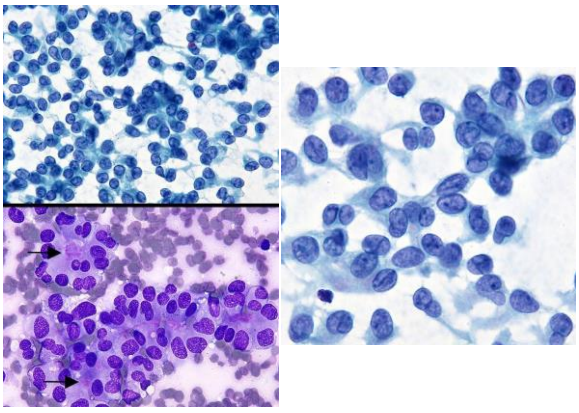
- "Mucin Producing Neoplastic Cyst", consistent with .....
- Negative (or positive) for high-grade dysplasia or carcinoma

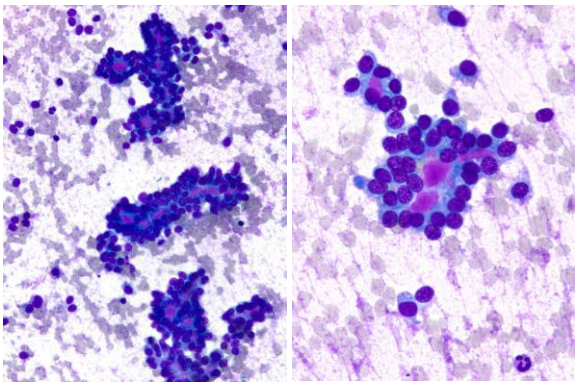


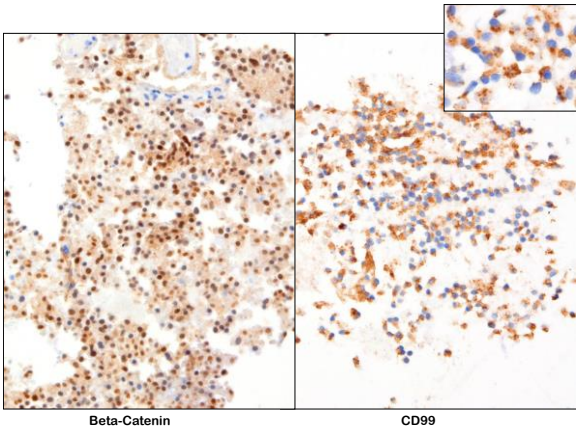
Solid-Pseudopapillary Neoplasm











Beta-Catenin CD99