Mass General Brigham

WHO Reporting Systems in Cytopathology

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No disclosures

Outline:
Introduction
WHO Reporting Systems

Acknowledgment:
Drs. Fernando Schmitt
Andrew Field
Ivan Chebib

The Pathology Report

Legal document of communication between pathologist and clinician
Communicates the results of testing
Provides information for patient treatment and management- importantly, risk of malignancy
Quality Parameters

- Timeliness
- Accuracy
- Completeness
- Conformance with current agreed standards
- Consistency and clarity of communication

Standardized Pathology Terminology

- Should be uniform among pathologists and universally understood by clinicians
- Must reflect our current understanding of the relevant disease entities
- Provide clinically relevant information to the treating physician to allow for proper patient management

Advantages of Standardized Terminology

- Unifies reporting of disease categories
- Reduces interobserver variability
- Improves intraobserver reproducibility
- Better aligns patient management options with interpretations
- Improves patient care

WHO Cytopathology Reporting Systems Sponsored by IARC/WHO And IAC

- ✓ MOU
  - IAC-IARC-WHO
  - 2020
- ✓ Organization
  - Standing Committee
  - Expert Editorial Board
    - Bibliometric/geographic
    - RA, Editors
  - Additional co-authors
- ✓ Follows tumor classification of WHO Blue Books
  - Hyperlinks between the books

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WHO Reporting Systems in Cytopathology

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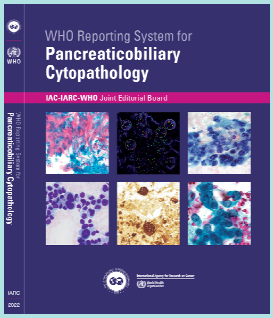
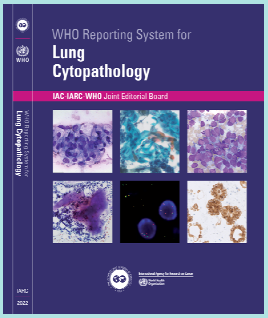
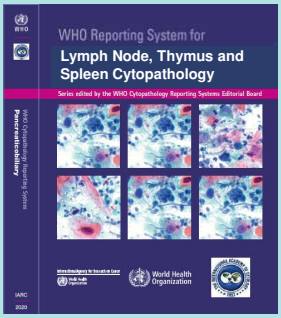
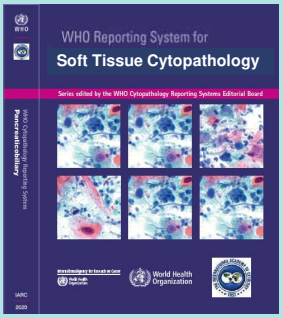




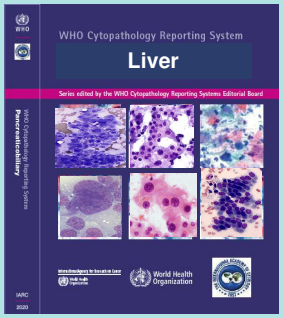


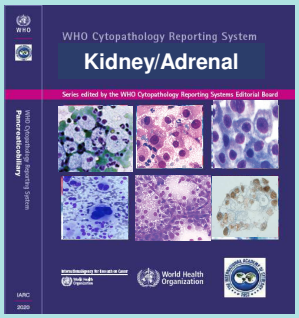


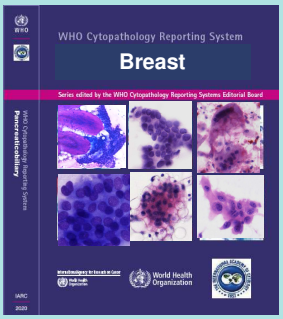
Mock-up of covers

WHO Reporting Systems in Cytopathology

In Development







Mock-up of covers

WHO Reporting Systems in Cytopathology Contents

- Introductory chapter on the role of cytopathology
- Techniques in acquiring and preparation of the specimens.
- Sections on ROSE and the use of imaging modalities.
- Role and best practice of ancillary testing.
- Chapters covering each category with an introduction, definitions, discussion and background, and ROM as well as management recommendations.

WHO Reporting Systems in Cytopathology
Contents

- Each category chapter has sections on the lesions/tumors that commonly are found in that category.
- Each lesion/tumor has subheadings for brief clinical presentation, imaging and histopathology (linked to the corresponding WHO tumor classification books) and then "key diagnostic cytopathological criteria" followed by a discussion, differential diagnosis and ancillary testing.
- Each category chapter includes "sample reports"

WHO Reporting Systems in Cytopathology
The Standardized Cytopathology Report

- **Demographic information:**
- -patient's name, date of birth, address, patient identifiers, date of request, and laboratory accession number
- -referring doctor and contact details

- **Type of Specimen:**
- -sputum, bronchial wash, bronchial lavage, bronchial brush, FNAB (EBUS, transthoracic), BDB, pancreas FNA, pancreas mass or cyst, lymph node (location), soft tissue mass (location)

- **Clinical & Imaging information:**
- -site, size (mm), imaging (ultrasound, CXR, tomogram, CT, MRI) features
- -previous cytopathology procedures and results and previous other biopsy results when available

- **Diagnostic Category:** (example: Malignant)
  - *-using terminology not a number*

- **Diagnosis:** *-specific diagnosis or differential diagnosis*

- *Comment, microscopic description optional (preferred if diagnosis is indeterminate)*

WHO Reporting Systems in Cytopathology

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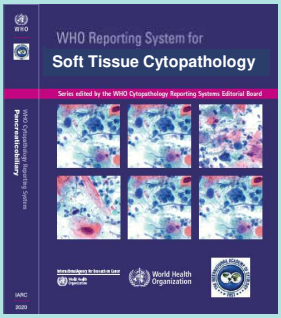

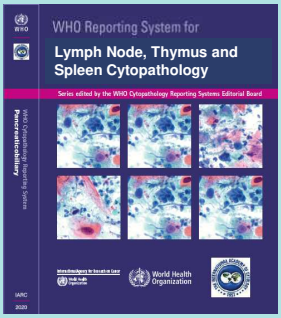

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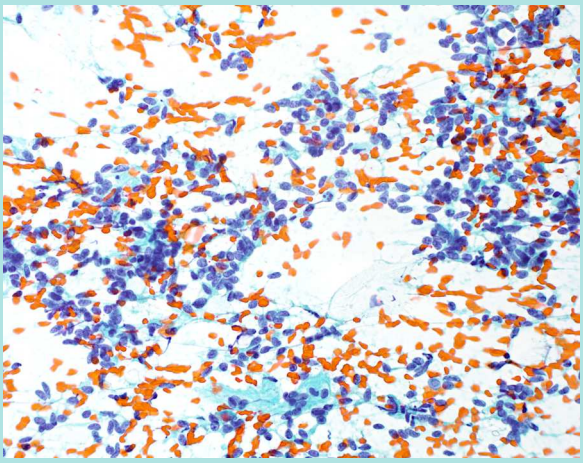
Diagnostic Categories

1. Insufficient/Inadequate/Non-diagnostic
2. Benign
3. Atypical
4. Soft Tissue neoplasm of uncertain malignant potential (STNUMP)
5. Suspicious for Malignancy
6. Malignant

Soft Tissue Neoplasm Of Uncertain Malignant Potential (STNUMP)

Specific Entities with uncertain malignant potential:

- Dermatofibrosarcoma protuberans
- Solitary fibrous tumor
- Inflammatory myofibroblastic tumor
- Angiomatoid fibrous histiocytoma
- Gastrointestinal stromal tumor
- Myoepithelial neoplasms
- PEComa



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Diagnostic Categories

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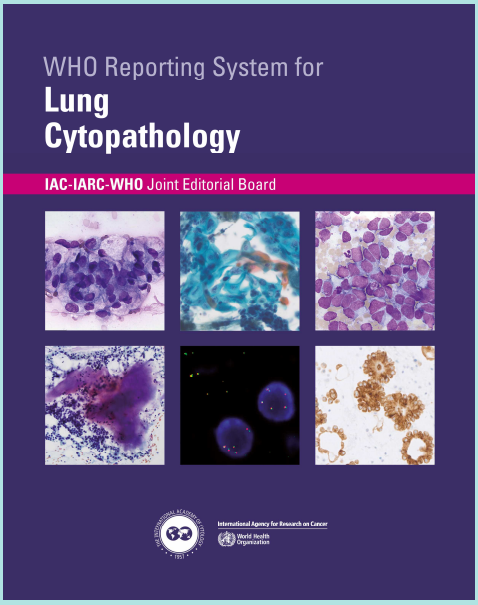
2. Benign
3. Atypical
4. Suspicious for Malignancy
5. Malignant



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WHO Reporting System for Lung Cytopathology

World Health Organization

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0.2: How to cite this volume
0.3: Foreword with changes from the book, including corrigenda

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2.0.0.2: The role of lung cytopathology
2.0.0.3: Diagnostic categories and report structure
2.0.0.4: Risk of malignancy and management recommendations

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Diagnostic Categories with ROM and Management for Lung FNAB

Diagnostic category	Estimated ROM[a]	Clinical management options[b]
"Insufficient/Inadequate/Non-diagnostic"	43–53%	Correlate with CLIN-IMG-MICRO, ideally discuss at an MDT meeting, and perform repeat FNAB with or without CNB
"Benign"	19–64%	Correlate with CLIN-IMG-MICRO; if these confirm a benign diagnosis, then routine follow-up at 3–6 months; if no correlation, perform repeat FNAB with or without CNB
"Atypical"	46–55%	Correlate with CLIN-IMG-MICRO, and ideally discuss at an MDT meeting; if all show a benign diagnosis, then routine follow-up at 3–6 months; if no correlation, perform repeat FNAB with ROSE with or without CNB
"Suspicious for malignancy"	75–88%	Correlate with CLIN-IMG-MICRO, and ideally discuss at an MDT meeting; if all four support a diagnosis of malignancy, consider definitive treatment; if no correlation that lesion is malignant, perform repeat FNAB with ROSE with or without CNB
"Malignant"	87–100%	Correlate with CLIN-IMG-MICRO, and ideally discuss at an MDT meeting; if all four support a diagnosis of malignancy, provide definitive treatment; if no correlation that lesion is malignant, consider repeat FNAB with ROSE with or without CNB

Diagnostic Categories with ROM and Management for Sputum, Bronchial Washing and Bronchial Brushing

Diagnostic category	Estimated ROM[a]	Clinical management options[b]
"Insufficient/Inadequate/Non-diagnostic"	Sputum sample: 0–100% BW: 38–81% BB: 0–75%	Consider repeating the sampling or use BB/BW (in case of sputum sample) and/or FNAB, depending on CLIN-IMG-MICRO
"Benign"	Sputum sample: 0–42% BW: 38–42% BB: 32–38%	Correlate with CLIN-IMG-MICRO; if these confirm a benign diagnosis, then routine follow-up at 3–6 months; if no correlation, consider new sampling
"Atypical"	Sputum sample: 86–100% BW: 62–86% BB: 79–100%	Correlate with CLIN-IMG-MICRO; if these are "Benign", repeat; if "Atypical" or "Suspicious for malignancy", perform BB/BW or FNAB with or without CNB
"Suspicious for malignancy"	Sputum sample: 100% BW: 83–100% BB: 75–100%	Correlate with CLIN-IMG-MICRO, and perform BB/BW or FNAB with or without CNB; these cases need to be discussed at MDT meetings
"Malignant"	Sputum sample: 100% BW: 98–100% BB: 94–100%	Correlate with CLIN-IMG-MICRO, and perform BB/BW or FNAB with or without CNB to confirm diagnosis before definitive treatment

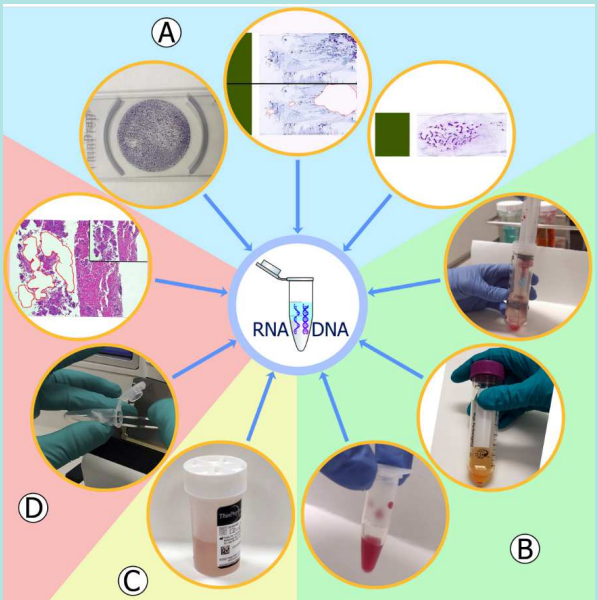
Different types of FNAB techniques and indications

Source:

Type of FNAB	Indications	Advantages	Limitations
Percutaneous transthoracic FNAB	New or enlarging solitary lung nodules on CXR or CT that are not amenable to diagnosis by bronchoscopy	High diagnostic yield Avoids open lung biopsy	Risk of pneumothorax
Ultrasound-guided	Sonographically visible subpleural or superficial lesions that are in contact with the chest wall	Quick and easy to perform	Only for superficial lesions
CT-guided	For deep parenchymal lesions	Deep lesions can be sampled	Time-consuming
	Endobronchial lesions		
	Peribronchial parenchymal lesions		
	Bronchial submucosal lesions		
Transbronchial/endobronchial FNAB without imaging guidance (blind/conventional TBFNAB)	Mediastinal, hilar, and subcarinal lymph nodes or hilar mass lesions for staging lung cancer, diagnosis of granulomatous diseases, lymphoma, extrapulmonary metastasis, or workup of nonspecific mediastinal lymphadenopathy	High sensitivity	Limited accessibility of mediastinum
EBUS-TBFNAB (lung)	Same as conventional TBFNAB	Can also access peripheral pulmonary lesions with the help of radial probe (radial EBUS) Can access nodal stations 10 (hilar), 11 (interlobar), and partial 12 (lobar)	Cannot access posteroinferior mediastinum and upper lobe lesions Costly; limited availability
EBUS-TBFNAB (lymph nodes)	Mediastinal lymphadenopathy of stations 8 (para-oesophageal, below carina) and 9 (pulmonary ligament)	Can be done safely alongside EBUS in a single session	n/a

EBUS, endobronchial ultrasound; EBUS-TBFNAB, endobronchial ultrasound–guided transbronchial FNAB; n/a, not applicable; TBFNAB, transbronchial FNAB.

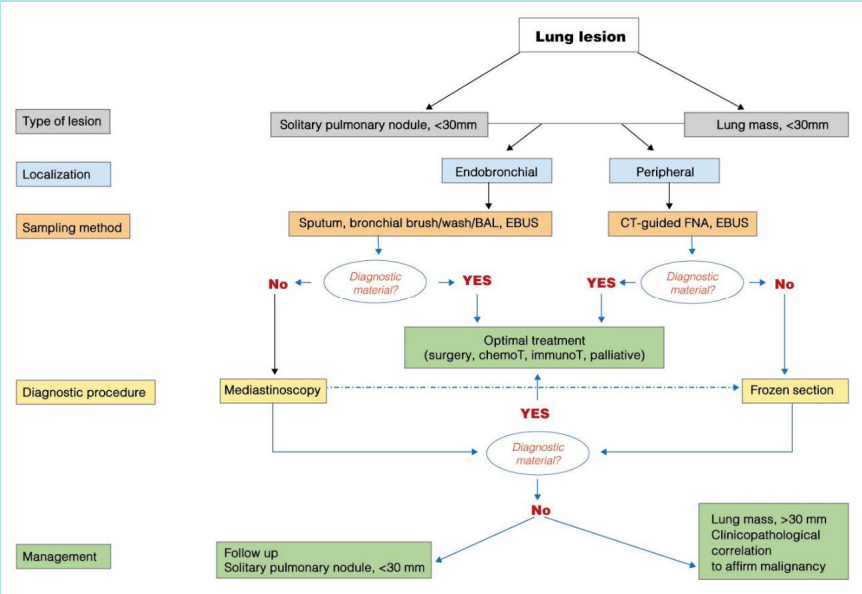
(from WHO Reporting System for Lung Cytopathology, Chapter 2)



Legend: Different types of cytological samples. **A** Direct smears (with/without microdissection/macrodissection). Pap-stained and Giemsa-stained and/or unstained slides. Cell scraping preferred. **B** Needle-rinse, supernatant, and fresh samples. **A** and **B** give high-quality DNA/RNA. **C** Optimal quality for extraction of DNA/RNA. **D** Cell blocks; long formalin fixation can lead to C>T or G>A artefacts.

(from WHO Reporting System for Lung Cytopathology, Chapter 2; source Maria Lozano)

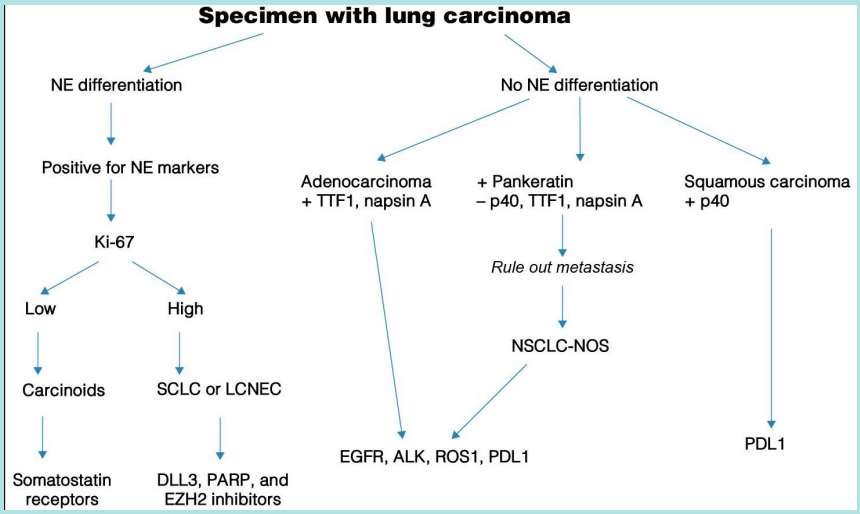
Management Algorithm for Insufficient/Inadequate/Nondiagnostic Specimen



(from WHO Reporting System for Lung Cytopathology, Chapter 8; Source Sule Canberk Schmitt)

Algorithm or Evaluating Lung FNAB

(from WHO Reporting System for Lung Cytopathology, Chapter 2; source Claire Michael)



Legend: Immunocytochemistry (ICC) algorithm for subtyping lung cancer. LCNEC, large cell neuroendocrine carcinoma; NE, neuroendocrine; NSCLC, non-small cell lung carcinoma; PARP, poly (ADP-ribose) polymerase; SCLC, small cell lung carcinoma; TTF1, thyroid transcription factor 1.

Differential Diagnosis of Mesothelioma

(from WHO Reporting System for Lung Cytopathology, Chapter 7; Source Claire Michael)

Feature	Mesothelioma	Reactive mesothelium	Carcinoma
Gross examination of pleural fluid:			
Consistency	Thick, tar-like	Thin	Generally thin
Appearance	Serosanguineous or bloody	Serosanguineous	Serosanguineous or bloody
Background:			
Clear	Some cases	Most cases	Some cases
Bloody	Frequently	Rare cases[a]	Most cases
Obscuring matrix	Frequent (hyaluronan)	Absent	In cases with mucin
Inflammation	May be present	Frequent	May be present
Low magnification:			
Cellularity	Strikingly high[b]	Moderate to high	Usually high
Tissue fragments	Plentiful, vary in size	Few, small	May be numerous, little variation in size
Single cells	Alone or combined with tissue fragments	Most cases	Alone or combined with tissue fragments
Populations	Monotonous population of mesothelial cells with wide variation in size	Monotonous population of mesothelial cells with minimal variation in size	Alien population in background of mesothelial cells
Tissue fragments:			
Shape	Predominantly 3D, berry-like morules with scalloped borders or spheres	Predominantly 2D tissue fragments with scalloped borders	3D tissue fragments with common cell borders
Architecture	Variable size and complexity, sometimes very complex branching papillae	Mostly simple and small	Variable complexity depending on primary
Collagenous core	Occasionally present and may be conspicuous	Rare	Uncommon, fibrovascular cores in papillary tumours
Hollow tissue fragments	May be present	Absent	Not characteristic

Immunostains for Work-up of Pulmonary Metastases

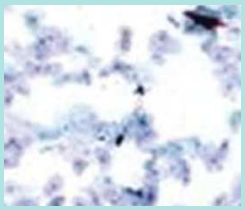
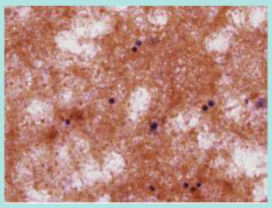
(from WHO Reporting System for Lung Cytopathology, Chapter 7; Source Zubair Baloch)

Site of origin	Immunocytochemistry profile[a]
Gastrointestinal tract	
Oesophagus (adenocarcinoma)	CK7+, CK20−, TTF1−, CDX2+/−, CEA+, EMA (MUC1)−/+, MUC5AC−/+, SATB2−
Stomach	CK7+, CK20+, TTF1−, CEA+, CDX2−/+, EMA (MUC1)−/+, MUC5AC−/+
Colon and rectum	CK7−, CK20+, CDX2+, SATB2+, MOC31+
Breast	CK7+, CK20−, GATA3+, mammaglobin+/−, GCDFP-15−/+, ER+, PR+, TTF1
Melanoma	SOX10+, melan-A+, MART1+, S100+, HMB45+, CK7−, CK20−
Pancreas (adenocarcinoma)	CK7+, CK20+, SMAD4 (DPC4)−/+, CK17+/−, VHL protein−, maspin+, S100+, MOC31+, MUC5AC+
Liver (hepatocellular)	CK7−, CK20−, HepPar1+, AFP+, GPC3+, ARG1+, CD10+, polyclonal CEA+, monoclonal CEA−
Genitourinary tract	
Urinary bladder (urothelial)	CK7+, CK20+/−, GATA3+, p63+, p40+, CK5/6+, S100+, 34βE12 (CK903)+, uroplakin+, thrombomodulin+
Prostate (adenocarcinoma)	CK7−, CK20−, PSA+, NKX3-1+, PAP+, AMACR (P504S)+
Ovary (serous)	CK7+, CK20−, PAX8+, ER+, WT1+, TTF1−, TFF3−, GATA3−
Ovary (clear cell)	CK7+, CK20−, VHL protein+, napsin A+, WT1−, ER−, AFP−
Ovary (mucinous)	CK7+, CK20−, SMAD4 (DPC4)+, CA125+, CDX2+/−
Endometrium	CK7+, CK20−, ER+, PR+, PAX8+, CEA+ (foci of squamous metaplasia)
Uterine cervix (adenocarcinoma)	CK7+, CK20−, p16+, CEA+, PR−, PAX8+/−
Kidney	
Clear cell	CK7−, PAX8+, PAX2+, CAIX+, CD10+, RCCm+, AE1/AE3+, CAM5.2+, EMA+, AMACR+/−, GATA3−, TTF1−
Clear cell papillary	CK7+, PAX8+, CAIX+, CD10−, RCCm+/−, AMACR−, GATA3−/+ (rare cases)

The WHO Reporting System for Lung Cytopathology

Insufficient/Inadequate/Non diagnostic

- Provides no useful diagnostic information (in a specific clinical context)
  - ✓ Insufficient cellularity
  - ✓ Cellular degeneration
  - ✓ Hemorrhagic samples
  - ✓ Bad preservation of cells
- Any atypia should be reported as such and put under the atypical or "suspicious" category.
- Incidence: around 16% (few studies)
- Reported ROM: 43-53% (few studies, different samples)

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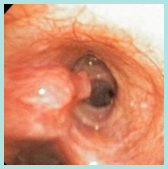
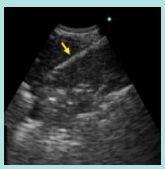
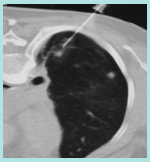
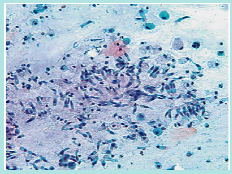
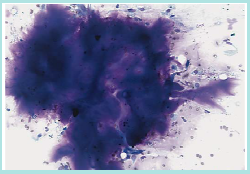
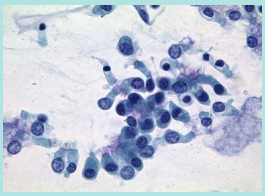
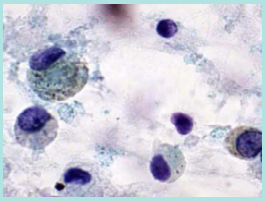
Insufficient/Inadequate/Non diagnostic

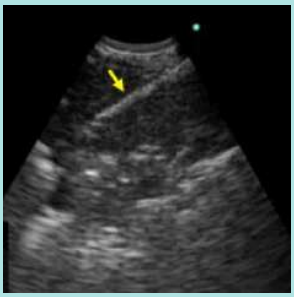
68 y-old man with pulmonary lesion/nodule

The WHO Reporting System for Lung Cytopathology

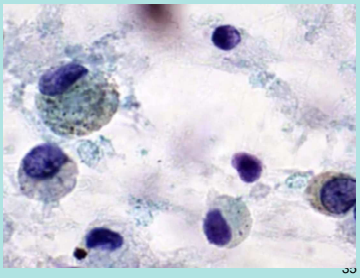
Example Report

2 cm well round mass in the lung



- Insufficient/Inadequate/Nondiagnostic
- Only macrophages (see note)

- Note: The biopsy does not explain a well-defined lung mass.



The WHO Reporting System for Lung Cytopathology

Benign

- *A specimen categorized as 'Benign' demonstrates unequivocal benign cytopathological features, which may or may not be diagnostic of a specific process or benign neoplasm.*

- INCIDENCE: around 50% * (Few studies)
- Reported ROM: 19-64% (few studies, different samples)
- MAIN CAUSES: inflammatory/infectious diseases/benign neoplastic lesions
- MANAGEMENT: Correlate with CLIN-IMG-MICRO and if these confirm benign, routine follow-up 3-6 months. If no correlation consider new sampling.

The WHO Reporting System for Lung Cytopathology

5.0: Diagnostic category: Benign

- 5.0.0.1: Introduction
- 5.0.0.2: Definition
- 5.0.0.3: Discussion and background
- 5.0.0.4: Risk of malignancy and management recommendations

5.1: Inflammatory processes

- 5.1.0.1: Acute inflammation and suppuration
- 5.1.0.2: Histiocytic, lymphocytic, and eosinophilic inflammatory patterns
- 5.1.0.3: Granulomatous disorders
- 5.1.0.4: Inflammatory and reactive changes in glandular cells and squamous cells

5.2: Benign neoplastic lesions

- 5.2.0.1: Pulmonary hamartoma
- 5.2.0.2: Sclerosing pneumocytoma
- 5.2.0.4: Bronchial papillomas
- 5.2.0.5: Salivary gland tumours
- 5.2.0.8: PEComa
- 5.2.0.9: Spindle cell tumours
- 5.2.0.10: Meningiomas
- 5.2.0.11: Granular cell tumour
- 7.0.1.3: Ectopic thyroid and parathyroid tumours

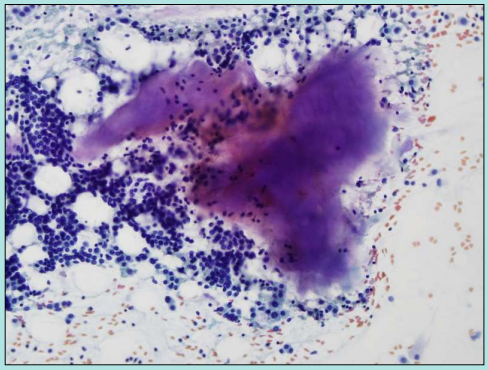
5.2.1: Sample reports

The WHO Reporting System for Lung Cytopathology

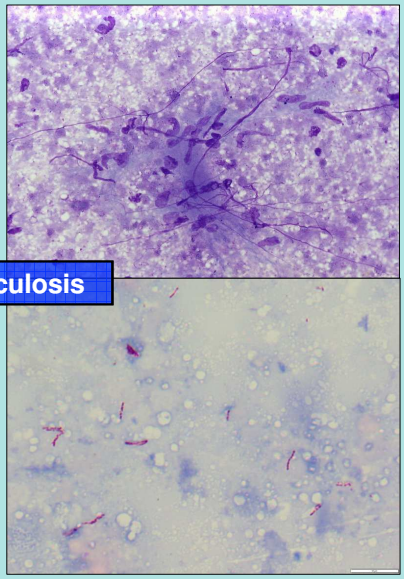
Example Report

Female 40y-old, 1.5 cm well round mass in the lung periphery

- Satisfactory for Evaluation
- Benign
- Pulmonary hamartoma (consistent with)

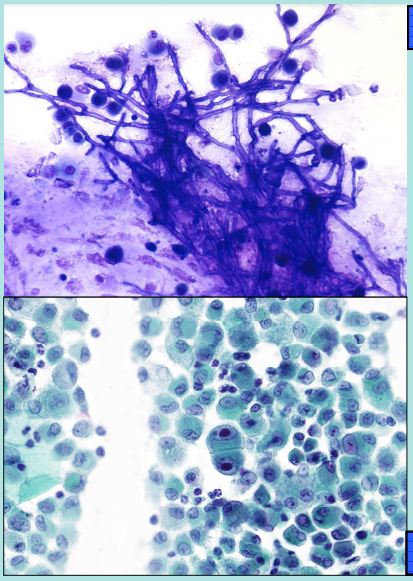


Source: Longwen Cheng and Matthew Zarka, Chapter 5: International System for Reporting Lung Cytopathology, 2022



Tuberculosis

Source: Marianne Engels, Chapter 5: WHO Reporting System for Lung Cytopathology, 2022



Aspergilosis

CMV

Source: Lara Pijuan , Chapter 5: WHO Reporting System for Lung Cytopathology, 2022

The WHO Reporting System for Lung Cytopathology

Atypical

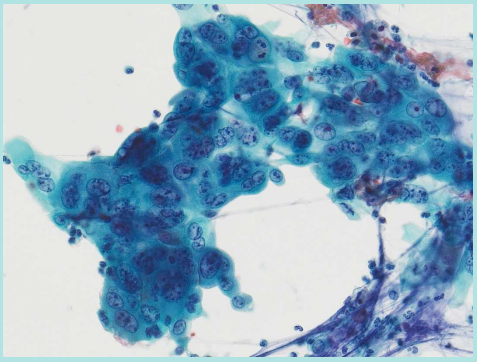
- *A specimen categorized as 'Atypical' demonstrates features predominantly seen in benign lesions and minimal features that may raise the possibility of a malignant lesion, but with insufficient features either in number or quality to diagnose a benign or malignant lesion.*
- INCIDENCE: around 5% (few studies)
- Reported ROM: 46-55% (few studies, different samples)
- MAIN CAUSES: reactive changes (metaplasia, hyperplasia), infectious (viral), post-therapy changes
- MANAGEMENT: Correlate with CLIN-IMG-MICRO, and if these are benign, repeat in case of exfoliative cytology or follow-up at 3-6 months after MDT in case of FNAB. If clinical or image are atypical or suspicious for malignancy, then perform BB/BW or FNAB with or without CNB.

The WHO Reporting System for Lung Cytopathology

Example Report

Male 70y-old, previous history of radiochemotherapy for SCLC.

- Satisfactory for Evaluation
- Atypical
- Atypia in metaplastic squamous and glandular cells. See note.
- Note: Previous history of therapy is noted. Clinical and imaging correlation are recommended.



Source: Prof Lukas Bubendorf

The WHO Reporting System for Lung Cytopathology

Suspicious for Malignancy

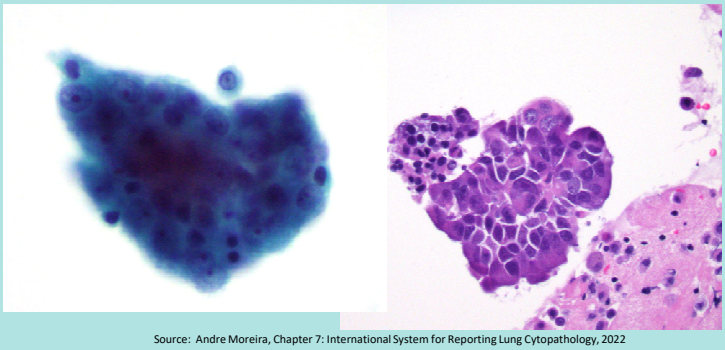
- *This diagnostic category applies to samples that demonstrate some features suggestive of malignancy but insufficient either in number or quality to make an unequivocal diagnosis of malignancy.*
- INCIDENCE: around 5% (Few studies)
- Reported ROM: 75-88% (few studies, different samples)
- MAIN CAUSES: intrinsic characteristics of the tumor (low-grade), extreme reactive atypia.
- MANAGEMENT: Correlate with CLIN-IMG-MICRO and ideally discuss at a MDT meeting. If no correlation that lesion is malignant, perform repeat FNAB with ROSE with or without CNB.

The WHO Reporting System for Lung Cytopathology

Example Report

CT-guided FNAB of a lung mass.

- Satisfactory for Evaluation
- Suspicious (for Malignancy)
- Neoplasm with features suspicious for (adeno)carcinoma. Tissue for confirmatory ancillary studies is not available.



Source: Andre Moreira, Chapter 7: International System for Reporting Lung Cytopathology, 2022

The WHO Reporting System for Lung Cytopathology

Malignant

- *A specimen classified as "Malignant" demonstrates unequivocal cytomorphologic features for malignancy. An attempt should be made to further subclassify the neoplasm based on cytomorphology and, if necessary, by ancillary tests.*
- INCIDENCE: around 20% * (Few studies)
- Reported ROM: 87-100% (few studies, different samples)
- MAIN CAUSES: primary and second malignancies.
- MANAGEMENT: Correlate with CLIN-IMG-MICRO, and ideally discuss at a MDT meeting. If all FOUR support a diagnosis of malignancy, provide definitive treatment. If no correlation that lesion is malignant, consider repeat FNAB with ROSE with or without CNB

The WHO Reporting System for Lung Cytopathology

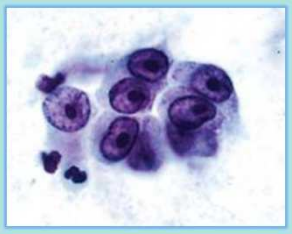
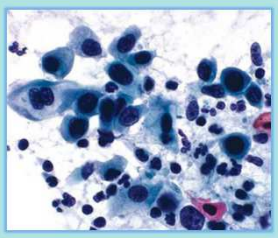
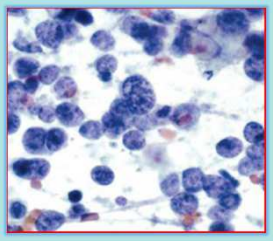
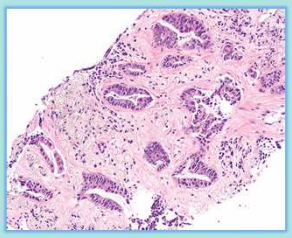
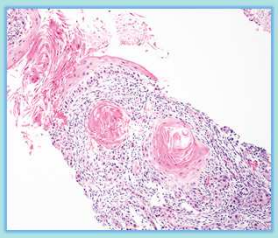
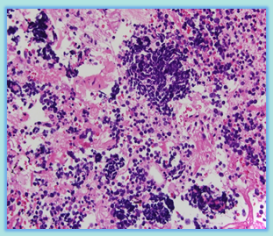
8.1: Specific malignant lesions
- 8.1.1: Non-small cell carcinomas
  - 8.1.1.1: Adenocarcinoma of the lung
  - 8.1.1.2: Squamous cell carcinomas
  - 8.1.1.3: Non-small cell carcinoma NOS
- 8.1.2: Other specific carcinomas
  - 8.1.2.1: Salivary gland-type carcinomas
  - 8.1.2.2: Adenosquamous carcinoma
  - 8.1.2.3: Pleomorphic carcinoma
  - 8.1.2.4: Pulmonary blastoma
  - 8.1.2.5: Carcinosarcoma
  - 8.1.2.6: NUT carcinoma
  - 8.1.2.7: Thoracic SMARCA4-deficient undifferentiated tumour

8.2: Neuroendocrine neoplasms
- 8.2.1: Neuroendocrine tumours
  - 8.2.1.1: Carcinoid/neuroendocrine tumours of the lung
- 8.2.2: Neuroendocrine carcinomas
  - 8.2.2.1: Small cell lung carcinoma
  - 8.2.2.2: Large cell neuroendocrine carcinoma

8.3: Lymphoproliferative diseases
- 8.3.0.1: Lymphomas
- 8.3.0.2: Pulmonary Langerhans cell histiocytosis
- 8.3.0.3: Erdheim-Chester disease

8.4: Other malignancies
- 8.4.0.1: Spindle cell tumours
- 5.2.0.7: Paraganglioma
- 8.4.0.2: Diffuse pleural mesothelioma
- 8.4.0.3: Primary germ cell tumours of the mediastinum
- 8.4.0.4: Pulmonary and thoracic metastases
- 8.4.0.5: Angiosarcoma
- 8.4.1: Sample reports

LUNG CANCER
Morphological Aspects

Adenocarcinoma	Squamous Cell Ca	Small Cell Ca
		
		

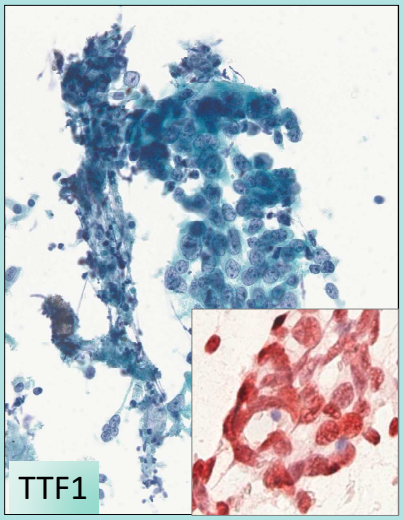
The WHO Reporting System for Lung Cytopathology

Example Report

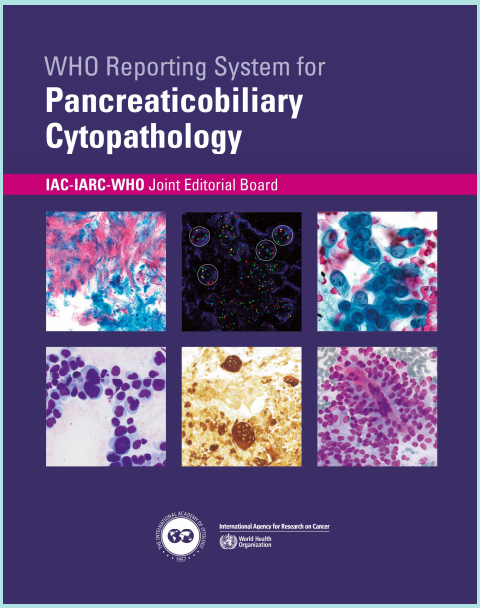
Male 75y-old, heavy smoker, lung mass.

- Satisfactory for Evaluation
- Malignant
- NSCLC favor Adenocarcinoma

- Note: Immunohistochemical stains show the tumor cells to be positive for TTF1 and negative for P40 supporting the diagnosis.



Source: Prof Lukas Bubendorf



April 2023

How to Cite Whole Volume:

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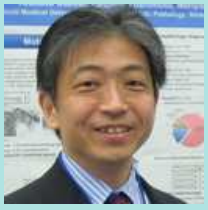
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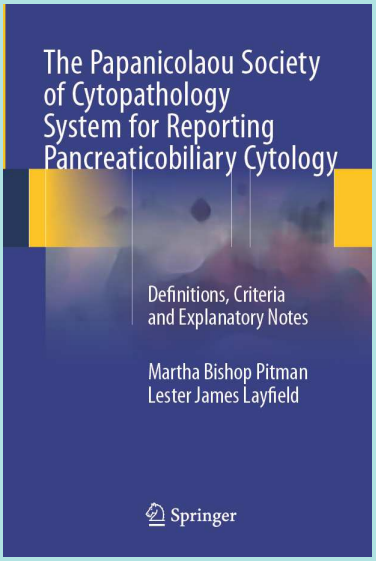


2015

Standardized Terminology and Nomenclature for Pancreaticobiliary Cytology: The Papanicolaou Society of Cytopathology Guidelines

Diagn Cytopathol. 2014 Apr;42(4):338-50.

Martha B. Pitman, M.D.,[1] Barbara A. Centeno, M.D.,[2] Syed Z. Ali, M.D.,[3] Muriel Genevay, M.D.,[4] Ed Stelow, M.D.,[5] Mari Mino-Kenudson, M.D.,[1] Carlos Fernandez-del Castillo, M.D.,[6] C. Max Schmidt, M.D.,[7] William Brugge, M.D.,[8] Lester Layfield, M.D.,[9]

Table 1 Diagnostic categories of PSC system.

Diagnostic category	Examples of diagnostic entities
I. Nondiagnostic	Acellular aspirate with no evidence of a mucinous etiology
	Gastrointestinal contamination
	Benign pancreatic parenchyma, if a well-defined mass is identified on imaging
II. Negative for malignancy	Benign pancreatic parenchyma, if a well-defined mass is not identified on imaging
	Acute pancreatitis
	Chronic pancreatitis
	Autoimmune pancreatitis
	Pseudocyst
	Lymphoepithelial cyst
	Ectopic splenic tissue
III. Atypical	Atypical ductal cells, obscured by artifact
IV. Neoplastic: benign	Serous cystadenoma
	Lymphangioma
IV. Neoplastic: other	Neuroendocrine tumor, well-differentiated
	Intraductal papillary mucinous neoplasm (including all grades of dysplasia)
	Mucinous cystic neoplasm (including all grades of dysplasia)
	Solid pseudopapillary neoplasm
V. Suspicious for malignancy	Rare markedly atypical epithelial cells, insufficient in quality or quantity for positive or malignant diagnosis
VI. Positive or malignant	Pancreatic ductal adenocarcinoma
	Cholangiocarcinoma
	Acinar cell carcinoma
	Neuroendocrine carcinoma, poorly differentiated
	Pancreatoblastoma
	Lymphoma
	Metastatic malignancy

Abbreviation: PCS, Papanicolaou Society of Cytopathology.
Data from Pitman et al.[5]

Table 3 Absolute risk and relative risk of malignancy of the diagnostic categories in the PCS system.

Diagnostic category	Absolute risk of malignancy (%)	Relative risk	*P* value (relative to benign category)
I. Nondiagnostic	7.7	7.7	0.07
II. Negative for malignancy	1.0	1.0	NA
III. Atypical	28.0	28.0	0.001[a]
IV. Neoplastic: benign	0.0	0.0	1.00
IV. Neoplastic: other, all grades of atypia	30.3	30.3	<0.001[a]
With low-grade atypia	4.3	4.3	0.23
With high-grade atypia	90.0	90.0	<0.001[a]
V. Suspicious for malignancy	100.0	100.0	<0.001[a]
VI. Positive or malignant	100.0	100.0	<0.001[a]

Abbreviations: NA, not applicable; PCS, Papanicolaou Society of Cytopathology.
[a]Statistically significant ($P < 0.05$).

Journal of the American Society of Cytopathology (2019) 8, 120–127

Pancreatic Tumor Classification:
WHO Digestive System Tumours, 5th Edition

10: Tumours of the pancreas

10.0: Tumours of the pancreas: Introduction

10.3.6: Epithelial tumours

- 10.1: Benign epithelial tumours and precursors
  - 10.1.1: Acinar cystic transformation of the pancreas
  - 10.1.2: Serous neoplasms of the pancreas
  - 10.2.1: Pancreatic intraepithelial neoplasia
  - 10.2.2: Pancreatic intraductal papillary mucinous neoplasm
  - 10.2.3: Pancreatic intraductal oncocytic papillary neoplasm
  - 10.2.4: Pancreatic intraductal tubulopapillary neoplasm
  - 10.2.5: Pancreatic mucinous cystic neoplasm
- 10.3: Malignant epithelial tumours
  - 10.3.1: Pancreatic ductal adenocarcinoma
  - 10.3.3: Pancreatic acinar cell carcinoma
  - 10.3.4: Pancreatoblastoma
  - 10.3.5: Solid pseudopapillary neoplasm of the pancreas
- 11.6: Pancreatic neuroendocrine neoplasms
  - 11.6b: Pancreatic neuroendocrine neoplasms: Introduction
  - 11.6.1.1: Non-functioning pancreatic neuroendocrine tumours
  - 11.6.1: Functioning pancreatic neuroendocrine tumours
    - 11.6.1.2: Insulinoma
    - 11.6.1.5: Gastrinoma
    - 11.6.1.6: VIPoma
    - 11.6.1.3: Glucagonoma
    - 11.6.1.4: Somatostatinoma
    - 11.6.1.8: ACTH-producing neuroendocrine tumour
    - 11.6.1.7: Serotonin-producing neuroendocrine tumour
  - 11.6.2: Pancreatic neuroendocrine carcinoma
  - 11.6.3: Pancreatic MiNENs

WHO Reporting System for PB Cytopathology

World Health Organization

1.0: Chapter 1: Introduction to the WHO Reporting System for Pancreaticobiliary Cytopathology
- 1.0.0.1: Background
- 1.0.0.2: The role of pancreaticobiliary cytopathology
- 1.0.0.6: Integration of clinical, radiological, and key FNAB cytopathological features with ancillary testing in a diagnostic approach
- 1.0.0.3: Diagnostic categories and report structure
- 1.0.0.4: Risk of malignancy and management recommendations

2.0: Chapter 2: Pancreaticobiliary cytopathology techniques
- 2.1: Sampling methods and tissue triage
  - 2.1.0.1: FNAB techniques and specimen management for solid pancreatic masses
  - 2.1.0.2: FNAB techniques and specimen management for pancreatic cysts
  - 2.1.0.3: FNAB techniques and specimen management for bile duct brushings
  - 2.1.0.4: Percutaneous FNAB and specimen management
  - 2.1.0.5: Rapid onsite evaluation
- 2.2: Ancillary testing
  - 2.0.0.1: Introduction: The role of ancillary testing
  - 2.2.0.1: Immunocytochemistry
  - 2.2.0.2: In situ hybridization
  - 2.2.0.3: Molecular testing
  - 2.2.0.4: Biochemical testing of cyst fluid

3.0: Chapter 3: Diagnostic category: Insufficient/Inadequate/Non-diagnostic
- 3.0.0.1: Introduction
- 3.0.0.2: Definition
- 3.0.0.3: Discussion and background
- 3.0.0.5: Risk of malignancy and management recommendations
- 3.0.1: Sample reports: Insufficient/Inadequate/Non-diagnostic

4.0: Chapter 4: Diagnostic category: Benign / Negative for malignancy
- 4.0.0.1: Introduction
- 4.0.0.2: Definition
- 4.0.0.3: Discussion and background
- 4.0.0.4: Risk of malignancy and management recommendations
- 4.0.1: Benign non-neoplastic processes
  - 4.0.1.1: Normal pancreatic and biliary parenchyma and contaminants
  - 4.0.1.2: Acute pancreatitis
  - 4.0.1.3: Cholangitis
  - 4.0.1.4: Chronic pancreatitis
  - 4.0.1.5: Groove/paraduodenal pancreatitis
  - 4.0.1.6: Autoimmune and IgG4-related pancreatitis
  - 4.0.1.7: Lymphoepithelial cyst
  - 4.0.1.8: Pseudocysts
  - 4.0.1.9: Splenule (accessory spleen)
- 4.0.2: Benign neoplastic processes
  - 4.0.2.1: Serous cystadenoma
  - 4.0.2.2: Schwannoma
  - 4.0.2.3: Lymphangioma
  - 4.0.2.4: Other rare benign neoplasms
- 4.0.3: Sample reports: Benign / Negative for malignancy

5.0: Chapter 5: Diagnostic category: Atypical
- 5.0.0.1: Introduction
- 5.0.0.2: Definition
- 5.0.0.3: Discussion and background
- 5.0.0.4: Risk of malignancy and management recommendations

6.0: Chapter 6: Diagnostic category: Pancreaticobiliary neoplasm, low-risk/grade
- 6.0.0.1: Introduction
- 6.0.0.2: Definition
- 6.0.0.4: Discussion and background
- 6.0.0.3: Risk of malignancy and management recommendations
- 6.0.1: Specific lesions
  - 6.0.1.1: Pancreatic intraepithelial neoplasia, low-grade
  - 6.0.1.2: Biliary intraepithelial neoplasia, low-grade
  - 6.0.1.3: Pancreatic intraductal papillary mucinous neoplasm, low-grade
  - 6.0.1.4: Intraductal papillary neoplasm of the bile duct, low-grade
  - 6.0.1.5: Mucinous cystic neoplasm, low-grade
  - 6.0.1.6: Other lesions (including spindle cell tumours)
- 6.0.2: Sample reports: Pancreaticobiliary neoplasm, low-risk/grade

7.0: Chapter 7: Diagnostic category: Pancreaticobiliary neoplasm, high-risk/grade
- 7.0.0.1: Introduction
- 7.0.0.2: Definition
- 7.0.0.4: Discussion and background
- 7.0.0.3: Risk of malignancy and management recommendations
- 7.0.1: Specific lesions
  - 7.0.1.1: Pancreatic intraepithelial neoplasia, high-grade
  - 7.0.1.2: Biliary intraepithelial neoplasia, high-grade
  - 7.0.1.3: Pancreatic intraductal papillary mucinous neoplasm, high-grade
  - 7.0.1.4: Intraductal papillary neoplasm of the bile duct, high-grade
  - 7.0.1.5: Mucinous cystic neoplasm, high-grade
  - 7.0.1.6: Intraductal oncocytic papillary neoplasm
  - 7.0.1.7: Intraductal tubulopapillary neoplasm
- 7.0.2: Sample reports: Pancreaticobiliary neoplasm, high-risk/grade

8.0: Chapter 8: Diagnostic category: Suspicious for malignancy
- 8.0.0.1: Introduction
- 8.0.0.2: Definition
- 8.0.0.3: Discussion and background
- 8.0.0.4: Risk of malignancy and management recommendations
- 8.0.1: Sample reports: Suspicious for malignancy

9.0: Chapter 9: Diagnostic category: Malignant
- 9.0.0.1: Introduction
- 9.0.0.2: Definition
- 9.0.0.4: Discussion and background
- 9.0.0.3: Risk of malignancy and management recommendations
- 9.0.1: Specific lesions
  - 9.0.1.1: Cholangiocarcinoma
  - 9.0.1.2: Pancreatic ductal adenocarcinoma
  - 9.0.1.3: Pancreatic acinar cell carcinoma
  - 9.0.1.4: Neuroendocrine tumour
  - 9.0.1.5: Neuroendocrine carcinoma
  - 9.0.1.6: Pancreatoblastoma
  - 9.0.1.7: Solid pseudopapillary neoplasm
  - 9.0.1.8: Pancreatic lymphomas
  - 9.0.1.9: Metastases to the pancreas
  - 9.0.1.10: Other lesions (including spindle cell tumours)
- 9.0.2: Sample reports: Malignant

	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,	Malignant	7

Table 1. The World Health Organization System for Reporting Pancreatic Cytopathology: implied risk of malignancy and clinical management options by diagnostic category for Pancreatic FNAB.

Diagnostic category	Estimated risk of malignancy (%)[a]	Clinical Management Options[b]
Insufficient/inadequate/nondiagnostic	5 – 25	Repeat FNAB
Benign/Negative for Malignancy	0 – 15	Correlate clinically
Atypical	30 – 40	Repeat FNAB
Pancreatic Neoplasm: low risk/low-grade (PaN-Low)	5 – 20	Correlate clinically
Pancreatic Neoplasm: high risk/high-grade (PaN-High)	60 – 95	Surgical Resection in surgically fit patients Conservative management optional
Suspicious for Malignancy	80 – 100	If patient to be surgically managed, treat as positive If patient requires pre-operative therapy, repeat FNAB
Malignant	99 – 100	Per clinical stage

Abbreviation: FNAB, fine-needle aspiration biopsy.
[a] Estimated risks of malignancy are based on retrospective and prospective studies with risk analysis based on pancreatic neoplasia with low-grade and high-grade cytopathological atypia.
[b] Management options for patients with pancreatic lesions may depend on a variety of factors, including clinical and imaging characteristics and the overall functional status of the patient. Some clinical management suggestions are outlined as above.

Hoda RS, Arpin RN 3rd, Rosenbaum MW, Pitman MB. Risk of malignancy associated with diagnostic categories of the proposed World Health Organization International System for Reporting Pancreaticobiliary Cytopathology. Cancer Cytopathol. 2021 Oct 8. doi: 10.1002/cncy.22514. Epub ahead of print. PMID: 34623767.

Table 2. The World Health Organization International System for Reporting Pancreaticobiliary Cytopathology: implied risk of malignancy and clinical management options by diagnostic category for Bile Duct Brushing Specimens.

Diagnostic category	Estimated risk of malignancy (%)[a]	Clinical management options[b]
Insufficient/inadequate/nondiagnostic	28 – 69	Repeat ERCP with cholangioscopy, brushing, and biopsies
Benign/Negative for Malignancy	26 – 55	Correlate clinically
Atypical	25 – 77	Repeat ERCP with cholangioscopy, brushing, and biopsies; consider ancillary testing with FISH and/or NGS
Pancreatic Neoplasm-low-grade (PaN-low)	NA[c]	NA
Pancreatic Neoplasm-high-grade (PaN-high)	NA[c]	NA
Suspicious (for malignancy)	74 – 100	Repeat sampling with ancillary testing (FISH and/or NGS) or, if other factors support malignancy, surgical intervention; for neoadjuvant therapy, repeat ERCP with cholangioscopy/brushings/biopsies/ancillary studies
Malignant	96 – 100	Per clinical stage

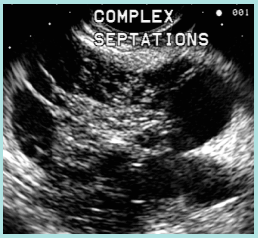
Abbreviation: ERCP, endoscopic retrograde cholangiopancreatography; FNAB, fine-needle aspiration biopsy; FISH, fluorescence in-situ hybridization; NA, not available/not applicable; NGS, next-generation sequencing.

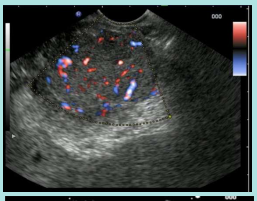
[a] Estimated risks of malignancy are based on retrospective and prospective studies with risk analysis based on pancreatic neoplasia with low-grade and high-grade cytologic atypia {10049415,24167030,26596524,28411396,32649050,34800330,35163571}.

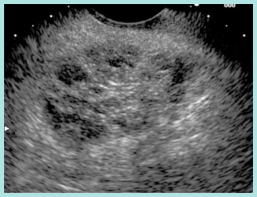
[b] Management options for patients with bile duct strictures may depend on a variety of factors, including clinical and imaging characteristics and overall functional status of the patient. Some clinical management suggestions are outlined as above.

[c] Cytological criteria for premalignant neoplasms of the bile duct are lacking and, thus, there are no data on bile duct categorization in the PaN-low and PaN-high categories.

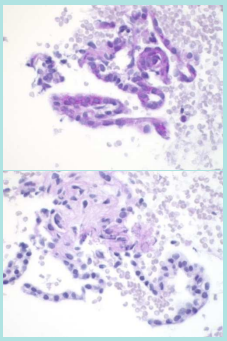
Clinical and Imaging Features



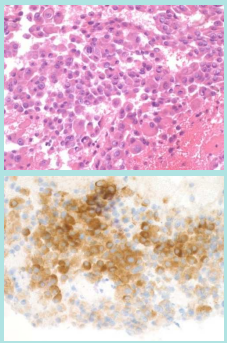




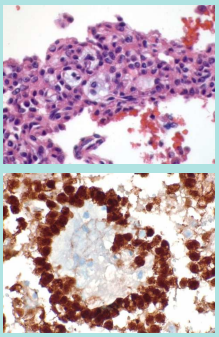
Cytomorphology, Special Stains and Immunohistochemistry



PAS and PASD



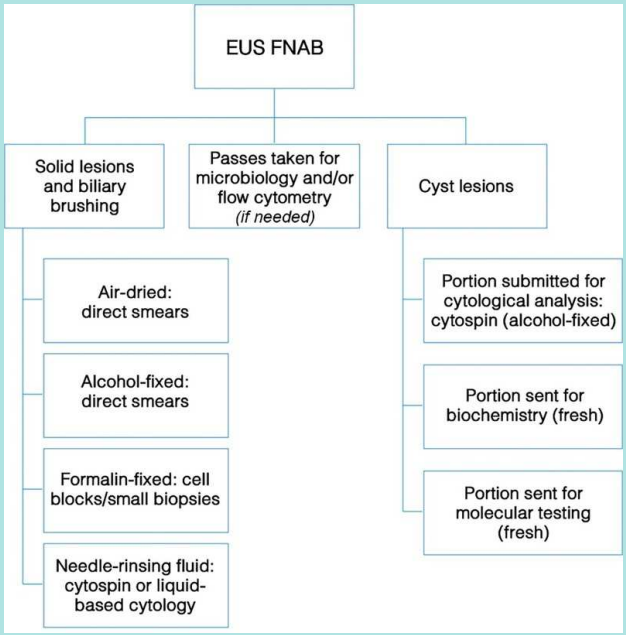
Synaptophysin



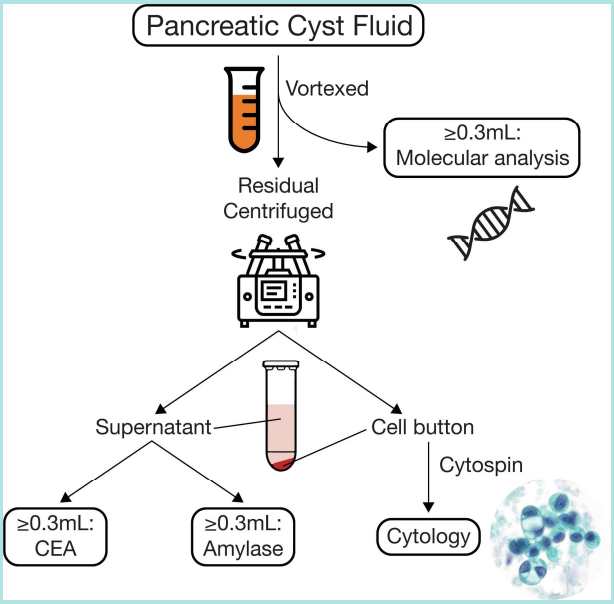
Beta catenin

Biochemical and Molecular analysis of Cyst Fluid

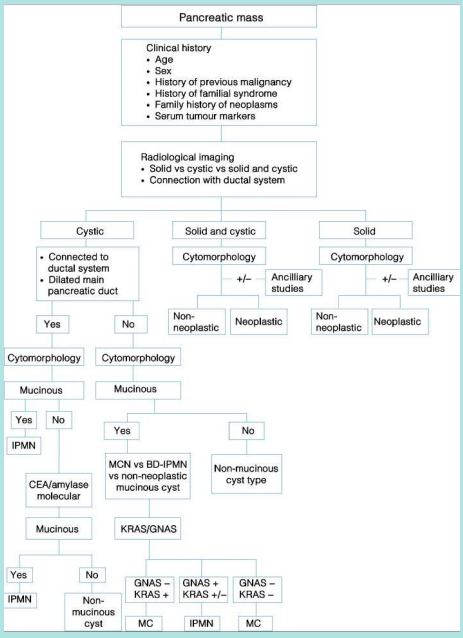
Cyst	Biochemical tests		Molecular Tests					
	CEA	Amy	KRAS	GNAS	3p25 (VHL)	P53	P16 (CDKN2A/INK4A)	SMAD4
PCT	↓	↑↑	-	-	-	-	-	-
SCA	↓↓	↓↓	-	-	+	-	-	-
IPMN	↑↓	↑↑	+	+	-	+[a]	+[a]	+[a]
MCN	↑↓	↓↑	+	-	-	+[a]	+[a]	+[a]



(from WHO Reporting System for PB Cytopathology, Chapter 2; Source Carlos de Andrea)



(from WHO Reporting System for PB Cytopathology, Chapter 2; Source Lisa Zhang)

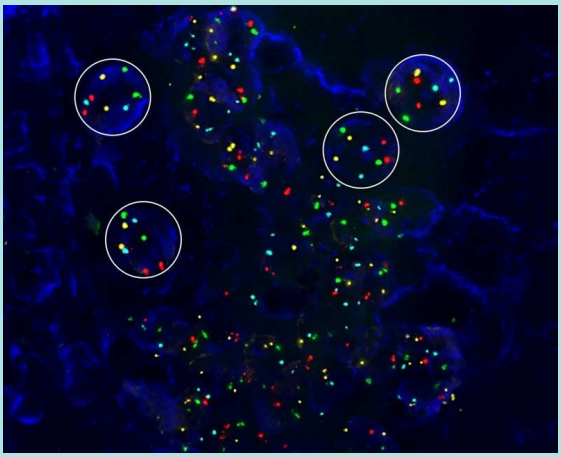


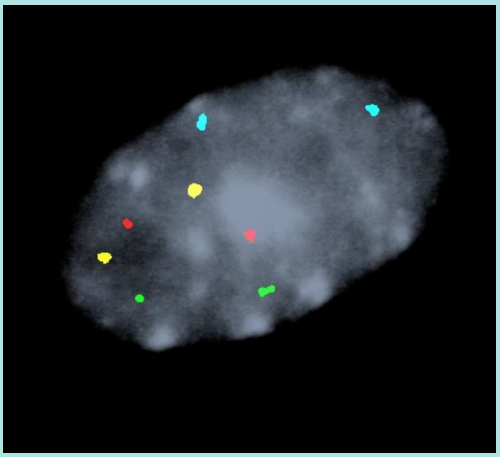
(from WHO Reporting System for PB Cytopathology, Chapter 1; Source Barbara Centeno)

ICC stain	Target	Diagnostic utility	Limitations
SMAD4	Loss of nuclear staining	Adenocarcinoma	Strong staining in non-tumour disorders and other tumours; lost in ~50% of adenocarcinomas
p53	Positive nuclear staining	Adenocarcinoma	Also mutated in high-grade intraepithelial neoplasia
Mesothelin	Positive cytoplasmic staining	Adenocarcinoma	Focal staining in pancreatitis
IMP3	Strong cytoplasmic staining	Adenocarcinoma	Focal staining in pancreatitis
S100P	Strong cytoplasmic and nuclear staining	Adenocarcinoma	Strong staining of gastric epithelium
Monoclonal CEA	Strong cytoplasmic staining	Adenocarcinoma	
CA125 (MUC16)	Strong cytoplasmic staining	Adenocarcinoma	
VHL protein	Loss of membranous and cytoplasmic staining	Adenocarcinoma	Membranous and cytoplasmic expression in normal biliary and pancreatic ductal cells; loss in AIP
Synaptophysin	Strong, diffuse cytoplasmic staining	Neuroendocrine neoplasms	Focal staining in other tumours and normal islet cells
Chromogranin A	Strong to patchy cytoplasmic staining	Neuroendocrine neoplasms	Patchy staining, sometimes weak
INSM1	Strong, diffuse nuclear staining	Neuroendocrine neoplasms	Focal staining in other tumours
Trypsin	Strong cytoplasmic granular staining	Acinar cell carcinoma and other acinar proliferations	High background staining; focal staining in other tumours
Chymotrypsin	Strong cytoplasmic granular staining	Acinar cell carcinoma and other acinar proliferations	High background staining; focal staining in other tumours
BCL10	Cytoplasmic staining	Acinar cell carcinoma and other acinar proliferations	
CD99	Perinuclear dot-like pattern	Solid pseudopapillary neoplasm	Specific
β-Catenin	Strong nuclear staining	Solid pseudopapillary neoplasm	Nuclear staining in other tumours, but usually much more high-grade (acinar cell carcinoma)

(from WHO Reporting System for PB Cytopathology, Chapter 2; Source Barbara Centeno)

FISH of BDB





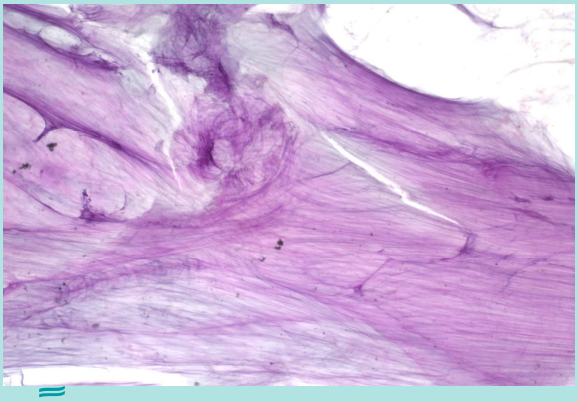
Four fluorescence-labelled DNA probes targeting the centromeric region of chromosomes 3 (SpectrumRed), 7 (SpectrumGreen), and 17 (SpectrumAqua), as well as the chromosomal locus 9p21 (SpectrumGold). Targeted FISH shows a negative result: encircled are non-overlapping cell nuclei with two signals for each probe (diploid pattern), supporting a benign diagnosis.

(from WHO Reporting System for PB Cytopathology, Chapter 3; Sources Spasenija Savic Prince and Amy Clayton)

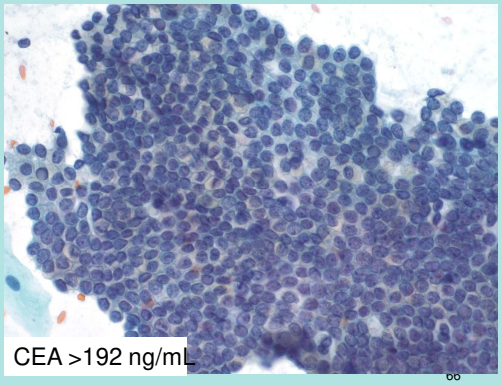
1. Insufficient/inadequate/non-diagnostic

- Is a specimen that for qualitative and/or quantitative reasons does not permit a diagnosis of the targeted lesion
- Precise terminology is user-dependent
- Includes normal pancreatic epithelium with defined mass on imaging (optional to use benign + caveat)
- ROM is up to 25% for pancreas FNA; but 69% for BDB
- Use of ancillary tests can decrease use of this category, e.g. biochemical testing of cyst fluid
- Repeat FNA/brushing is warranted

NOT
insufficient/inadequate/
non-diagnostic

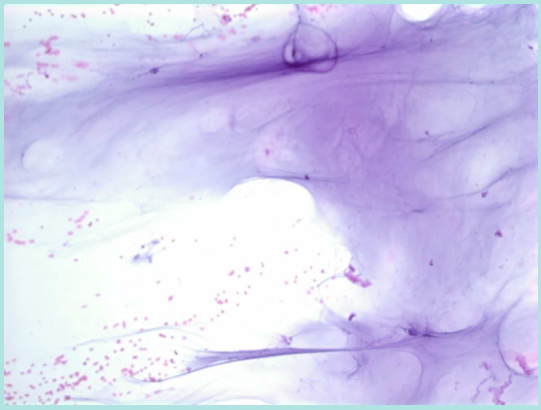


OR



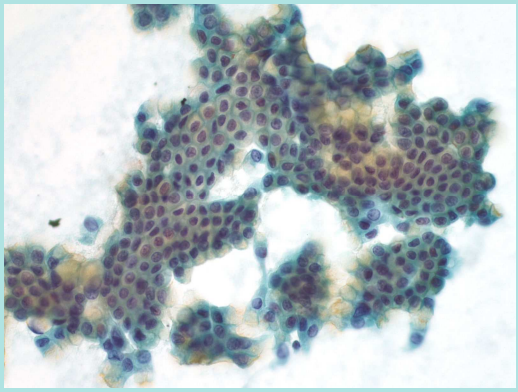
Example Report
3 **cm unilocular cyst**

Evaluation limited by absent cyst lining epithelium
Pancreaticobiliary Neoplasm- low risk/low-grade
Thick, colloid-like extracellular mucin consistent with a neoplastic mucinous cyst. See note.
Note: No epithelial component is identified. No necrosis is present. Correlation with imaging required.



EXAMPLE REPORT
2 unilocular cyst in the pancreatic tail

- Satisfactory for Evaluation
- Pancreaticobiliary Neoplasm- low risk/low-grade
- Cyst fluid with elevated CEA (1250 ng/mL) supportive of a neoplastic mucinous cyst. See note.
- Note: Gastric foveolar epithelium is present likely gastric contamination. No high-grade epithelial atypia is present, and no background necrosis is seen. Correlation with imaging features required.



2. Benign/Negative (for Malignancy)

- ✓Is a specimen that demonstrates unequivocal benign cytopathological features, which may or may not be diagnostic of a specific process or benign neoplasm.
- ✓Non-neoplastic and benign neoplastic lesions (e.g. SCA)
- ✓Includes normal pancreatic epithelium without a defined mass on imaging or with mass on imaging with a specific caveat
- ✓ROM for pancreatic FNA = 0-15%
- ✓ROM for BDB = 25-55%
- ✓Management is conservative with clinical correlation

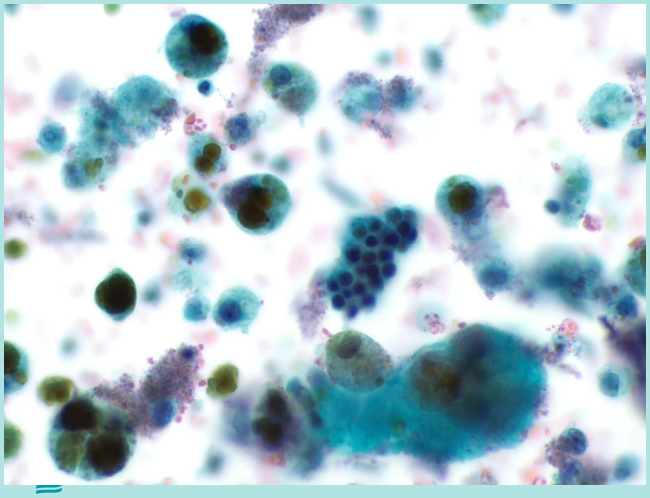
2. Benign/Negative (for malignancy)

4.0.1: Benign non-neoplastic processes
- 4.0.1.1: Normal pancreatic and biliary parenchyma and contaminants
- 4.0.1.2: Acute pancreatitis
- 4.0.1.3: Cholangitis
- 4.0.1.4: Chronic Pancreatitis
- 4.0.1.5: Groove/para-duodenal pancreatitis
- 4.0.1.6: Autoimmune and IgG4-related Pancreatitis
- 4.0.1.7: Lymphoepithelial Cyst
- 4.0.1.8: Pseudocyst
- 4.0.1.9: Splenule (accessory spleen)

4.0.2: Benign neoplastic processes
- 4.0.2.1: Serous Cystadenoma
- 4.0.2.2: Schwannoma
- 4.0.2.3: Lymphangioma
- 4.0.2.4: Other Rare Benign Neoplasms (leiomyoma, granular cell tumors, hemangioma, etc)

2. Benign/Negative (for Malignancy)

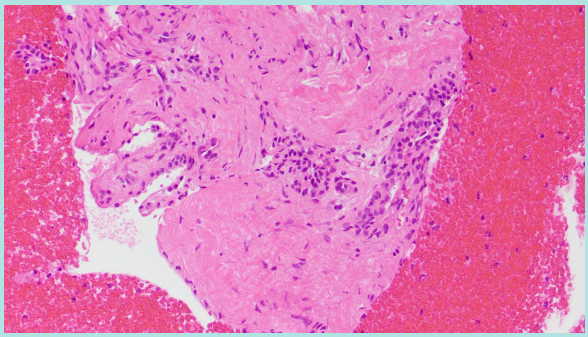
Serous Cystadenoma

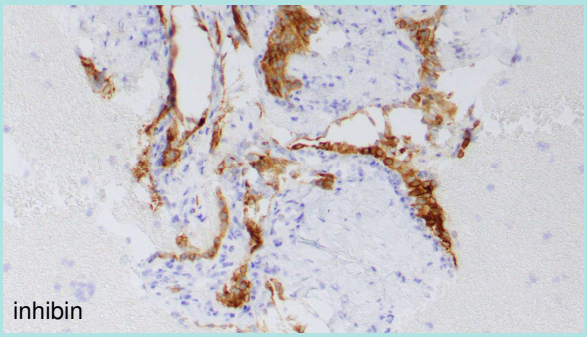


- Multilobulated, multicystic mass
- Cuboidal , glycogen-rich, non-mucinous epithelium
- +/- hemosiderin-laden macrophages
- Low CEA, low amylase (<250 U/L)
- 3p (VHL) gene mutation (+/-)

2. Benign/Negative (for Malignancy)

Serous Cystadenoma – fork tipped needle





inhibin

3. Atypical

- ✓ A specimen that demonstrates features predominantly seen in benign lesions and minimal features that may raise the possibility of malignant lesions, but with insufficient features either in number or quality to diagnose a benign, PaN-Low, PaN-High or malignant process or lesion.
- ✓ ROM for pancreatic FNA is 30-40%
- ✓ ROM for BDB is 25-77%
- ✓ Clinical management is repeat procedure, preferably with FISH and/or NGS for BDB

4. Pancreatic neoplasm: low risk/ low-grade (Pan-low)

- ✓ A specimen categorized as 'Pancreaticobiliary neoplasm: low risk/low-grade' has features of an intraductal and/or cystic neoplasm with low-grade epithelial atypia.
- ✓ Extracted from the 'Neoplastic: Other' category of the Papanicolaou System for Reporting Pancreaticobiliary Cytology
- ✓ Low-grade epithelial atypia encompasses low-grade and intermediate-grade dysplasia and has a low risk of disease progression.

4. Pancreatic neoplasm: low risk/ low-grade (Pan-low)

- ✓ Category is not likely to be used for BDB
  - More likely to use “atypical’ category
- ✓ Incorporates ancillary studies
  - CEA, amylase, NGS (if available)
- ✓ ROM pancreatic FNA = 5-20%
- ✓ ROM in BDB is not established
- ✓ Clinical management is usually conservative

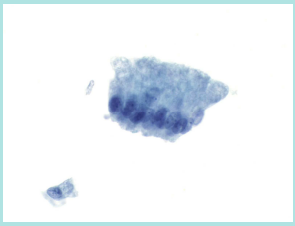
4. Pancreatic neoplasm: low risk/ low-grade (Pan-low)

6.0.1: Specific lesions:
- 6.0.1.1: Pancreatic intraepithelial neoplasia: low-grade
- 6.0.1.2: Biliary intraepithelial neoplasia: low-grade
- 6.0.1.3: Intraductal papillary mucinous neoplasm - low-grade
- 6.0.1.4: Intraductal papillary mucinous neoplasm of the bile duct - low-grade
- 6.0.1.5: Mucinous Cystic Neoplasm-low-grade
- 6.0.1.6: Others (inc spindle cell tumours)

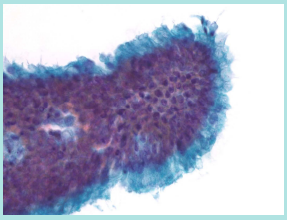
4. Pancreatic neoplasm: low risk/ low-grade (Pan-low)

- Thick, colloid-like ECM **or**
- LGA **or**
- Elevated CEA >192 ng/mL **and**
- Absent HGA and necrosis

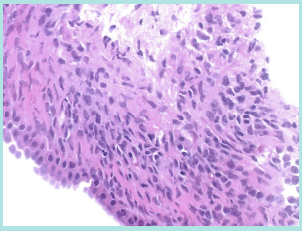
Neoplastic mucinous cyst, NOS



IPMN-LG



MCN-LG



5. Pancreatic neoplasm: high risk/ high-grade (Pan-high)

- ✓ A specimen categorized as 'Pancreaticobiliary neoplasm: high risk/high-grade' has features of an intraductal and/or cystic neoplasm with high-grade epithelial atypia
- ✓ Extracted from the 'Neoplastic: Other' category of the Papanicolaou System for Reporting Pancreaticobiliary Cytology
- ✓ High-grade epithelial atypia encompasses high-grade dysplasia and possibly carcinoma and has a high risk of disease progression.

5. Pancreatic neoplasm: high risk/ high-grade (Pan-high)

- ✓ The category is not likely to be used in BDB
  - Use “suspicious for malignancy” instead
- ✓ ROM in pancreatic FNA is 60-95%
- ✓ ROM in BDB is not established
- ✓ Clinical management is surgical resection for pancreatic lesions

5. Pancreatic neoplasm: high risk/ high-grade (Pan-high)

7.0.1: Specific lesions:

- 7.0.1.1: Pancreatic intraepithelial neoplasia - high-grade
- 7.0.1.2: Biliary intraepithelial neoplasia - high-grade
- 7.0.1.3: Intraductal papillary mucinous neoplasm of the pancreas - high-gra
- 7.0.1.4: Intraductal papillary neoplasm of the bile duct - high-grade
- 7.0.1.5: Mucinous cystic neoplasm - high-grade
- 7.0.1.6: Intraductal oncocytic papillary neoplasm
- 7.0.1.7: Intraductal tubulopapillary neoplasm

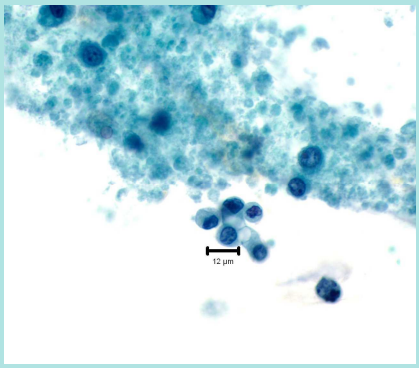
5. Pancreatic neoplasm: high risk/ high-grade (Pan-high)

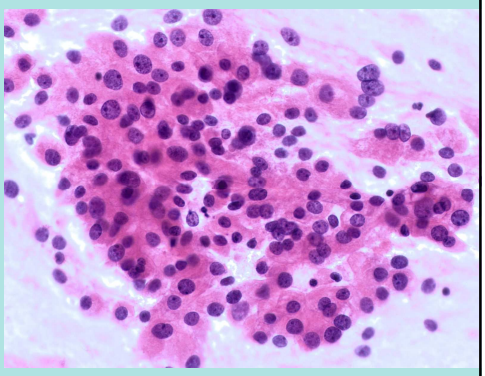
IPMN-HG

IOPN

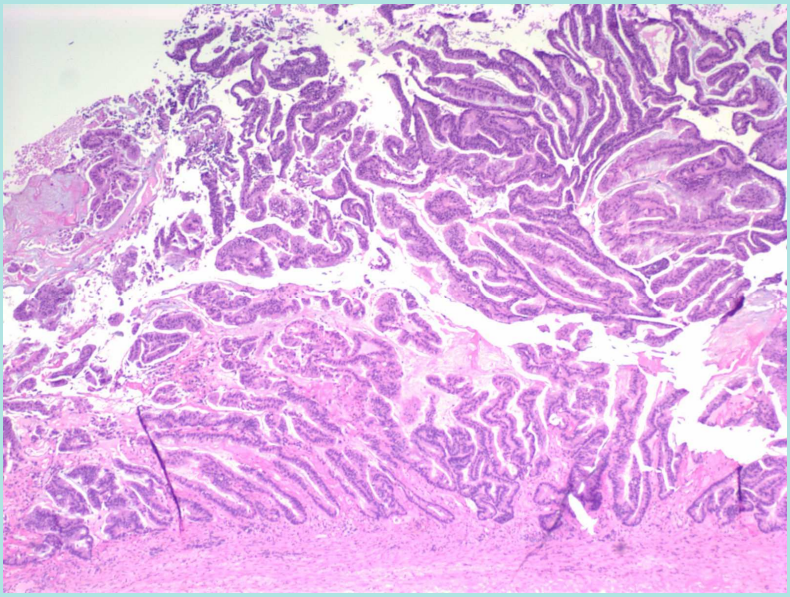
High-grade Epithelial Atypia

- < 12µ duodenal enterocyte
- Increased N/C ratio
- Nuclear membrane abnormalities
- Abnormal chromatin pattern
- Prominent nucleoli +/-
- Variable residual cytoplasmic mucin
- Background necrosis in most cases
- Background inflammation variable

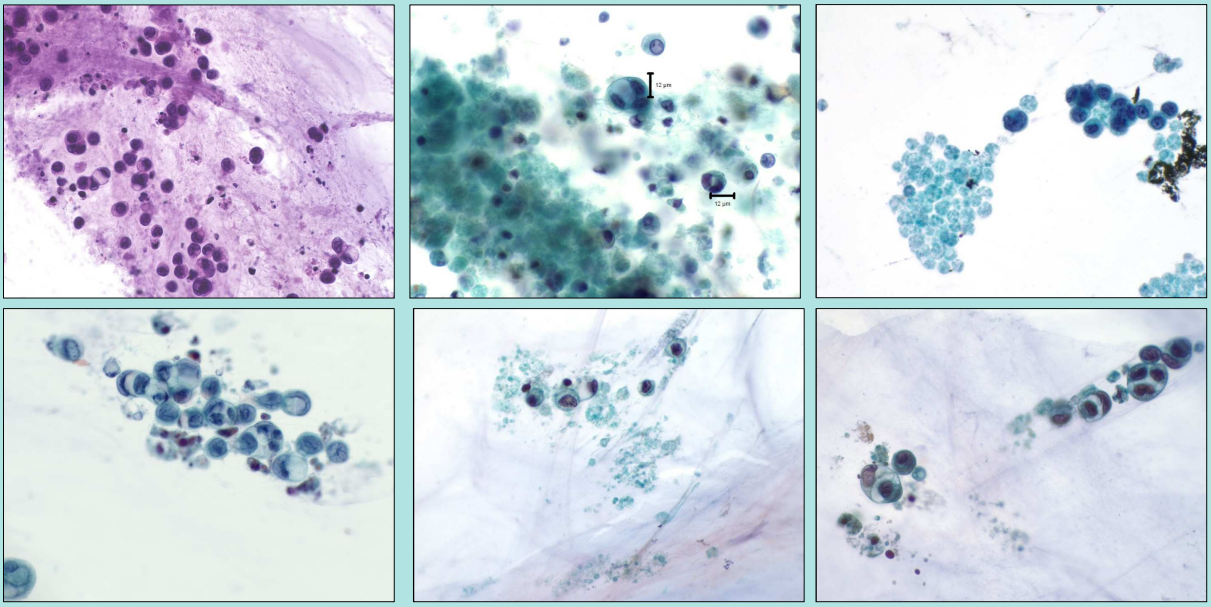




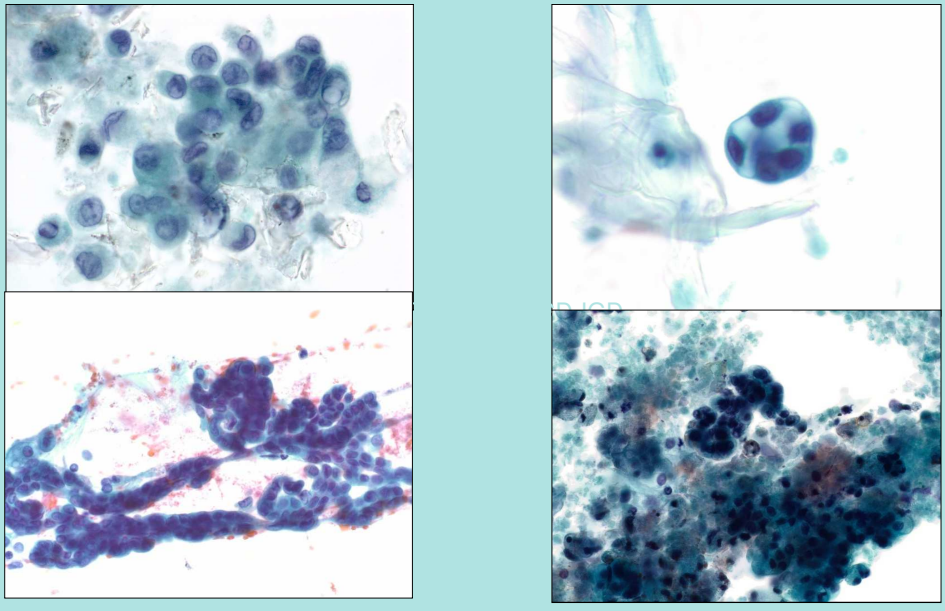
IPMN with HGD



HGA in Mucinous Cysts



Morphological Overlap with LGA and HGA



6. Suspicious (for Malignancy)

- ✓ A specimen that demonstrates features that quantitatively and/or qualitatively fall short of an unequivocal diagnosis of malignancy.
- ✓ ROM for pancreatic FNA = 80-100%
- ✓ ROM for BDB is 74-100%
- ✓ Management is repeat FNA/BDB for neoadjuvant therapy, or surgical resection in the appropriate clinical setting

7. Malignant

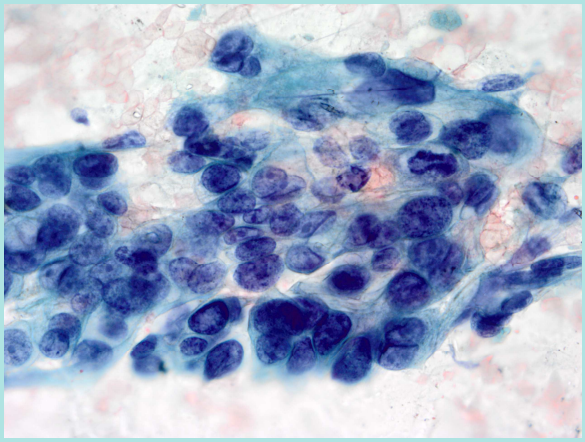
- ✓ A specimen that demonstrates unequivocal cytopathological features of malignancy.
- ✓ ROM for pancreatic FNA = 99-100%
- ✓ ROM for BDB is 96-100%
- ✓ Management is per clinical stage

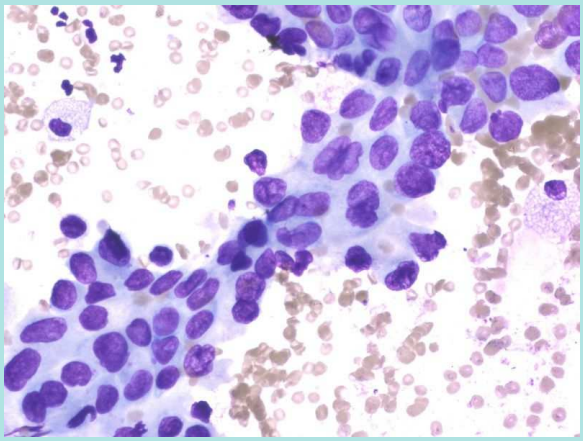
7. Malignant

9.0.1: Specific Lesions
- 9.0.1.1: Cholangiocarcinoma
- 9.0.1.2: Pancreatic ductal adenocarcinoma
- 9.0.1.3: Pancreatic acinar cell carcinoma
- 9.0.1.4: Neuroendocrine tumour
- 9.0.1.5: Neuroendocrine carcinoma (small and large cell types)
- 9.0.1.6: Pancreatoblastoma
- 9.0.1.7: Solid-pseudopapillary neoplasm
- 9.0.1.8: Primary non-Hodgkin lymphoma (general overview; small versus large cell types)
- 9.0.1.9: Metastasis to the pancreas
- 9.0.1.10: Others (inc spindle cell tumours)

7. Malignant

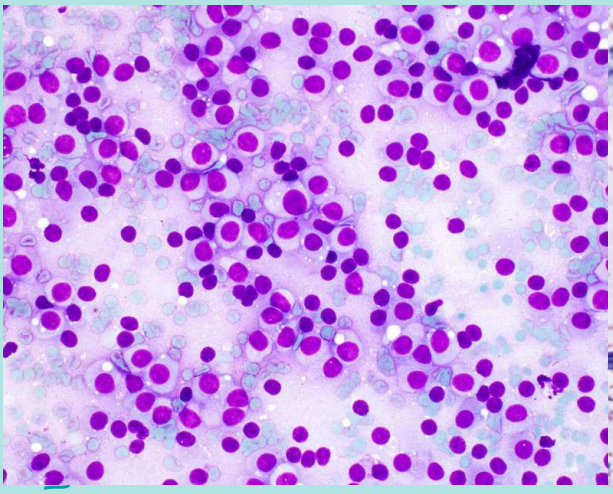
PDAC



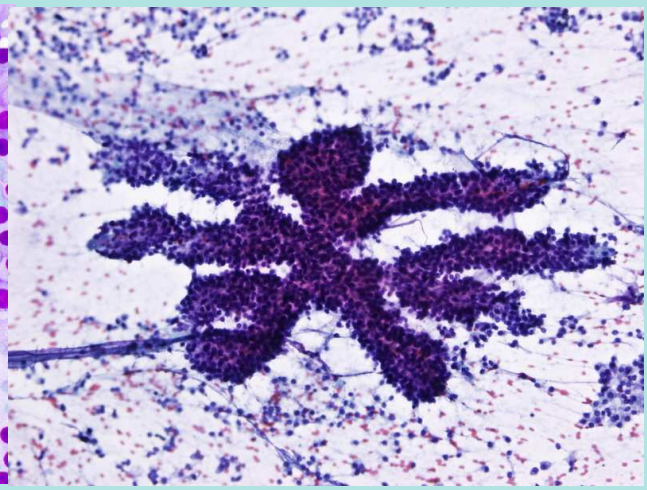


7. Malignant

PanNET



SPN



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