Mass General Brigham

Pancreatic Cysts

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No disclosures

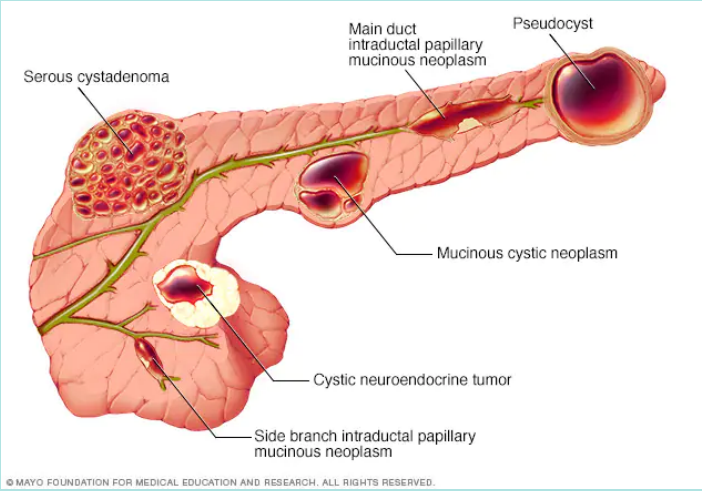
Outline:

Biopsy Technique
Tissue Triage
Biochemical testing
Molecular testing
Cytomorphology
Reporting

Pancreatic Cysts

Differential Diagnosis

- Pseudocyst
- Lymphoepithelial cyst
- Serous cyst
- Mucinous cyst
  - (MCN and IPMN)
- Cystic degeneration of typically solid tumors
  - PanNET
  - SPN
  - other
- Other more rare cysts



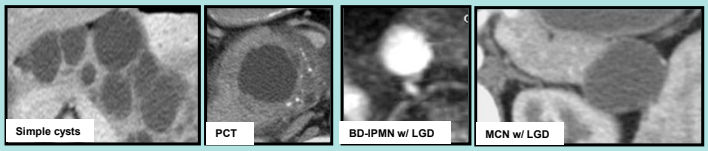
Cytology Interpretation

Multimodal Approach

- Clinical Information
  - Patient age and gender
  - Symptoms
  - Past medical history
- Radiological Information
  - Location of mass in the pancreas (and thus organ traversed for EUS)
  - Cyst characteristics
    - Size, contours, invasion
    - Cyst structure: uni- or multilocular; thick/thin wall, Ca++, nodule/mass in the wall
    - Gross cyst contents: thick, viscous, thin, water, clear, brown
- Biochemical tests: CEA, amylase, glucose
- Molecular tests: *KRAS, GNAS, TP53, SMAD4, CDKN2A/p16*

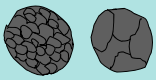
Pancreatic Cysts: CT

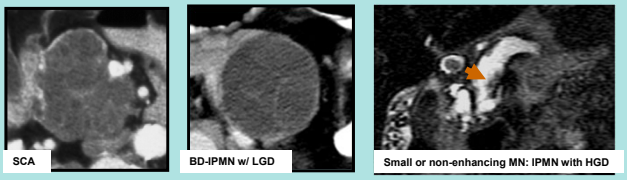
unilocular



Benign imaging

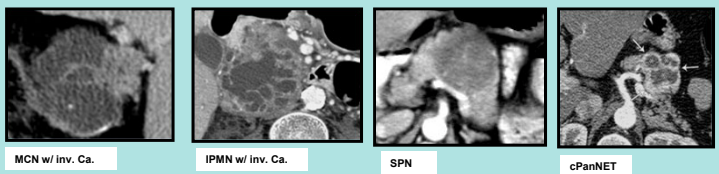
multilocular





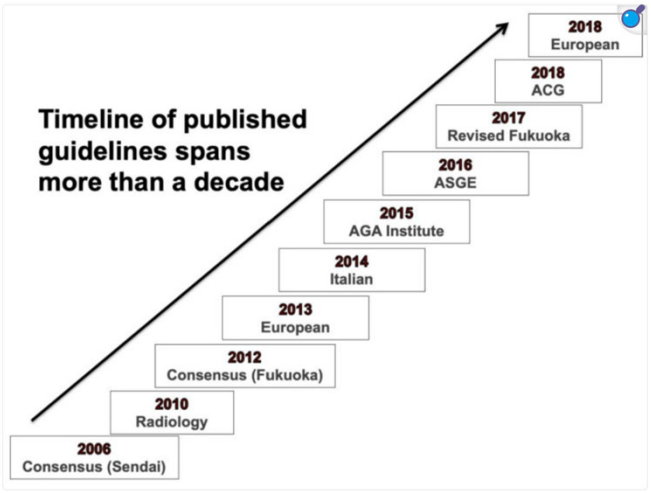
Benign to Worrisome imaging

complex



Worrisome to High-risk imaging

Figure 1.



Timeline of published guidelines for the management of pancreatic cystic lesions.

Mohapatra S, Krishna SG, Pannala R. Pancreatic Cystic Neoplasms: Translating Guidelines into Clinical Practice. Diagnostics (Basel). 2023 Feb 16;13(4):749.

Table 1. Guideline performance for referral to EUS.

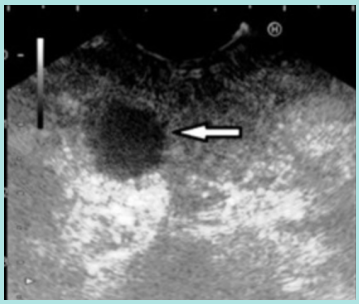
	AGA 2015	Fukuoka 2012	*P* value
Sensitivity	17.6%	35.3%	0.031
Specificity	94.5%	66.1%	<0.001
Positive Predictive Value	50.0%	24.5%	0.154
Negative Predictive Value	78.6%	76.6%	0.747
Accuracy	76.2%	58.7%	<0.001

Lee A, Kadiyala V, Lee LS. Evaluation of AGA and Fukuoka Guidelines for EUS and surgical resection of incidental pancreatic cysts. Endosc Int Open. 2017 Feb;5(2):E116-E122.

Imaging Morphology: Cysts

Unilocular
- ✓ **Pseudocyst- thick wall**
- ✓ BD-IPMN- thin wall

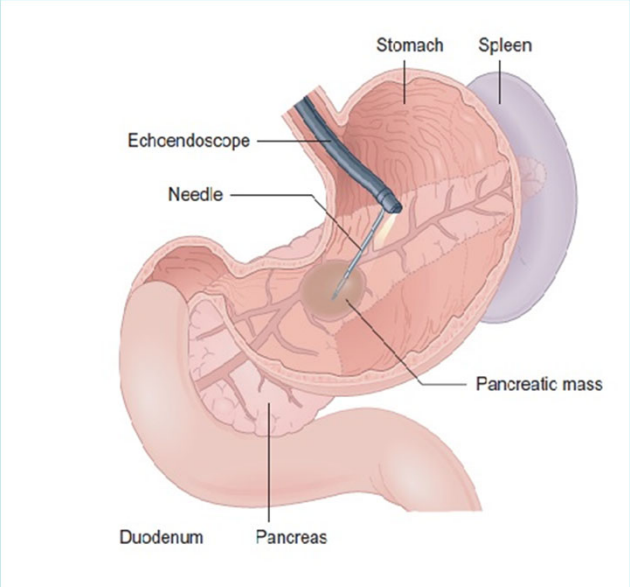
Multilocular
- ✓ **SCA- lobular borders**
- ✓ MCN- round; thick wall
- ✓ BD-IPMN- **connect to MPD**



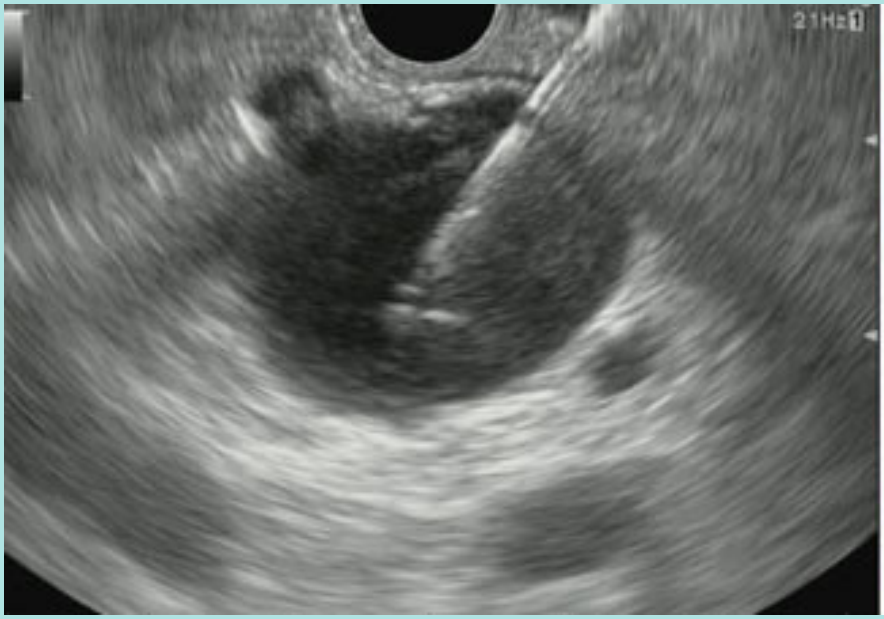
Unilocular with thick wall
- ✓ **Cystic NET**
- ✓ Pseudocyst

Biopsy Technique: EUS-FNA

Transduodenal: head

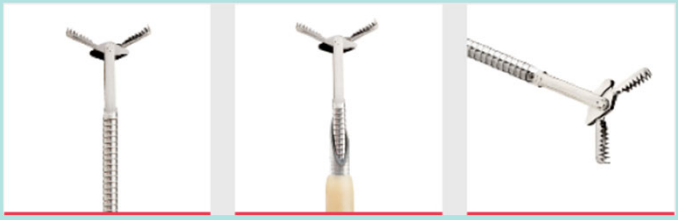


Transgastric: body and tail

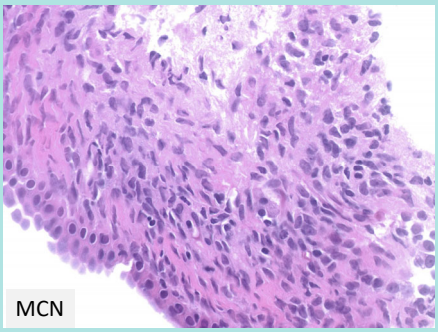


Garcia-Garcia de Paredes, Ana, et al. "Current clinical and research fluid biomarkers to aid risk stratification of pancreatic cystic lesions." *Revista Espanola de Enfermadades Digestivas* [REED], vol. 113, no. 10, Oct. 2021, pp. 714+

Moray Micro-forceps biopsy



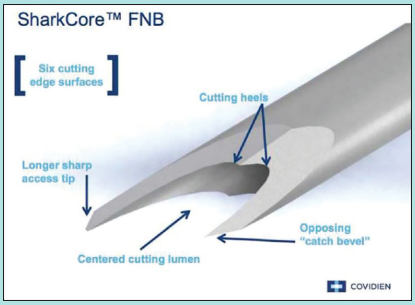
IPMN

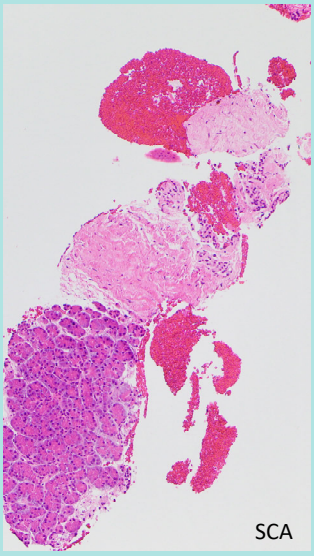


MCN

Zhang ML, Arpin RN, Brugge WR, Forcione DG, Basar O, Pitman MB. Moray micro forceps biopsy improves the diagnosis of specific pancreatic cysts. Cancer Cytopathol. 2018 Jun;126(6):414-420.

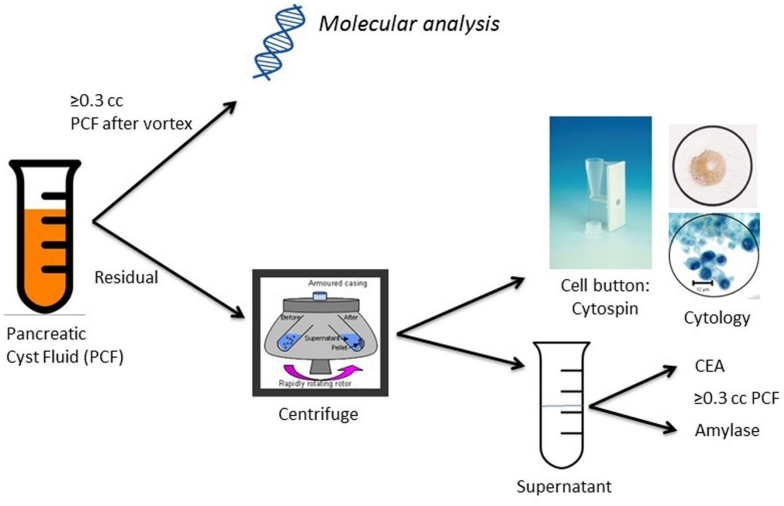
Next Generation Needles



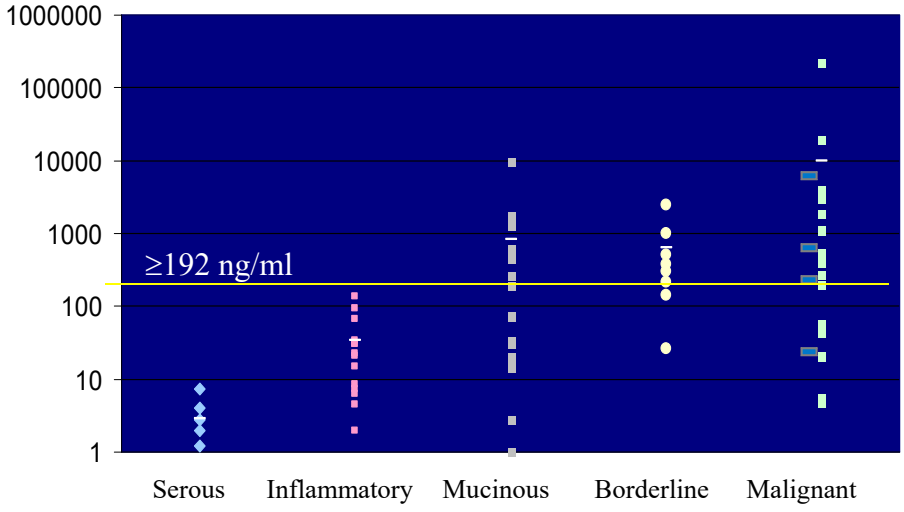


Acquire- Boston Scientific

Pancreatic Cyst Fluid Triage



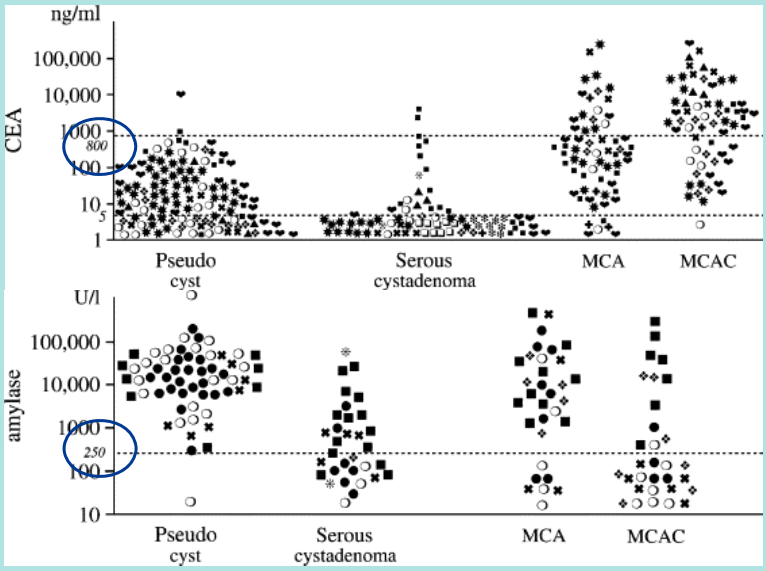
CEA by cyst fluid analysis



Gastroenterology. 2004 May;126(5):1330-6.

CFA cut-off levels lab and study dependent

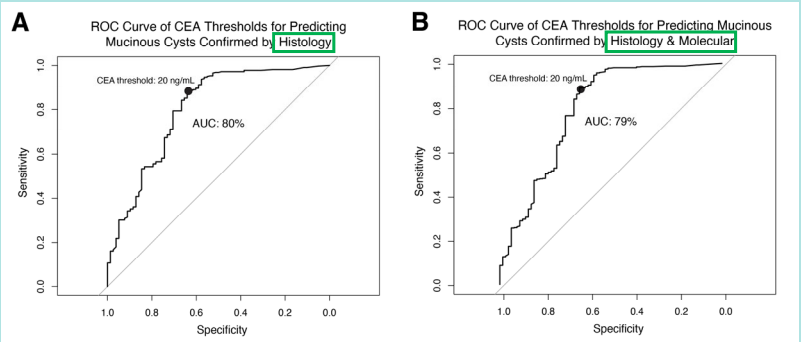
(van der Waaij, et. al. Cystfluid analysis in the differential diagnosis of pancreatic cystic lesions: a pooled analysis. Gastrointes Endosc. 2005; 62:383)



CEA >800ng/ml	**Neoplastic mucinous cysts**
CEA <5ng/ml	**Serous cystadenoma Pseudocyst**
Amylase <250 U/L	**Not a pseudocyst**

•. 2024 Mar 7;73(4):629-638.
•. 2024 Mar 7;73(4):629-638.

N=39



N=63

	Cysts with histological confirmation			Cysts with histological OR molecular confirmation		
CEA threshold (ng/mL)	Sensitivity	Specificity	# of False positive cases	Sensitivity	Specificity	# of False positive cases
20	0.89	0.64	30	0.89	0.64	28
110	0.68	0.73	22	0.64	0.73	21
192	0.56	0.78	18	0.51	0.78	17
250	0.53	0.85	13	0.47	0.85	12
840	0.35	0.90	9	0.29	0.90	8
1202	0.30	0.95	5	0.25	0.95	4

Kwan M, Fernandez-del Castillo C, Pitman MB, Zhang ML (Gut. 2024 Mar 7;73(4):629-638.

Intracystic Glucose and Carcinoembryonic Antigen in Differentiating Histologically Confirmed Pancreatic Mucinous Neoplastic Cysts

Zachary L. Smith, DO[1,2,*], Sagarika Satyavada, MD[2,*], Roberto Simons-Linares, MD[3], Shaffer R.S. Mok, MD, MBS[2,4], Bélen Martinez Moreno, MD[5], José Ramón Aparicio, MD[5] and Prabhleen Chahal, MD[3]

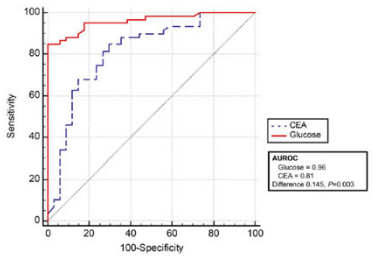


Figure 2. Receiver operating curves for glucose and CEA concentration from fresh cyst fluid in the differentiation of MNPC. AUROC, area under the receiver operating curve; CEA, carcinoembryonic antigen; MNPC, mucinous neoplastic pancreatic cyst.

Table 4. Glucose, CEA, and amylase concentration stratified by histologic type (median, range)

	Fluid diagnostic test		
Histologic diagnosis	Glucose (mg/dL)	CEA (ng/mL)	Amylase (U/L)
Main duct IPMN	2 (2–9)	568.5 (2.2–3,604)	8,356 (3–588,224)
Branch duct IPMN	4 (0–112)	58.9 (1.4–1,297)	5,113.5 (465–558,580)
Mixed IPMN	3 (2–24)	201.8 (4.3–298.9)	47,402.5 (275–202,909)
IPMN with invasive cancer	6.5 (1–86)	604.4 (22–3,872)	902 (2–93,300)
Mucinous cystic neoplasm	9 (2–34)	205 (56–10,001)	706 (3–86,700)
Mucinous cystic neoplasm with invasive cancer	10 (9–70)	10,000 (4,714–65,170)	35.5 (9–139)
Pseudocyst	71 (15–150)	108.1 (2.9–416)	71,376.7 (6,001–204,102)
Serous cystadenoma	86 (29–173)	1.8 (0.1–687.9)	124 (9–71,800)
Cystic neuroendocrine tumor	120 (92–446)	4.9 (0.7–26.7)	114 (9–150,000)
Other	37 (11–111)	11.3 (0.2–10,001)	88 (20–6,001)

CEA, carcinoembryonic antigen; IPMN, intraductal papillary mucinous neoplasm.

Am J Gastroenterol 2022;117:478–485.

CEA, Glucose and Amylase: Key Points

Elevated CEA (>~200 ng/ml) supports a mucinous cyst
- Does not distinguish IPMN from MCN
- Level does not correlate with malignancy
- Rare FP: PCT, GI duplication cyst, LEC

Glucose
- < 50 mg/dL supports a mucinous cyst
- >50 mg/dL supports a non-mucinous cyst

Amylase levels
- Elevated in the 1000's for most PCT
- Low amylase levels exclude a PCT
- Elevated level does not distinguish IPMN from MCN
  - MCN can have high amylase
  - IPMN can have low amylase

Molecular Tests: Key Points

KRAS
- Mutation(s) support a neoplastic mucinous cyst
  - Does not distinguish IPMN and MCN
  - Does not correlate with grade

GNAS
- Mutation supports IPMN over MCN
  - Does not correlate with grade

RNF43
- Mutation supports a mucinous cyst
  - Does not distinguish IPMN and MCN

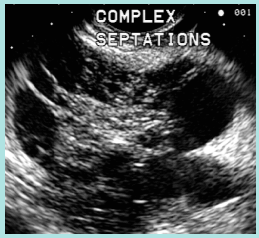
3p deletions
- 3p25, VHL gene, supports SCA
- Other 3p deletions also noted in SCA

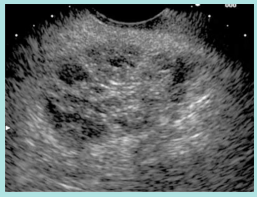
CTNNB1 (beta-catenin) deletion
- Mutation(s) support SPN

TP53* mutation**, ***CDKN2A loss, ***SMAD4*** loss support a HR cyst

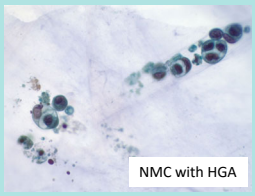
Cancer Cytopathol. 2017 Jan;125(1):41-47; Gastrointest Endosc. 2016 Jan;83(1):140-8; Surg Pathol Clin. 2022 Sep;15(3):455-468; Gastroenterology. 2023 Jan;164(

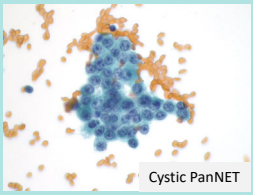
Clinical and Imaging Features

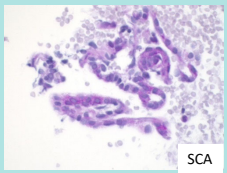


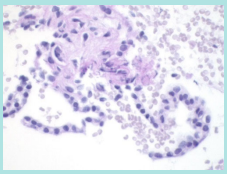


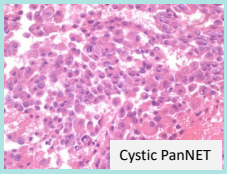
Multimodal Approach: Cytomorphology, Special Stains and Immunohistochemistry

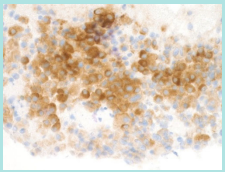

NMC with HGA

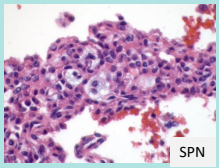

Cystic PanNET

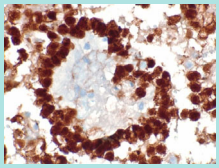

SCA


PAS and PASD


Cystic PanNET


Synaptophysin

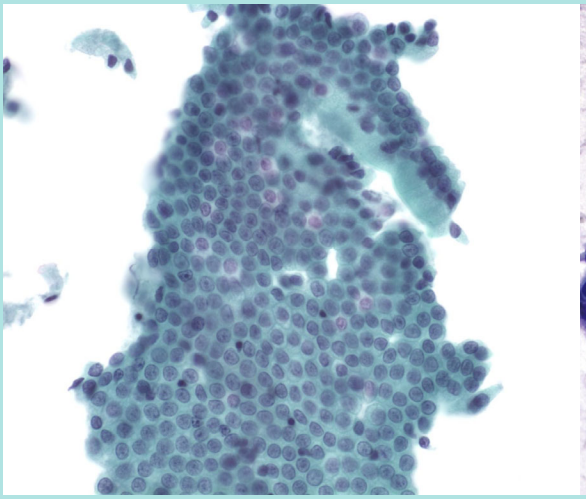

SPN

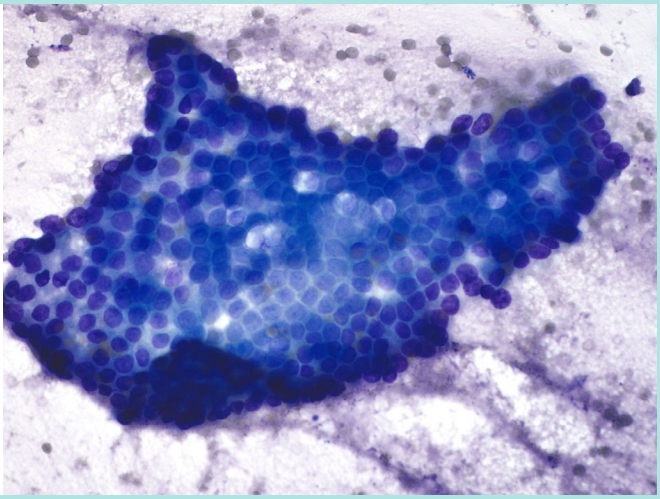

Beta catenin

Biochemical and Molecular analysis of Cyst Fluid

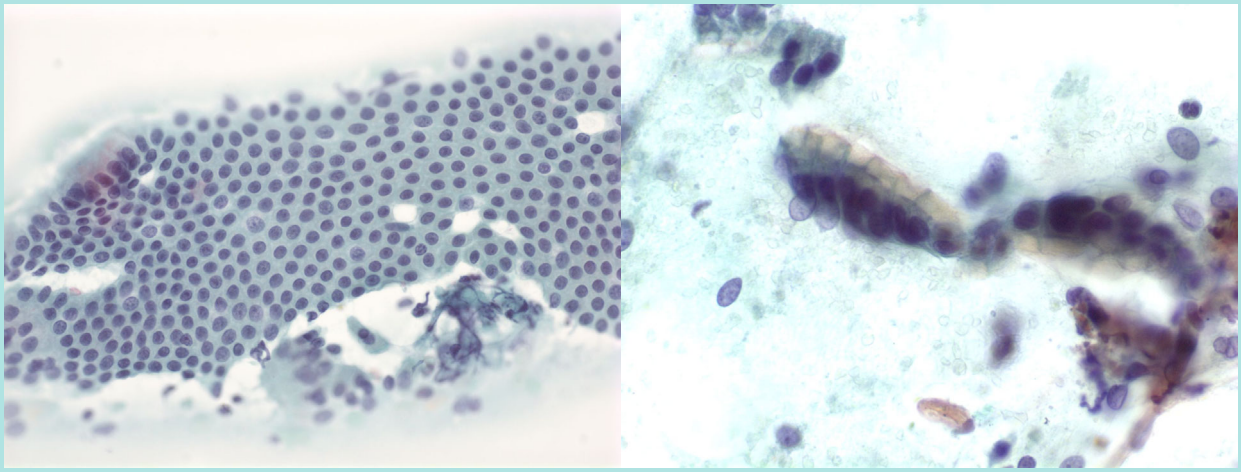
Cyst	Biochemical tests		Molecular Tests					
	CEA	Amy	KRAS	GNAS	3p25 (VHL)	P53	P16 (CDKN2A/INK4A)	SMAD4
PCT	↓	↑↑	-	-	-	-	-	-
SCA	↓↓	↓↓	-	-	+	-	-	-
IPMN	↑↓	↑↑	+	+	-	+[a]	+[a]	+[a]
MCN	↑↓	↓↑	+	-	-	+[a]	+[a]	+[a]

Duodenal Contamination





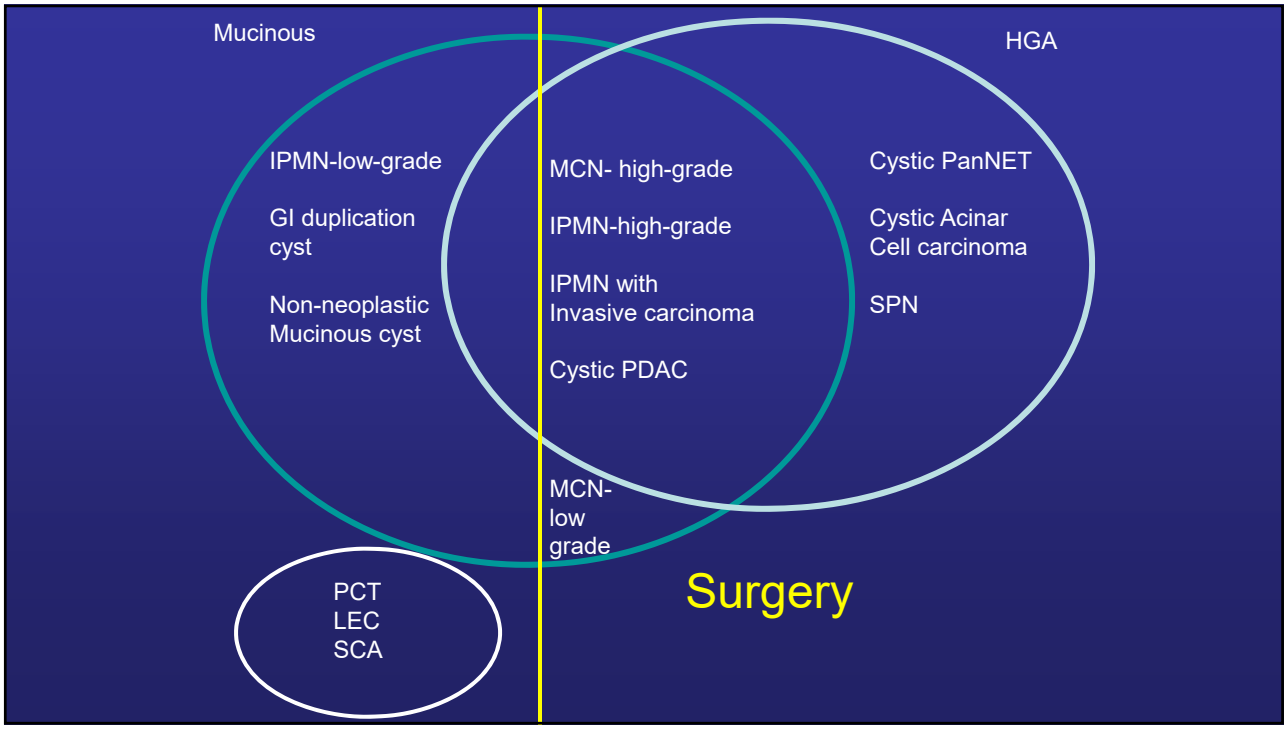
Gastric Contamination



Two basic questions for Cyst analysis

1) Is the cyst mucinous or non-mucinous?

2) Is the cyst low-risk/grade or high-risk/grade?



Solid-Pseudopapillary Neoplasm

- Clinical: **young female**
  - Up to 2.7% of exocrine tumors; 5% of cystic neoplasms
  - 89% in young women, mean age ~ 28 years
- Radiology: **solid and cystic**
  - shows complex, large solid and cystic neoplasm
  - Slight preference for the pancreatic tail

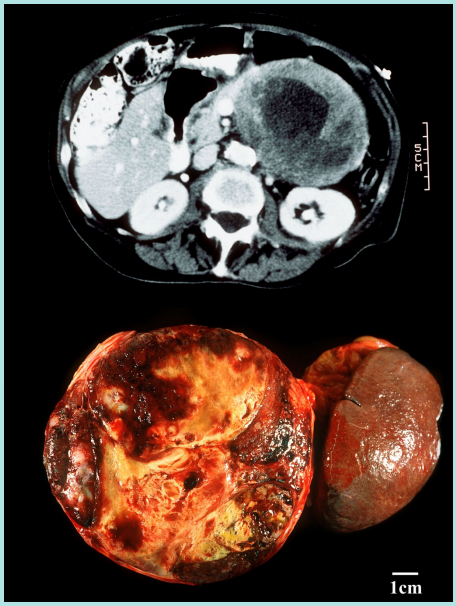
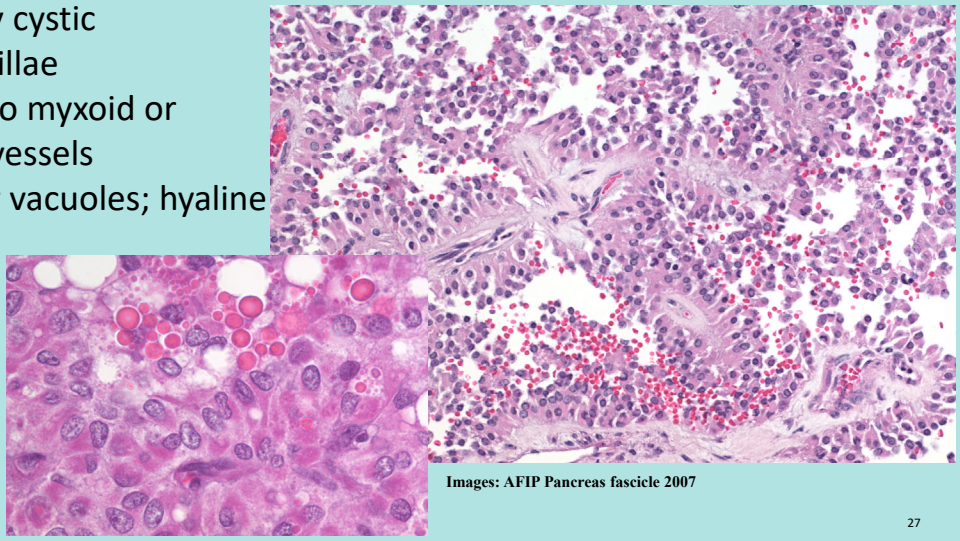


Image: AFIP Pancreas fascicle 2007

Solid-Pseudopapillary Neoplasm

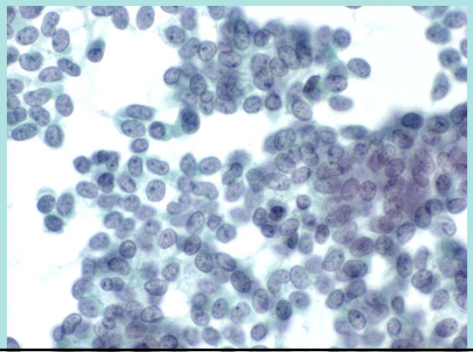
- Secondarily cystic
- Pseudopapillae
- Cells cling to myxoid or hyalinized vessels
- Perinuclear vacuoles; hyaline globules

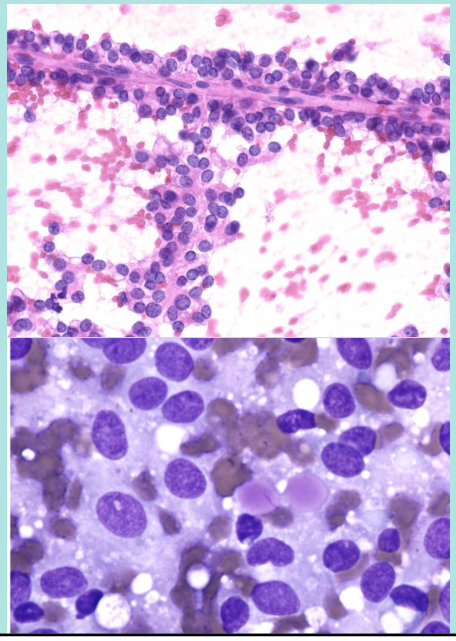


Images: AFIP Pancreas fascicle 2007

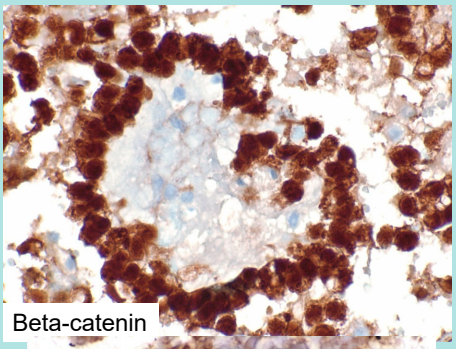
Classic Morphology: SPN

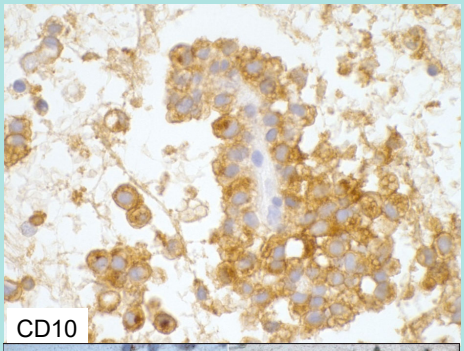
- Papillary branching
- Myxoid stroma
- Clinging cells and single cells
- Euchromatin
- Oval, indented, grooved nuclei
- Perinuclear vacuoles/globules

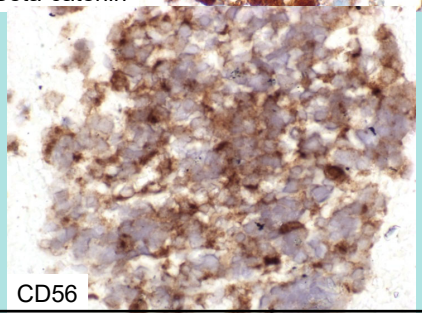


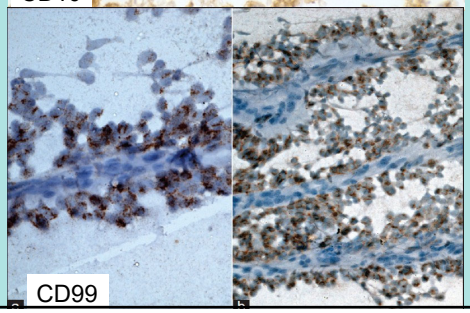


IHC: SPN


Beta-catenin


CD10


CD56


CD99

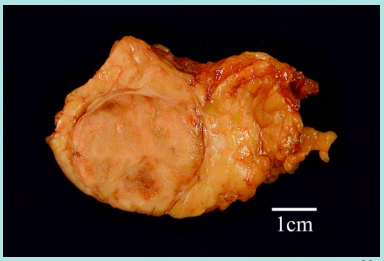
29

Ghosh R, Mallik SR, Mathur SR, Iyer VK. CD-99 immunocytochemistry in solid pseudopapillary tumor of pancreas: A study on fine-needle aspiration cytology smears. J Cytol 2013;30:151-5

Well-Differentiated Pancreatic Neuroendocrine Tumor

- Clinical: **middle age adult**
  - Any age; 40-50 y.o.; M=F
  - Slow growing
- Radiological: **round mass**
  - Pancreatic tail>>head/body
  - well-circumscribed
- Functional imaging-high levels of somatostatin receptor 2 (SSTR2) expression
  - Indium-111 (^{111}In) pentetreotide scan (Octreoscan™)-radiolabeled- use scintigraphy
  - Gallium-68 (^{68}Ga) DOTATATE- positron emitter- use PET/CT


https://radiologykey.com/pancreatic-neuroendocrine-tumors

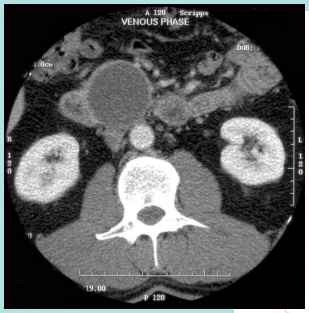


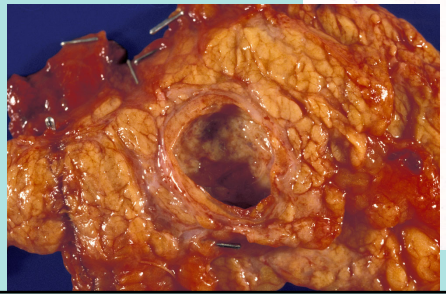
Images: AFIP Pancreas fascicle 2007

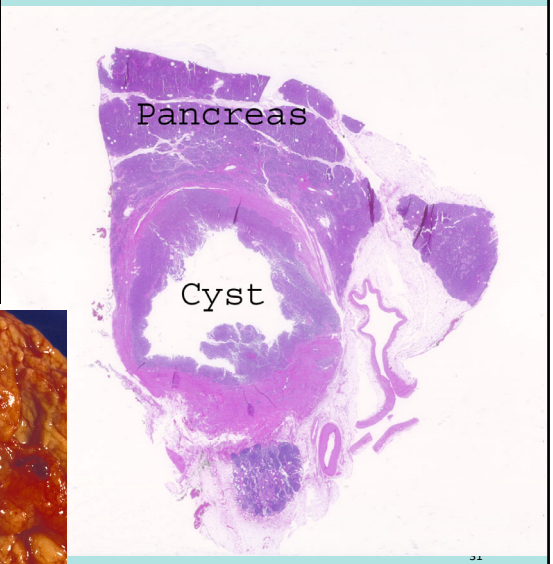
30

Cystic PanNET

- 10% of tumors are cystic
- Secondary change
- Can mimic primary cysts
- Clue to diagnosis on imaging is **"thick cyst wall"**

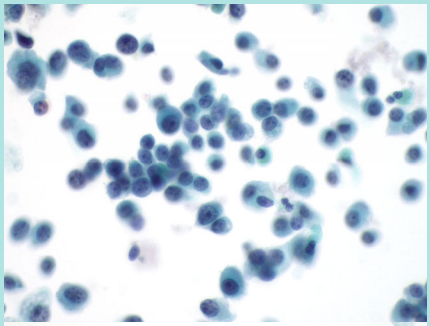


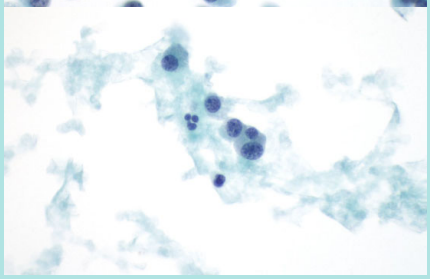




Cystic PanNET

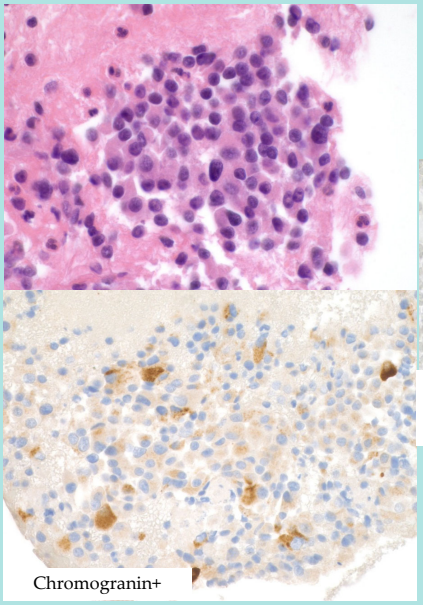
- Cytology is THE diagnostic test
  - CEA low
  - Amylase low
  - *KRAS/GNAS* negative
- Cells usually diagnostic when present



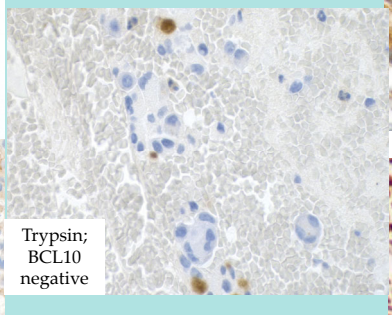


Morales-Oyarvide V, Yoon WJ, Ingkakul T, Forcione DG, Casey BW, Brugge WR, Fernández-del Castillo C, Pitman MB. Cystic pancreatic neuroendocrine tumors: the value of cytology in preoperative diagnosis. Cancer Cytopathol. 2014 Jun;122(6):435-44.

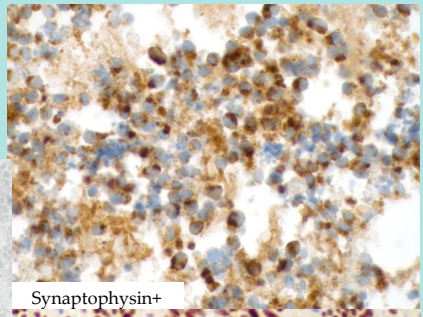
Ancillary Studies: PanNET



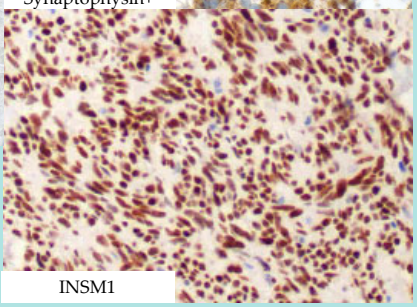
Chromogranin+



Trypsin; BCL10 negative



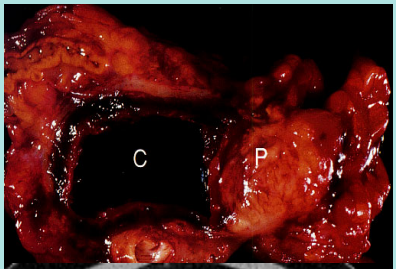
Synaptophysin+

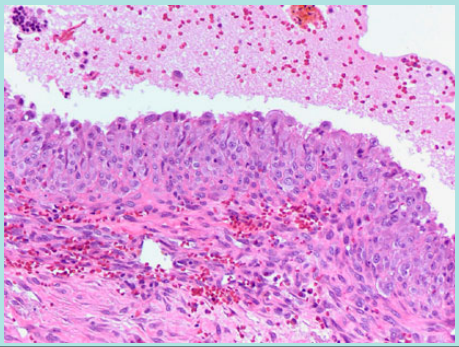


INSM1

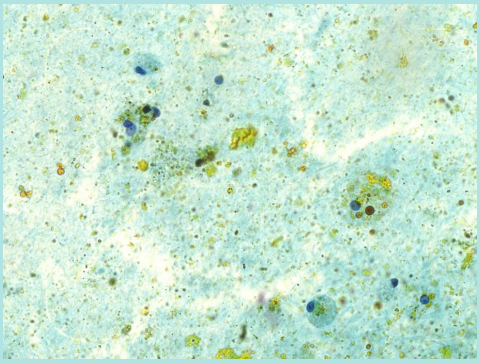
Pancreatic Pseudocyst

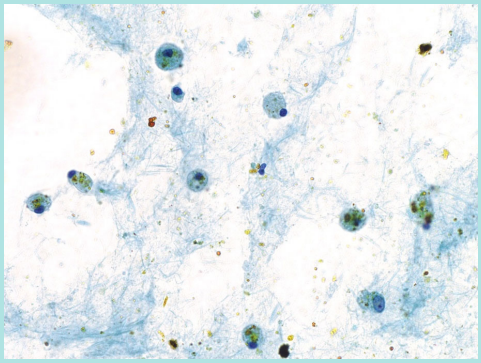
- Clinical: **pancreatitis**
  - From alcohol, trauma, surgery
- Radiology: **large cyst, high volume fluid**
  - Unilocular, non-septated
  - Thick walled
  - No mural nodule
- Histology
  - Cyst lining of
  - histiocytes and
  - inflammatory
  - cells





Pancreatic Pseudocyst: Cytology

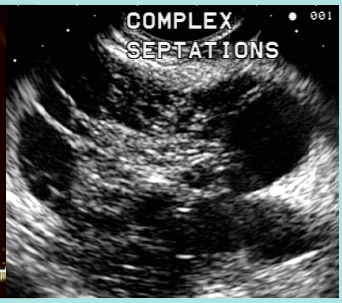


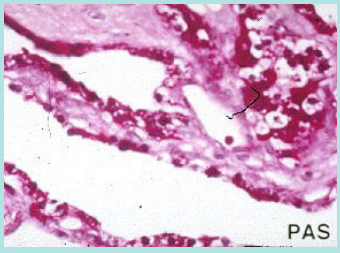


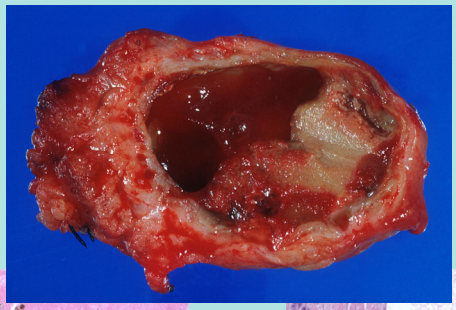
- cyst debris with blood, proteinaceous material and yellow hematoidin-like pigment (grossly brown and thin fluid)
- variable inflammation
- NO cyst lining epithelium (beware of contamination, mucin and epithelium)
- CEA low; amylase usually in the 1000's; no mutations

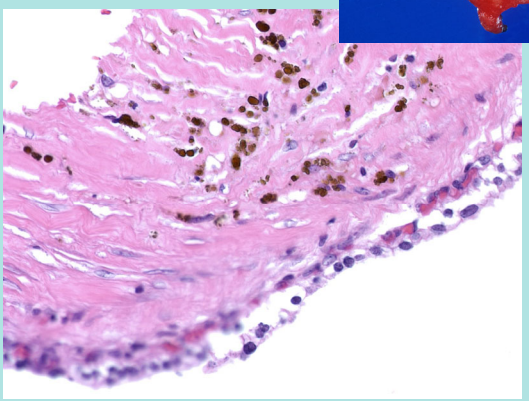
Serous Cystadenoma

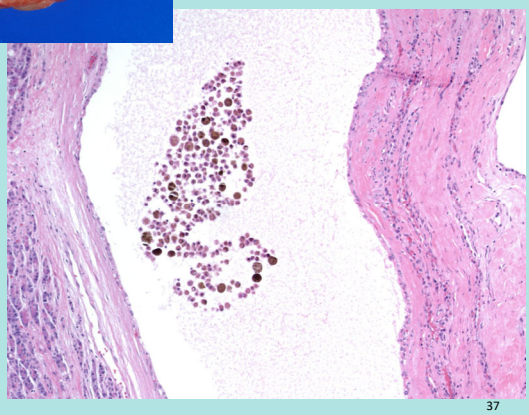
- Clinical: **asymptomatic, elderly female**
  - Benign, slow growing neoplasm women>>men, mean age 7th decade
  - Assocaited with VHL with deletion of 3p25 in most cases
  - Often asymptomatic, but can hemorrhage and cause pain
- Radiology: **multi-lobulated**
  - circumscribed
    - Microcystic with fibrous septae, central scar, calcifications in ~30-40%
- Histology
  - "glycogen-rich"
  - dPAS+ cuboidal
  - epithelium





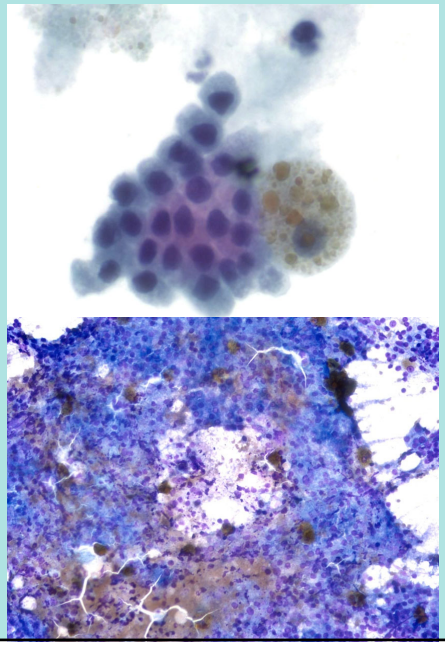






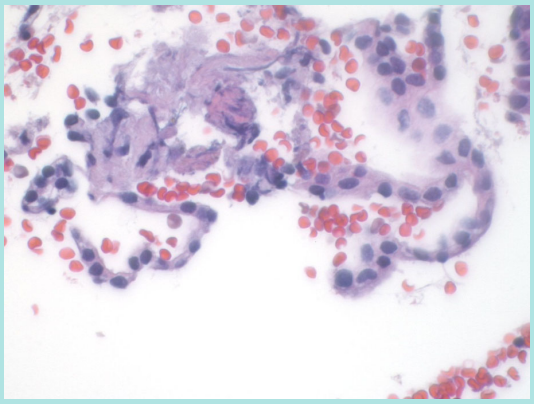
Serous Cystadenoma

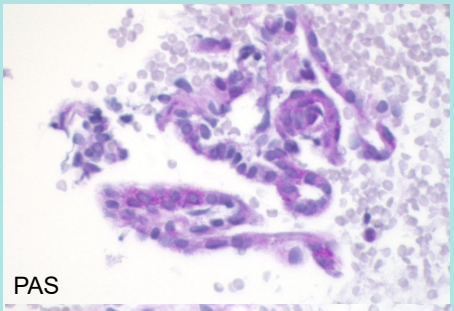
- Cuboidal non-mucinous epithelial cells
- Hemosiderin-laden macrophages in a clean or bloody, non-pseudocyst like background
- Grossly bloody or thin and clear
- CEA and amylase low
- NO *KRAS/GNAS*
- 3p deletions (3p25, VHL)



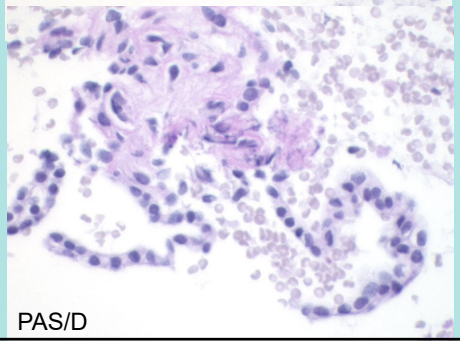
Cancer. 2008 Apr 25;114(2):102-10.

Serous Cystadenoma: Special Stains



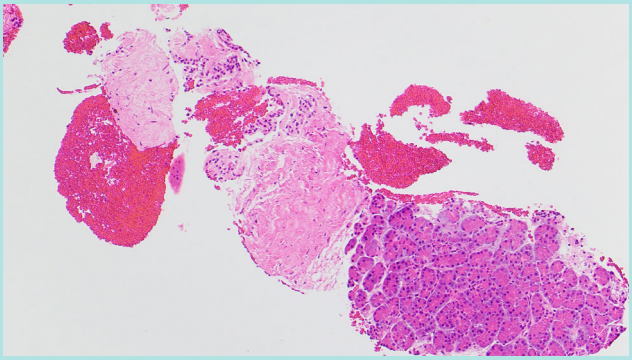


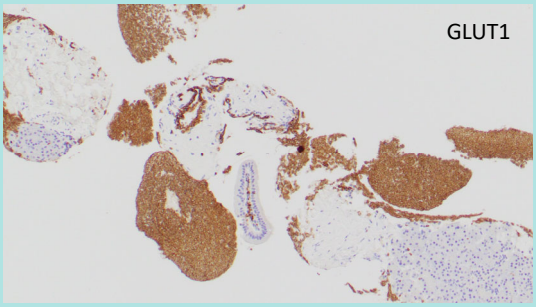
PAS



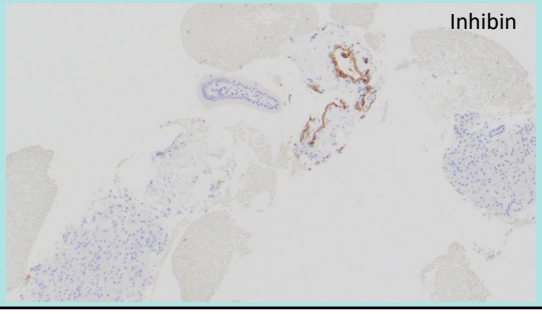
PAS/D

Serous Cystadenoma: Immunostains



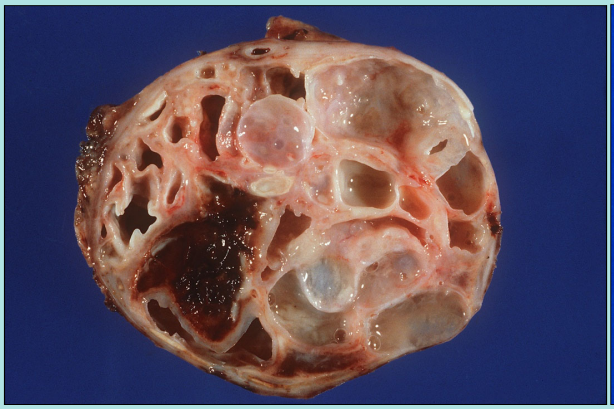


GLUT1

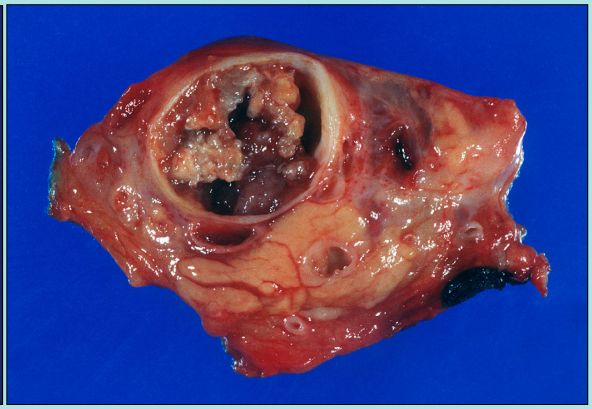


Inhibin

Neoplastic Mucinous Cysts



MCN

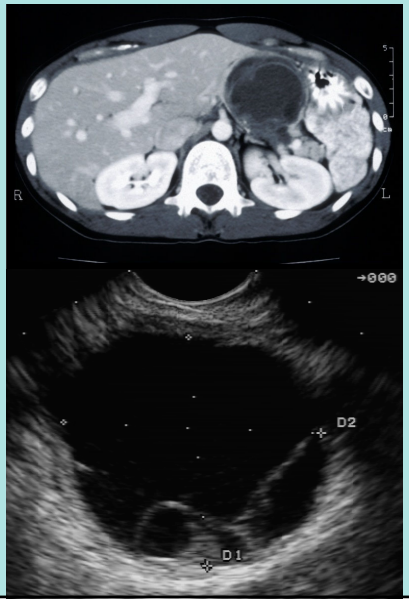


IPMN

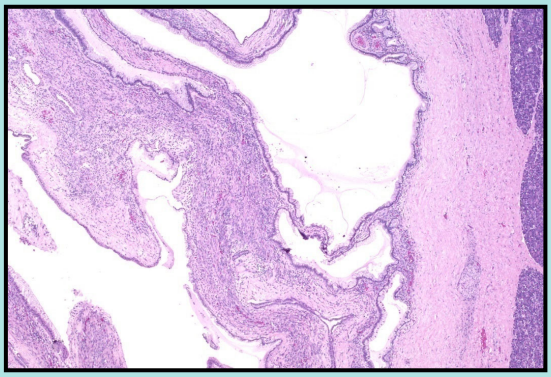
AFIP 4th Series Fascicle

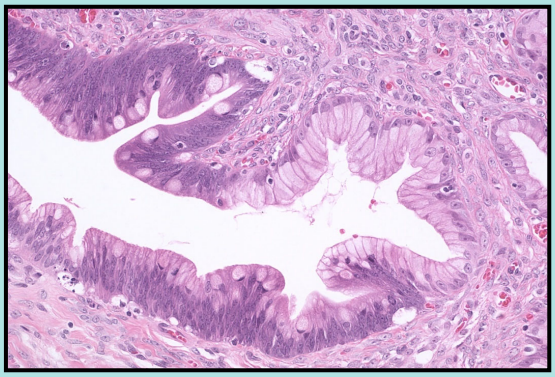
Mucinous Cystic Neoplasm

- Clinical: **middle age female**
  - F:M=20:1
  - Most are benign
  - Prognosis excellent for non-invasive completely resected tumors
  - Resection recommended despite grade
- Radiology: **multiloculated**
  - body and tail (90%)
  - do not communicate with the pancreatic ductal system
  - thick walled (Ca++ in 20%)
  - thin or thick septa



Mucinous Cystic Neoplasm

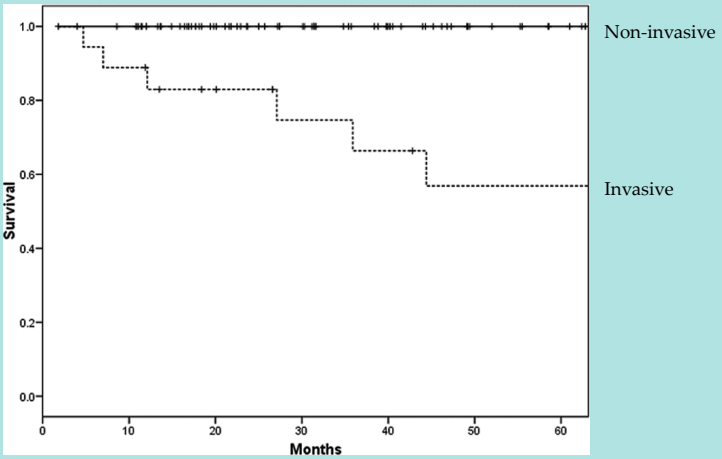




- Not associated with the pancreatic ducts
- Lined by mucinous, generally non-papillary epithelium
- Subepithelial "ovarian-like stroma" <u>required</u>
- Atypia may be very heterogeneous; invasion may be very focal, so the entire cyst should be submitted for histology

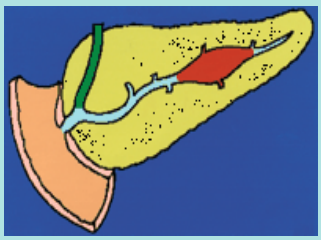
Mucinous Cystic Neoplasm is not an Aggressive Entity

(Crippa, et.al. Annals of Surgery 2008; 247:571-579

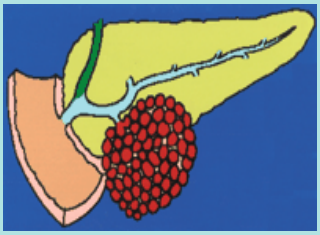


Intraductal Papillary Mucinous Neoplasm

Clinical: **elderly adult;** M:F ~ 1:1 in US

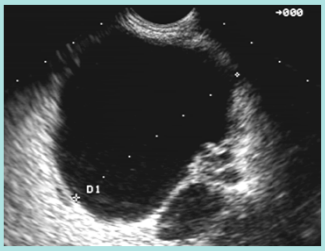


Main duct

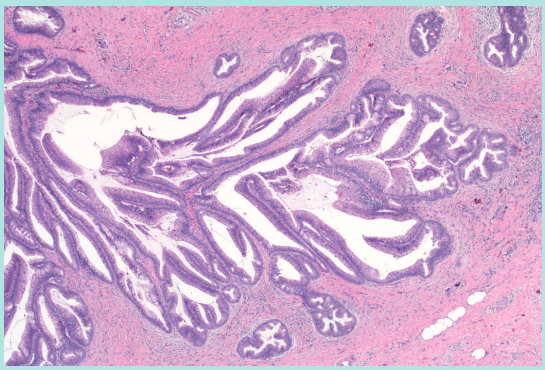


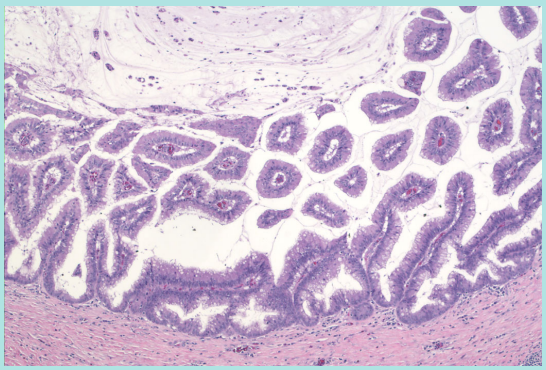
Branch duct

Combined



Intraductal Papillary Mucinous Neoplasm





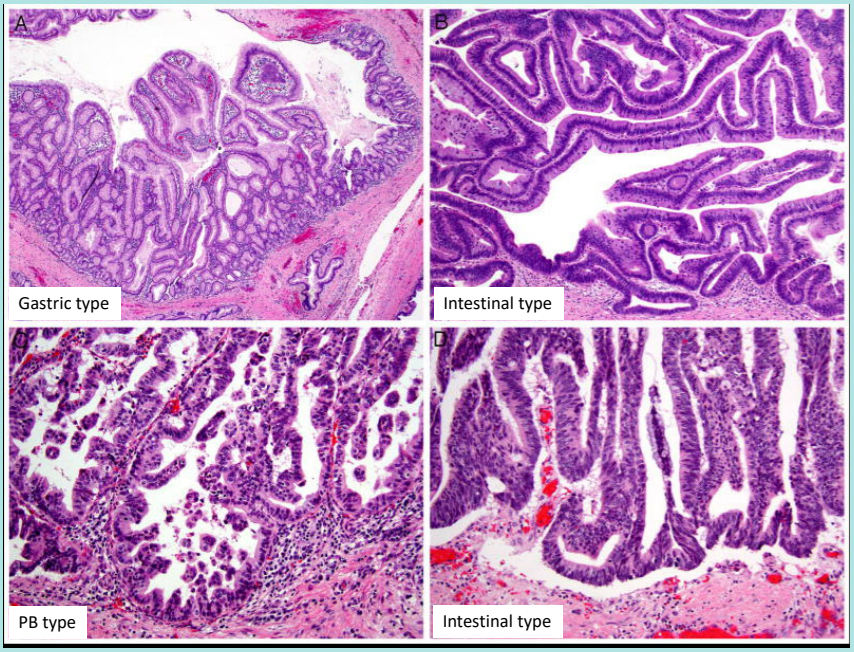
- Variously papillary mucinous epithelium of variable cell type and heterogenous atypia
- No association with ovarian-like stroma under the epithelium

AFIP 4th Series Fascicle

Two-tiered Grading of IPMN:

Low-grade
(low-intermediate grade dysplasia

High-grade
(high-grade dysplasia/carcinoma in-situ)



Am J Surg Pathol. 2015 Dec;39(12):1730-41.

Intraductal Oncocytic Papillary Neoplasm

Clinical: average 60 yo, M=F

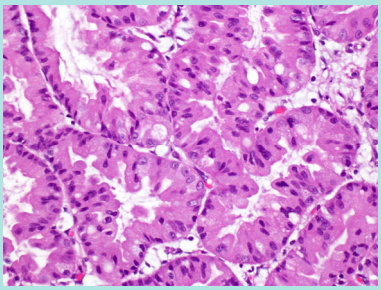
Imaging: Cystic to solid and cystic Pancreatic head; High PET uptake

Cytology = High risk/grade

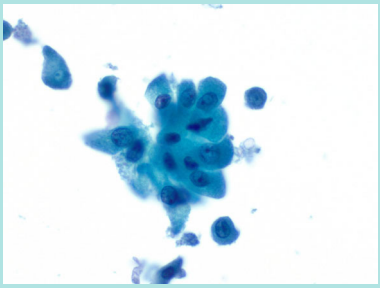
Biochemical: Low CEA

Molecular: recurrent rearrangements in *PRKACA* and *PRKACB*; no *KRAS* or *GNAS*

Prognosis: invasive carcinoma in about 30% of cases, but 5-year disease-specific survival rate approaches 100%



Olca Bastuck from WHO 5th edition of GI Tumours



Michelle Reid from WHO 1st edition of PB Reporting System

Management Guidelines for IPMN and MCN

(International consensus guidelines (revised)
Pancreatology. 2017(5):738-753.

MCN	• All MCNs are resected regardless of grade	
	Indication for Resection	**Indication for EUS-FNA**
IPMN	• Cytology suspicious or positive for malignancy, includes cytology with features of HGEA • Jaundice (tumour-related) • Enhancing mural nodule (> 5 mm) • MPD dilatation ≥ 10 mm	• Growth rate ≥ 5 mm over 2 years • Increased levels of serum CA19-9 • MPD dilatation between 5 and 9 mm • Cyst diameter ≥ 30 mm • Acute pancreatitis (caused by IPMN) • Enhancing mural nodule (< 5 mm) • Abrupt change in diameter of MPD with distal atrophy • Lymphadenopathy • Thickened or enhancing cyst walls

Modified from Barbara Centeno and the 1st edition of the WHO Reporting System for Pancreaticobiliary Cytopathology

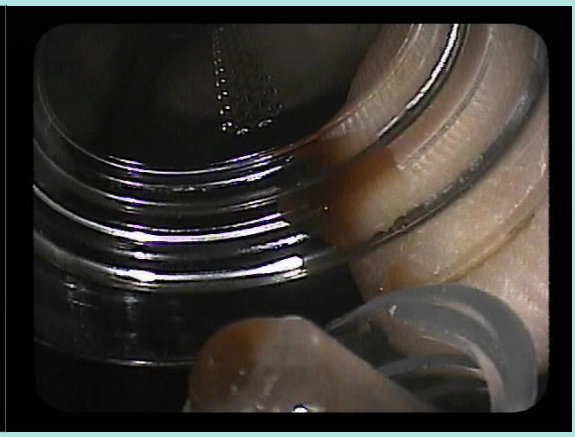
Two basic questions for Cyst analysis

1. Is the cyst mucinous or non-mucinous?
   1. **Gross examination**
   2. **Cytology**
   3. **CEA**
   4. ***KRAS/GNAS/RNF43***

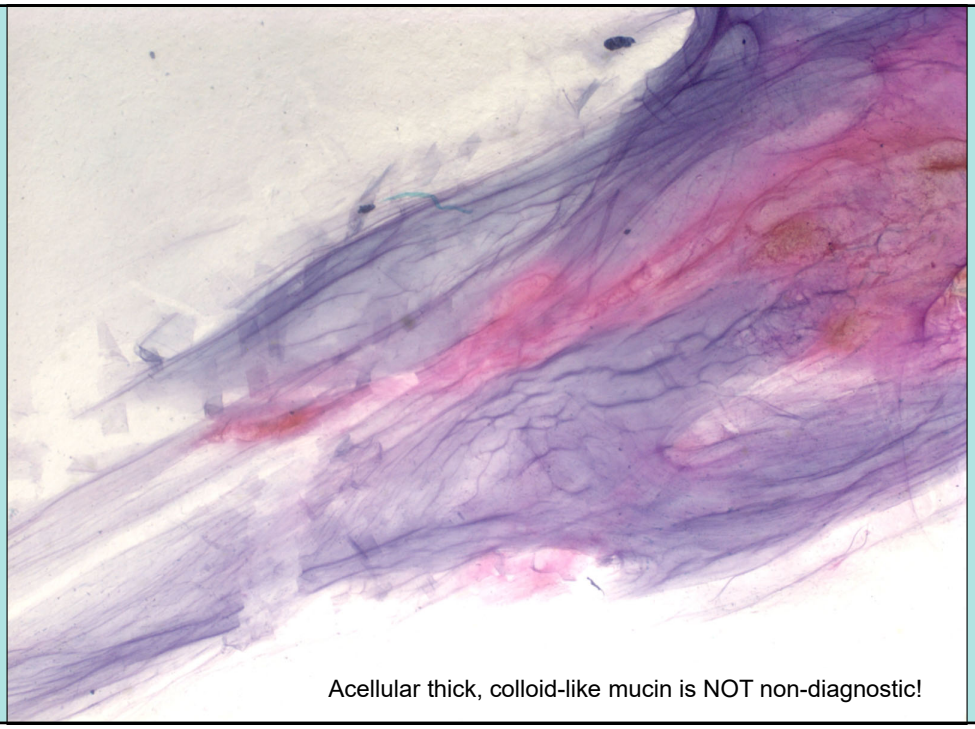
2. Is the cyst low-grade or high-grade?
   1. **Cytology!!**
   2. **Molecular analysis**

Gross Cyst Fluid

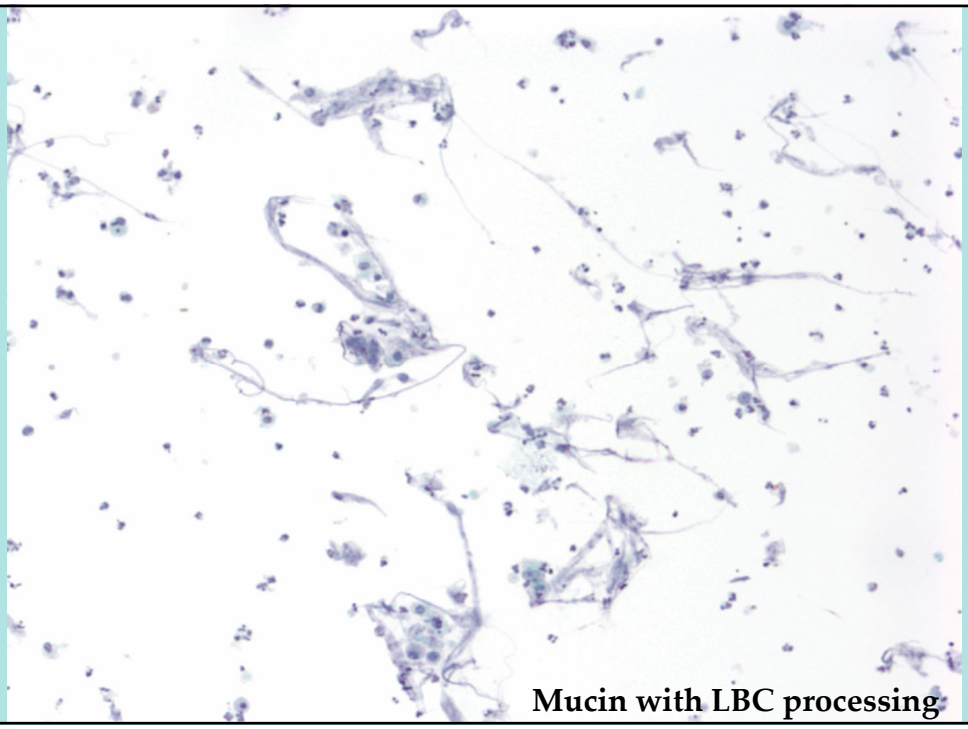
Mucinous cyst fluid



Pseudocyst fluid



Acellular thick, colloid-like mucin is NOT non-diagnostic!



Mucin with LBC processing

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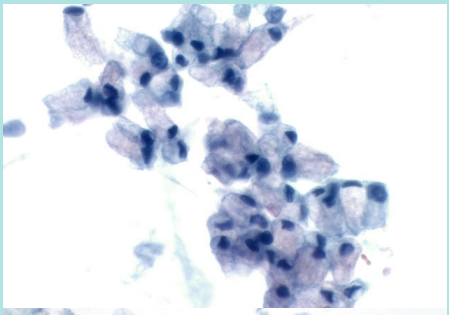
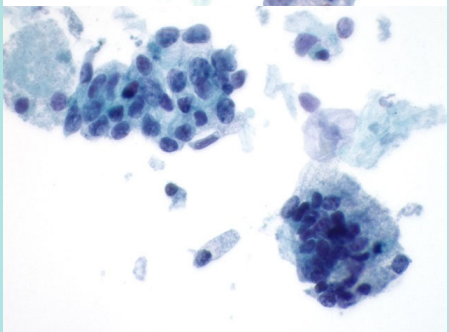
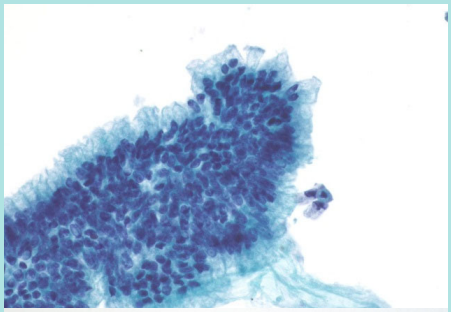
Mucinous Epithelium







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Ancillary Tests for Mucinous Neoplasia

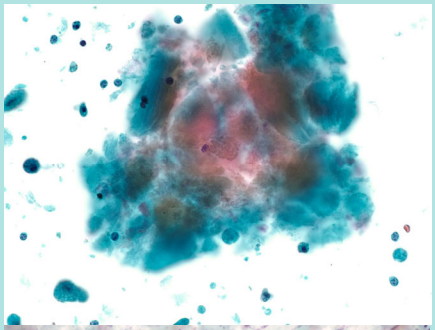
CEA > 192 ng/ml

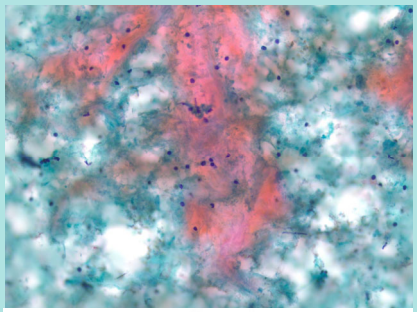
Molecular Analysis

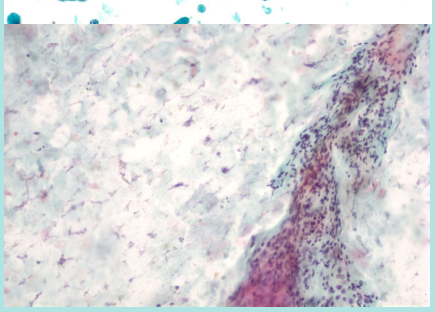
- *KRAS* mutation
- *GNAS* mutation
- *RNF43* mutation

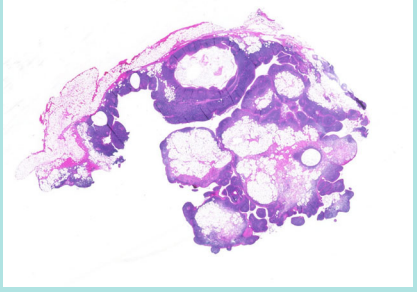
Lymphoepithelial cyst

- Anucleate squames and abundant keratinous debris
- Mature superficial squamous cells
- Lymphocytes variable and may be quite scant
- +/-Cholesterol clefts
- Elevated CEA (pitfall!)









Two basic questions for Cyst analysis

1. Is the cyst mucinous or non-mucinous?
   1. Gross examination
   2. Cytology
   3. CEA
   4. *KRAS/GNAS/RNF43*

2. Is the cyst low-grade or high-grade?
   1. **Cytology!!**
   2. **Molecular analysis**

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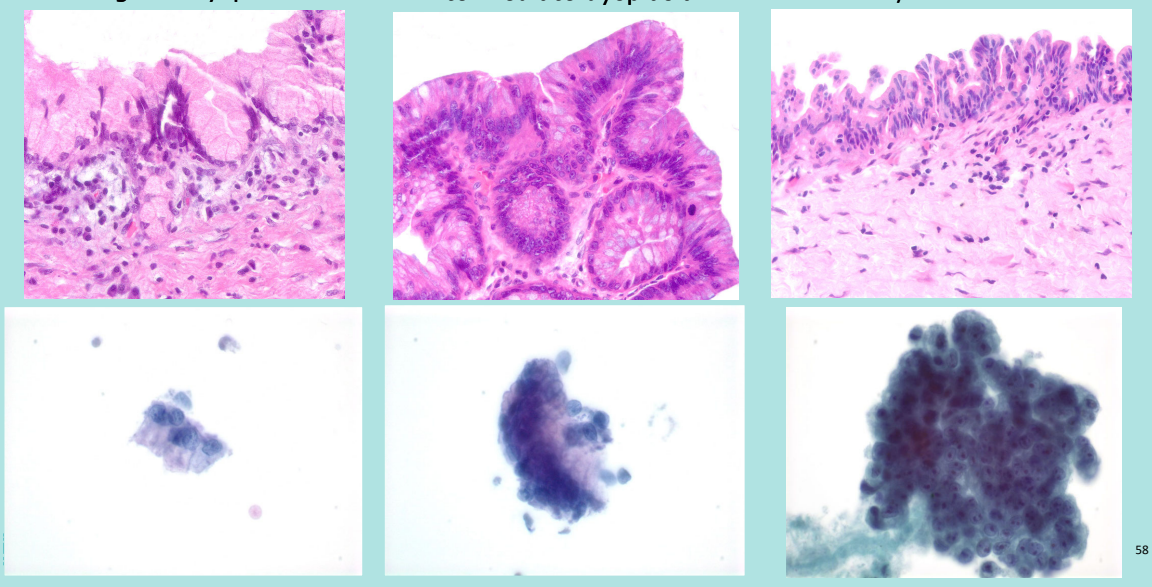
Intraductal Papillary Mucinous Neoplasm of the Pancreas: Cytologic Analysis and Correlation with Histologic Grade

PJ Michaels, EF Brachtel, BC Bounds, WR Brugge, and MB Pitman
(Cancer Cytopathol 2006; 108:174-179.)

Low grade dysplasia | Intermediate dysplasia | HGD/Carcinoma



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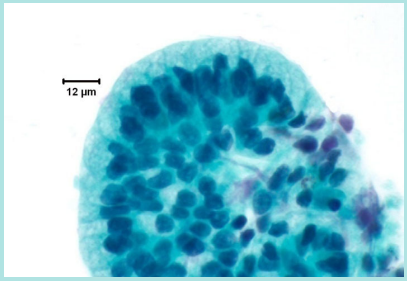
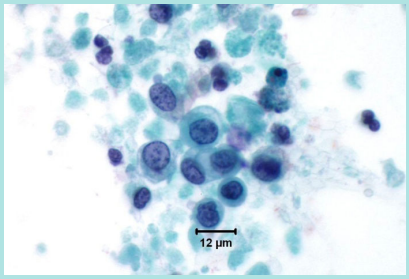
Cytological Criteria of High-Grade Epithelial Atypia in the Cyst Fluid of Pancreatic Intraductal Papillary Mucinous Neoplasms

Martha B. Pitman, MD, Barbara A. Centeno, MD, Ebubekir S. Daglilar, MD, William R. Brugge, MD, and Mari Mino-Kenudson, MD
Cancer Cytopathology 2014;122(1):40-47.

Reference duodenal enterocyte



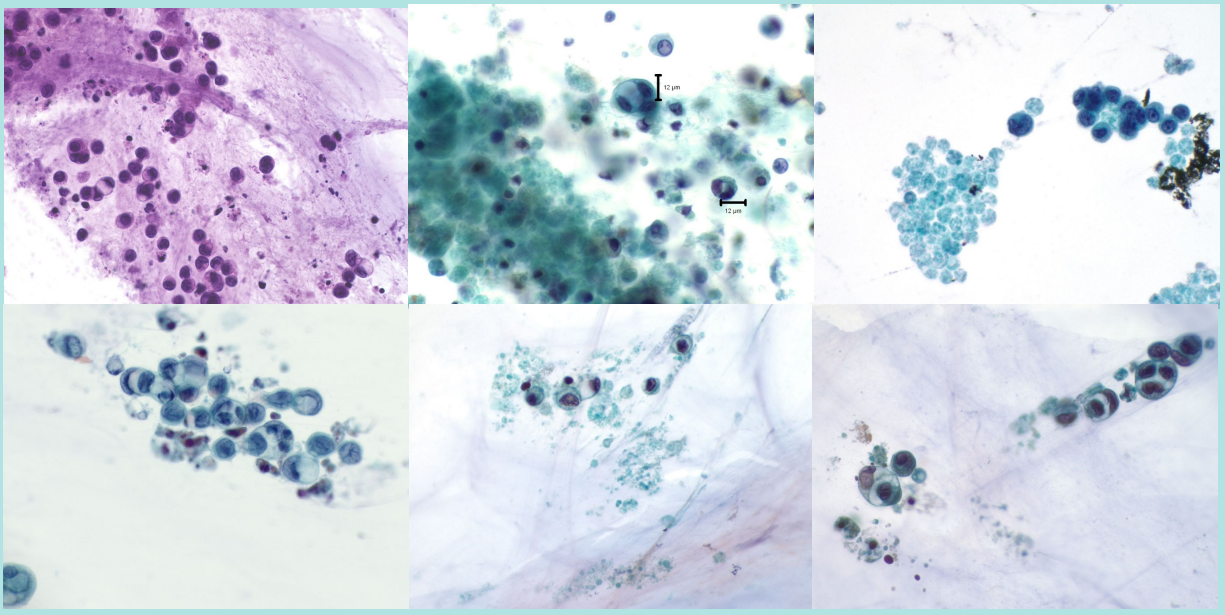
Low-grade



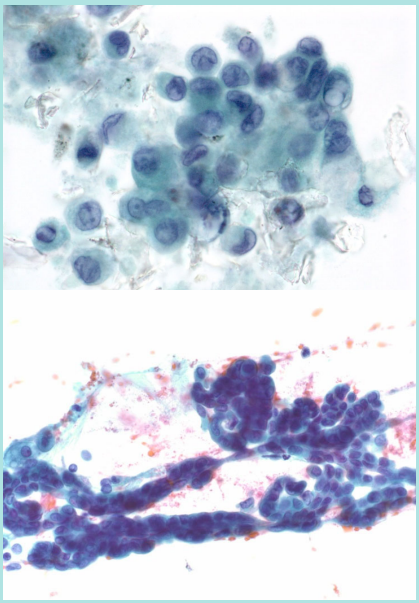
High-grade

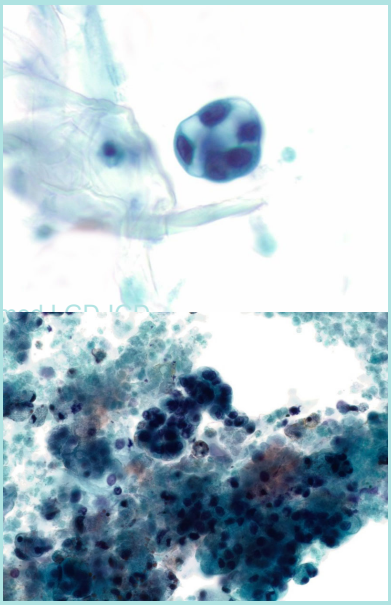
HGA is most accurately identified in mucinous cyst fluids by:
1. an increased N/C ratio,
2. an abnormal chromatin pattern
3. background necrosis

HGA in Mucinous Cysts



Morphological Overlap with LGA and HGA





Grading Epithelial Atypia in EUS-FNA of Intraductal Papillary Mucinous Neoplasms: An international interobserver concordance study

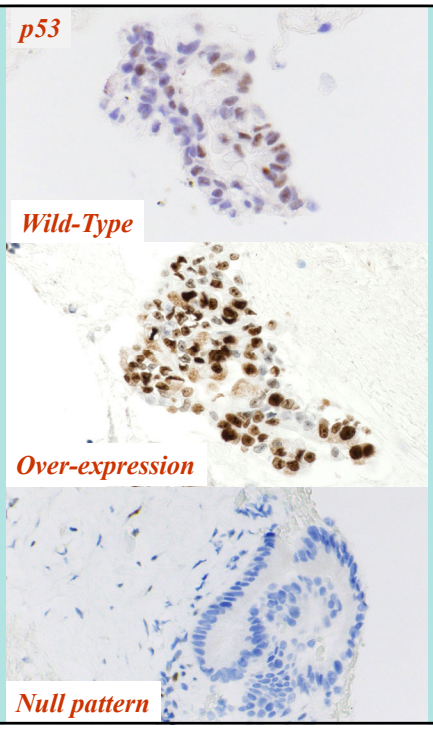
Martha B Pitman MD[1], Barbara A Centeno MD[2], Muriel Genevay MD[3], Ricardo Fonseca, MD[4] and Mari Mino-Kenudson MD[1].
Cancer Cytopathology 2013;121(12):729-736.

Table 3. Kappa Coefficient for Two-Tiered Cytological Grading of Branch-Duct IPMN Cyst Fluids

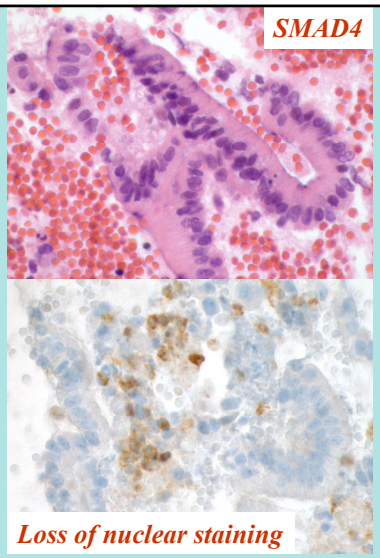
Grade	Four Reviewers	Randolph's Multirater Kappa	Two Reviewers*	Cohen's Kappa
0-2, 3-4	54%	0.45	87%	0.74
0-1, 2-4	52%	0.44	88%	0.71

* Two most experienced reviewers

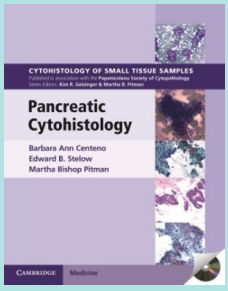
0= GI contamination; 1=LGD; **2= IGD**; 3= HGD and 4= PDAC

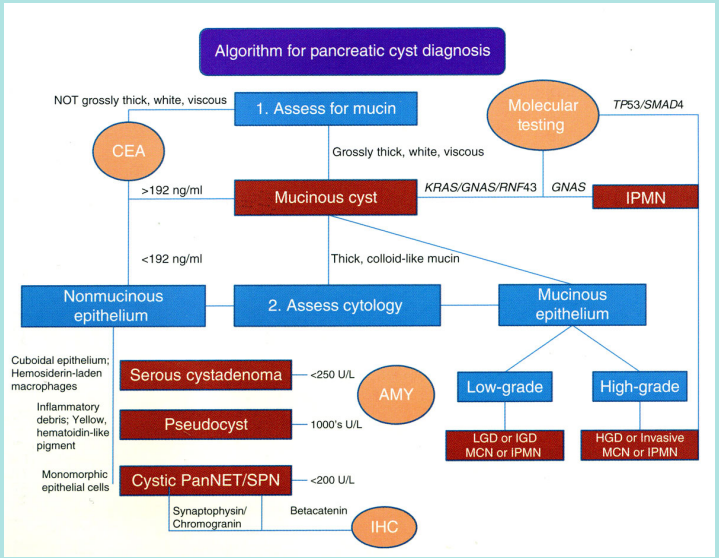


Ancillary Studies: HGA



Others:
p16- loss if nuclear staining
MTAP- loss if nuclear staining
Keratin 18-positive cytoplasmic staining

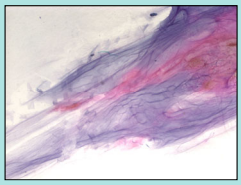




Diagnosis of a Mucinous Cyst

Mucin Production Established

○Thick, colloid-like extracellular mucin



○Cellular or inflammatory debris within the mucin
○Thin mucin covering the slide confirmed with

- ❖special stains for mucin (mucicarmine or Alcian blue pH2.5)
- ❖Elevated CEA (192 ng/ml is ~ 80% accurate)

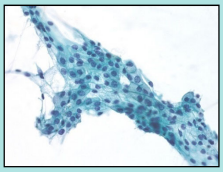
OR

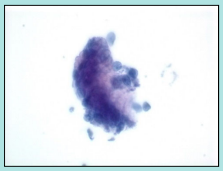
- ❖*KRAS/GNAS* mutation

And/OR

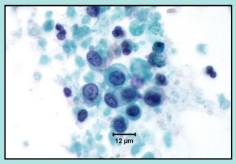
Neoplastic Epithelial Cells identified

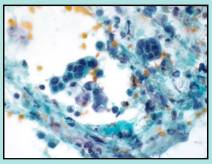
○Low-grade mucinous epithelium ,e.g. low-grade atypia (low-grade to intermediate-grade dysplasia)





○High-grade epithelium, e.g. high-grade atypia (at least high-grade dysplasia/carcinoma in-situ, but quality and quantity of atypia is insufficient for diagnosis of adenocarcinoma)





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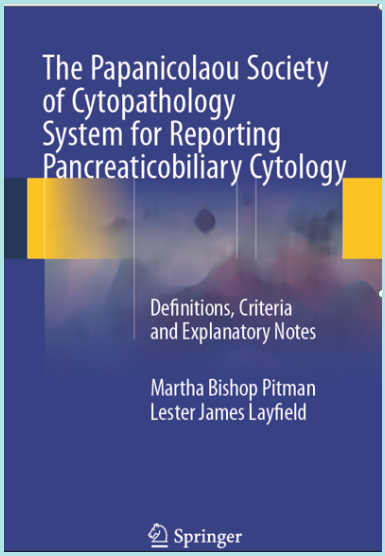
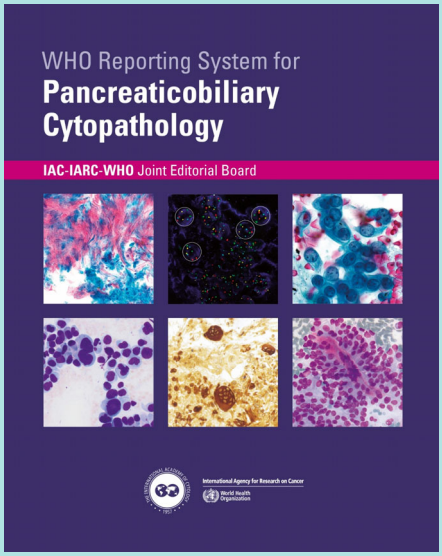
Reporting Systems for Pancreaticobiliary Cytology





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	PSC System		WHO System		
1	Nondiagnostic			Inadequate/insufficient/ nondiagnostic	1
2	Negative (for Malignancy)	Non-neoplastic only	Non-neoplastic and neoplastic (SCA)	Benign/Negative (for Malignancy)	2
3	Atypical			Atypical	3
4	Neoplastic				
4a	Neoplastic:Benign	SCA	low-grade MCN Low-grade IPMN Also, low-grade PanIN, BilIN	Pancreaticobiliary Neoplasm-low risk/low-grade (Pan-Low)	4
4b	Neoplastic:Other	IPMN,MCN, PanNET, SPN	High-grade MCN High-grade IPMN IOPN ITPN Also, high-grade PanIN, BilIN	Pancreaticobiliary Neoplasm-high risk/high-grade (Pan-High)	5
5	Suspicious (for malignancy)			Suspicious (for malignancy)	6
6	Positive (for malignancy)		PDAC, Acinar Cell ca., PanNET, PanNEC, SPN, PBL, other	Malignant	7

J Am Soc Cytopathol. 2023 Nov-Dec;12(6):395-406. doi: 10.1016/j.jasc.2023.04.007. Epub 2023 May 5.

One procedure-one report: the Re-Imagine Cytopathology Task Force position paper on small tissue biopsy triage in anatomic pathology

Amy Ly [1], Ronald Balassanian [2], Susan Alperstein [3], Amber Donnelly [4], Cindy McGrath [5], Aliyah R Sohani [6], Edward B Stelow [7], Michael J Thrall [8], M Lisa Zhang [6], Martha B Pitman [6]

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Conclusions

- One integrated pathology report provides advantages over 2 separate cytology and histology reports
  - Increase overall accuracy
  - Support judicious use of ancillary studies reducing redundancy
  - Allow for real-time cyto-histological correlation
  - Present one coordinated and comprehensive report and diagnosis to the patient and their care team

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A. PANCREAS, HEAD, FINE NEEDLE ASPIRATION:
DIAGOSTIC CATEGORY: MALIGNANT
DIAGNOSIS: Adenocarcinoma

B. PANCREAS, HEAD, FINE NEEDLE BIOPSY/CORE:
Desmoplastic stroma an detached gastrointestinal epithelium.
There is no evidence of malignancy.

Teaching Points

- ✓ Imaging features provide a clue to diagnosis
  - ➢ Multiple cysts along the duct likely IPMN
- ✓ Biochemical analysis
  - ➢ Elevated CEA supports a mucinous etiology
- ✓ Cytology is best test for assessing high-risk
  - ➢ HGA
  - ➢ Background necrosis
- ✓ Molecular analysis adds value to cytology
  - ➢ High-risk mutations support HGA diagnosis
    - TP53 mutation, SMAD4 deletion, CDKN2A deletion