The World Health Organization Reporting System for Pancreaticobiliary Cytopathology

Review and Comparison to the Papanicolaou Society of Cytopathology System

Martha B. Pitman, MD

• ***Context.***—**The World Health Organization (WHO) Reporting System for Pancreaticobiliary Cytopathology (WHO System) is the product of a joint venture between the World Health Organization, the International Academy of Cytology, and the International Agency for Research on Cancer. The WHO System revises the Papanicolaou Society of Cytopathology System for Reporting Pancreaticobiliary Cytology (PSC System) and replaces the 6-tiered system with a 7-tiered system.**

Objective.—**To explain the WHO System and the differences with the PSC System.**

Data Sources.—**The WHO System and the PSC System of Reporting Pancreaticobiliary Cytopathology.**

Conclusions.—**The diagnostic categories of the WHO System are "Insufficient/Inadequate/Nondiagnostic"; "Benign (Negative for Malignancy"'; "Atypical"; "Pancreaticobiliary Neoplasm, Low Risk/Low Grade (PaN-Low)"; "Pancreatic Neoplasm, High Risk/High Grade (PaN-High)"; "Suspicious for Malignancy"; and "Malignant." In the WHO System, the "benign" category includes both nonneoplastic and neoplastic lesions, so the "Neoplastic: Benign" category of the PSC system has been eliminated. Low-grade malignancies, pancreatic neuroendocrine tumors (PanNETs), and solid-pseudopapillary neoplasm (SPN) classified as "Neoplastic: Other" in the PSC System are classified as "Malignant" in the WHO System, leaving in the "Neoplasm" category intraductal lesions, which are divided into 2 new diagnostic categories: "Pancreaticobiliary Neoplasm (PaN)–Low Risk/Grade" and "PaN–High Risk/Grade." As with the PSC System, the WHO System advocates close correlation with imaging and encourages incorporation of ancillary testing into the final diagnosis, such as biochemical (carcinoembryonic antigen [CEA] and amylase) and molecular testing. The WHO System includes risk of malignancy per category, and reporting and diagnostic management options that recognize the variations in resources of low- and middle-income countries.**

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The World Health Organization (WHO), the International Academy of Cytology, and the International Agency for Research on Cancer (IARC), through a memorandum of understanding signed in 2020, are developing international standardized reporting systems in cytopathology that mirror the WHO Classification of Tumors series with links between the 2 series on the Web site and in the text. These evidence-based terminology systems have diagnostic categories with associated risks of malignancy (ROMs) and diagnostic management recommendations to facilitate diagnosis and patient management. Each standardized terminology system provides key diagnostic cytomorphologic features of specific lesions or neoplasms and provides a discussion of the differential diagnosis based on morphology alone, which is a benefit to pathologists in low-resource settings. Ancillary studies for diagnostic and prognostic evaluation are also covered.

Two books have been recently published—one on lung cytopathology[1] and one on pancreaticobiliary cytopathology,[2] the latter detailed below. Five other books are in development: lymph node, thymus, and spleen; soft tissue; liver; breast; and kidney/adrenal cytopathology.

A Standing Committee or "series editors" for these books includes co-chairs Ian Cree, MBSc, MBChB, PhD (recently retired and replaced by the new director of IARC, Dilani Lokuhetty, MBBS) and Andrew Field, MD; and Fernando Schmitt, MD, PhD; Martha Pitman, MD; and Ravi Mehrotra, MD, PhD (recently replaced by Bharat Rekhi, MD, of India). This Standing Committee oversees the organization, development, writing, and editing of the WHO Systems. Each specific terminology system has an Expert Editorial Board who are chosen on the basis of their expertise in the field and/or diversity of geographic representation.

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From the Department of Pathology, Harvard Medical School, Boston, Massachusetts; and the Department of Pathology, Massachusetts General Hospital, Boston.

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Corresponding author: Martha B. Pitman, MD, Department of Pathology, Massachusetts General Hospital, 55 Fruit Street, Warren 105C, Boston, MA 02114 (email: mpitman@partners.org).

Table 1. Comparison of the Papanicolaou Society of Cytopathology (PSC) and World Health Organization (WHO) Systems of Reporting Pancreaticobiliary Cytopathology

Diagnostic Category	PSC System		WHO System
I	Nondiagnostic	I	Unsatisfactory/Insufficient/Nondiagnostic
II	Negative (for Malignancy) Nonneoplastic lesions only	II	Benign/Negative (for Malignancy) Nonneoplastic and neoplastic lesions
III	Atypical	II	Atypical
IV	Neoplastic Benign Other Intraductal lesions–all grades PanNET and SPN	IV	PaN-Low Intraductal lesions–low risk/grade
		V	PaN-High Intraductal lesions–high risk/grade
V	Suspicious (for Malignancy)	VI	Suspicious (for Malignancy)
VI	Positive (for Malignancy)	VII	Malignant Includes PanNET and SPN

Abbreviations: PaN-High, pancreatic neoplasm, high risk/grade; PaN-Low, pancreatic neoplasm, low risk/grade; PanNET, pancreatic neuroendocrine tumor; SPN, solid-peudopapillary neoplasm.

The WHO Reporting System for Pancreaticobiliary Cytopathology (WHO System) revises the Papanicolaou Society of Cytopathology System for Reporting Pancreaticobiliary Cytology (PSC System) published in 2015.[3,4] The PSC system uses a 6-tiered system, and the WHO System uses a 7-tiered system. Differences between the 2 systems are illustrated in Table 1. Both systems advocate close correlation of the cytomorphology with ancillary testing, such as biochemical (carcinoembryonic antigen [CEA] and amylase) and molecular testing of pancreatic cyst fluid, as well as correlation with imaging features.[3] Doing so reduces the number of atypical and nondiagnostic reports, and increases both sensitivity and specificity of detecting neoplasia.[3,5–13]

There are significant differences between the WHO and the PSC systems. In the WHO System, the "benign" category includes both nonneoplastic and neoplastic lesions, so serous cystadenoma and other benign neoplasms are now classified as simply "Benign," and the "Neoplastic: Benign" category of the PSC system has been eliminated. Low-grade malignancies, pancreatic neuroendocrine tumors (PanNETs), and solid-pseudopapillary neoplasm (SPN) classified as "Neoplastic: Other" in the PSC System are now classified as "Malignant" category, as per the 5th edition of the WHO Classification of Tumours, *Digestive System Tumours*,[14] thus leaving in the "Neoplasm" category noninvasive premalignant lesions of the ductal system. Given the stark difference in the risk of malignancy of low-grade and high-grade intraductal lesions, 2 new diagnostic categories—pancreaticobiliary neoplasm–low risk/grade (PaN-Low) and pancreatic neoplasm–high risk/grade (PaN-High)—were created, which are selected on the basis of cytomorphologic grade of the epithelium.

The method of pancreaticobiliary sampling—fine-needle aspiration biopsy (FNAB) versus bile duct brushing (BDB)—is associated with different ROMs, and thus 2 tables are provided (Tables 2 and 3). With the redistribution of tumors in the benign, neoplastic, and malignant categories in the WHO System, the associated ROM for the diagnostic categories is better aligned than in the PSC System, which had an artificially low ROM in the "Neoplastic" category owing to the admixture of benign, low- and high-grade premalignant lesions and low-grade malignancies.[8,11,15–17] The ROM for BDB is higher per diagnostic category than for FNAB because of the higher threshold for a definitive malignant diagnosis on BDB owing to inherent underlying inflammatory conditions causing biliary stricture and the often-associated indwelling stents. Also, because criteria are lacking for the diagnosis of specific premalignant intraductal biliary neoplasms, the "PaN-Low" or "PaN-High" categories will likely not be used for BDB.

Table 2. The World Health Organization System for Reporting Pancreaticobiliary Cytopathology for Pancreatic Fine-Needle Aspiration Biopsy (FNAB): Implied Risk of Malignancy and Clinical Management Options by Diagnostic Category

Diagnostic Category	Estimated Risk of Malignancy, %	Clinical Management Options
1. Insufficient/Inadequate/Nondiagnostic	5–25	Repeat FNAB
2. Benign/Negative for Malignancy	0–15	Correlate clinically
3. Atypical	30–40	Repeat FNAB
4. Pancreatic Neoplasm–Low Grade (PaN-Low)	5–20	Correlate clinically
5. Pancreatic Neoplasm–High Grade (PaN-High)	60–95	Surgical resection in surgically fit patients Conservative management optional
6. Suspicious (for Malignancy)	80–100	If patient to be surgically managed, treat as positive If patient requires preoperative therapy, repeat FNAB
7. Positive (for Malignancy)	99–100	Per clinical stage

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Table 3. The World Health Organization System for Reporting Biliary Cytopathology: Implied Risk of Malignancy and Clinical Management Options by Diagnostic Category

Diagnostic Category	Estimated Risk of Malignancy, %	Clinical Management Options
Insufficient/Inadequate/Nondiagnostic	NA	Repeat ERCP with cholangioscopy, brushings, and biopsies
Benign/Negative for Malignancy	0–25	Correlate clinically
Atypical	25–50	Repeat ERCP with cholangioscopy, brushings, and biopsies; consider ancillary testing with FISH and/or NGS
Pancreatic Neoplasm–Low Grade (PaN-Low)	NA	NA
Pancreatic Neoplasm–High Grade (PaN-High)	NA	NA
Suspicious (for malignancy)	75–90	Repeat sampling with ancillary testing (FISH and/or NGS) or, if other factors support malignancy, surgical intervention; for neoadjuvant therapy, repeat ERCP with cholangioscopy and brushings/biopsies/ancillary testing
Malignant	96–100	Per clinical stage

Abbreviations: ERCP, endoscopic retrograde cholangiopancreatography; FISH, fluorescence in situ hybridization; NA, not available/applicable; NGS, next-generation sequencing.

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The 7 diagnostic categories of the WHO System are discussed below and selectively illustrated.

CATEGORY: INSUFFICIENT/INADEQUATE/ NONDIAGNOSTIC

The definition of an Insufficient/Inadequate/Nondiagnostic specimen is "one that for qualitative and/or quantitative reasons does not permit a diagnosis of the targeted lesion." In contrast to the 1 term of *Nondiagnostic* in the PSC System, 3 terms are listed as options given the variation in preference among institutions, but all institutions should select 1 term and use it consistently.[4] Rates for this category average 12%[18] and are associated with operator experience, biopsy technique, and use of rapid on-site evaluation.[19–21]

"Insufficient/Inadequate/Nondiagnostic" FNAB specimen classification may also be due to the nature of the lesion, one with extensive fibrosis for example, or from obscured tissue from mechanical or preparation artifact.

Cellularity for adequacy is not established in pancreaticobiliary cytopathology. While solid lesions or duct strictures with acellular to very paucicellular samples should be placed in this category, this is not true for cystic lesions. Thick, colloid-like extracellular mucin or elevated cyst fluid CEA levels are enough to classify the cyst as mucinous, even in the absence of an epithelial component.[22] Specimens containing only benign pancreatic acinar and/or ductal epithelial cells in the setting of a distinct solid or cystic lesion on imaging are best classified as "Insufficient/Inadequate/Nondiagnostic," since the FNAB does not explain the mass seen on imaging. But it is recognized within the WHO System that some laboratories choose to classify such cases as "Benign," describing what is present on the slides, and then adding a note or caveat in the report that the biopsy specimen most likely is not representative of the targeted lesion. Classifying a likely sampling error as "Benign", however, will inflate the ROM of the "Benign" category, impacting clinical confidence in a benign diagnosis.

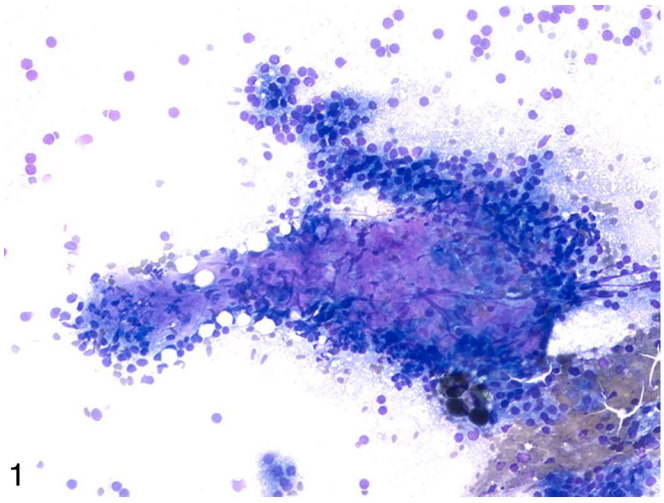
ROM for the "Insufficient/Inadequate/Nondiagnostic" category is based on retrospective and prospective studies and ranges from 5% to 25%.[8,11,15,18] For BDB specimens, the ROM is high at 28% to 69% owing to the sampling bias of targeting duct strictures with an inherently high risk of malignancy.[23–29]

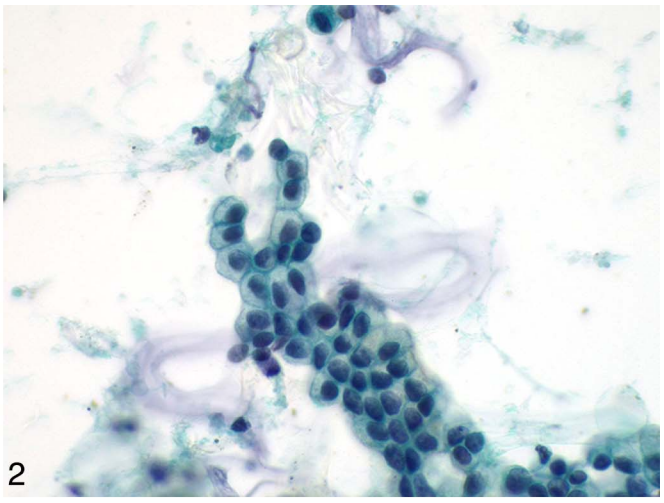
Diagnostic management recommendation of an "Insufficient/Inadequate/Nondiagnostic" sample is repeated biopsy in most cases. Patients clinically suspected of autoimmune pancreatitis may have a trial of steroids.[30] Brush cytopathology specimens evaluated with direct smears can be repeated by using liquid-based cytopathology to improve cellular preservation. Adding molecular testing to pancreatic cysts and BDBs may also help to identify high-risk lesions.[25,31–34]

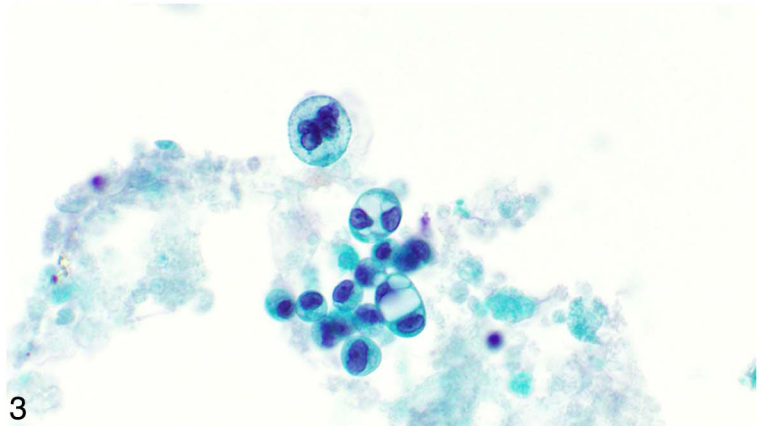
CATEGORY: BENIGN/NEGATIVE FOR MALIGNANCY

The definition of a specimen categorized as "Benign (Negative for Malignancy)" is one that "demonstrates unequivocal benign cytopathological features, which may or may not be diagnostic of a specific process or benign neoplasm."

The *Benign* term is new to the WHO System and added as an option to "Negative (for Malignancy)" as in the PSC System. This category includes both nonneoplastic and neoplastic entities, so SCA and other benign neoplasms are classified as "Benign" and not as "Neoplastic: Benign" as in the PSC System. Specific benign entities that can be diagnosed on cytology include acute pancreatitis, chronic pancreatitis, autoimmune pancreatitis, cholangitis, pseudocyst, lymphoepithelial cyst, accessory spleen (splenule), serous cystadenoma (SCA) (Figure 1), and other rare benign neoplasms such as lymphangioma and schwannoma. If a specific benign nonneoplastic condition or neoplasm is not recognized, a descriptive report is provided. The use of this diagnostic category implies that the cellularity of the sample is adequate and that there is no evidence of cytopathologic atypia. A sample composed of normal pancreatic tissue in the appropriate clinical setting, and in the absence of a distinct mass lesion, is appropriately placed in the "Benign" category. However, if there is a distinct, clearly defined mass on imaging, aspiration of only normal pancreatic tissue is best classified as "Insufficient/Inadequate/Nondiagnostic" to maintain a meaningful ROM in the "Benign" category.







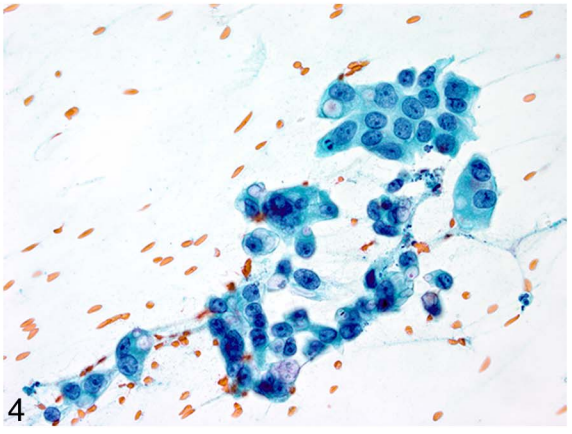


Figure 1. *Serous cystadenoma. Fibrous septum surrounded by bland, cuboidal, nonmucinous epithelial cells punctuated with hemosiderin-laden macrophages (direct smear, Diff-Quik, original magnification ×100).*

Figure 2. *Low-grade mucinous epithelium from a neoplastic mucinous cyst. Sheet of bland mucinous epithelial cells with evenly distributed uniform nuclei associated with extracellular mucin (cytospin, Papanicolaou, original magnification ×600).*

Figure 3. *High-grade mucinous epithelium from a neoplastic mucinous cyst. Small mucinous epithelium singly and in small loose cluster in a background of cellular necrosis (cytospin, Papanicolaou, original magnification ×600).*

Figure 4. *Ductal adenocarcinoma. Discohesive sheet of glandular cells with intracytoplasmic mucin vacuoles. Note the anisonucleolsis and irregularity of nuclear membranes (direct smear, Papanicolaou, original magnification ×600).*

The ROM in the "Benign" category on pancreatic FNAB ranges from 0% to 15%.[8,11,15,17] The ROM for a "Benign" BDB is as high as 55%,[23–29] owing to the high threshold for a malignant diagnosis in BDB samples.

Clinical management for a "Benign" diagnosis can be conservative. No further treatment is needed for lymphoepithelial cyst or splenule. Pseudocysts can be drained, and benign neoplasms observed. Surgical resection may be performed to alleviate symptoms. Corticosteroids are used in the treatment of autoimmune pancreatitis, which is why it is essential for cytopathologists to consider the possibility of the disease based on the FNAB.

CATEGORY: ATYPICAL

A specimen categorized as "Atypical" is one that "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, PaN-low, PaN-high, or malignant' process or lesion."

There is significant interobserver variability in the use of the "Atypical" category primarily based on the quality and quantity of the abnormal cells coupled with the experience of the pathologist. The inherent characteristics of the lesion sampled influence cellularity, and technical factors, such as preparation artifact, influence the sample quality.[35,36] Experience and expertise in interpreting pancreaticobiliary samples impact the use of the "Atypical" category.[37] The histopathologic correlate with this category is broad and ranges from benign to premalignant and malignant entities.[8–10,15,38–40]

The frequency of the "Atypical" category for FNAB of pancreas ranges from 0% to 14% with an average of 5.5%.[18,41] The frequency in BDB ranges from 11% to 39.8%, which is likely due to the reactive atypia inherent to primary sclerosing cholangitis, stents, and biliary stones.[24,42–44] Now that PanNETs and SPN are classified as "Malignant," an FNAB sample that is not diagnostic, but suspected, should be

classified as "Suspicious for Malignancy" and not "Atypical" as was the case in the PSC System. For BDB, the "Atypical" category is applied to cases in which the atypia observed is beyond that seen in reactive and inflammatory changes while quantitatively and qualitatively insufficient for categorization as "Suspicious for Malignancy." Low-grade biliary intraepithelial neoplasia and intraductal papillary neoplasm of the bile duct are entities described in the "Pan-Low" category but given the rarity of these lesions and the lack of well-defined diagnostic criteria, the mostly likely category will be "Atypical."[45,46] The known overlap in cytomorphology between reactive and reparative changes in bile duct epithelium—from stents, stones, and inflammation—and well-differentiated adenocarcinoma leads to a high use of the "Atypical" category.[47] The ROM of the "Atypical" category for FNAB of pancreas is 30% to 40% and for bile duct brushings, 25% to 50%.[8,11,15,23–26]

The management of an "Atypical" cytopathologic diagnosis should include multidisciplinary discussion, consensus review, expert consultation, the use of ancillary tests, and repeated sampling with ROSE. Adding ancillary testing with fluorescence in situ hybridization[48–51] and next-generation sequencing[32,33] has improved the classification of pancreatic cysts, and the sensitivity of detection of malignancy in BDB.[25,31,52,53] Consensus review or second opinion from experienced pancreaticobiliary cytopathologists may also help in changing this indeterminate diagnosis to a definitive diagnosis.[54]

CATEGORY: PANCREATIC NEOPLASM: LOW RISK/GRADE

A specimen categorized as "Pancreaticobiliary Neoplasm: Low Risk/Grade" is defined as one with features of an intraductal and/or cystic neoplasm with low-grade epithelial atypia. Intraductal neoplasia is graded as either low or high grade, with low-grade epithelial atypia representing low- to intermediate-grade dysplasia.[55,56] The ROM for the "PaN-Low" category is 4.3%.[57] Accurate grading of the epithelial atypia as low risk/grade, which includes intermediate-grade dysplasia, and distinguishing it from high-risk/grade atypia is challenging, requiring well-preserved epithelium and diagnostic experience.[58] Degeneration and reactive changes can cause low-grade cells to mimic high-grade cells. When in doubt, grade down and add a note to the report that some cells raise the possibility of a high-grade lesion.

This category can also be used even without epithelium if thick colloid-like mucin or cyst fluid CEA analysis shows an elevated CEA level supporting the diagnosis of mucinous neoplasia. If molecular data are also available at the time of diagnosis that support mucinous neoplasia (eg, *KRAS* or *GNAS* mutation; maybe from a prior FNAB), then this information can also be used to justify this diagnostic category. The absence of epithelium does not equate to a definitive diagnosis of a low-risk/grade cyst, but the absence of high-grade epithelial atypia or background necrosis supports the "PaN-Low" category, based on cytology.

Most intraductal lesions are intraductal papillary mucinous neoplasms (IPMNs), but distinction between a low-grade mucinous cystic neoplasm (MCN) and IPMN is usually not possible because the required ovarian-type stroma for a diagnosis of MCN is typically not identified in aspirated cyst contents. Low-grade IPMNs, most often from branch-duct cysts, produce scantily cellular specimens with columnar mucinous epithelium resembling gastric foveolar cells. Some nuclear elongation and pseudostratification can be seen (Figure 2).[59] The primary differential diagnosis for low-grade IPMN is gastric contamination, so knowing the part of the gastrointestinal tract punctured for the FNAB is very helpful.[60]

Patients with low-grade mucinous cysts have the option of surveillance depending on the clinical and imaging features.[61–63]

CATEGORY: PANCREATIC NEOPLASM: HIGH RISK/GRADE

A specimen categorized as "Pancreaticobiliary Neoplasm: High Risk/Grade" is one with features of an intraductal and/or cystic neoplasm with high-grade epithelial atypia (HGA).

PaN-high lesions include flat high-grade pancreaticobiliary intraepithelial neoplasia, intraductal mucinous and non-mucinous lesions with HGA (IPMN, intraductal papillary biliary neoplasm, intraductal oncocytic papillary neoplasm, and intraductal tubulopapillary neoplasm), and MCN with HGA.

HGA represents either high-grade dysplasia or invasive carcinoma because the difference cannot be distinguished with accuracy on cyst fluid cytology in most cases. PaN-high has an estimated ROM of 60% to 95%.[8,11,15,17] The "PaN-High" category provides a more flexible and less anxious patient management paradigm than the "Suspicious for Malignancy" category, particularly when conservative patient management is recommended. HGA has an 89% sensitivity and 98% specificity for detecting a high-risk cyst.[57]

HGA is defined as a cell smaller than a 12-μm duodenal enterocyte with high nuclear to cytoplasmic ratio and abnormal chromatin, which can be hypochromatic or hyperchromatic and with or without background necrosis[55] (Figure 3). When these criteria are used there is overall good interobserver agreement in distinguishing low-risk/grade from high-risk/grade cysts.[55,58,63–65] However, if intermediate-grade dysplasia is included in the grading scheme, it is virtually impossible to accurately stratify cysts with intermediate-grade dysplasia into low- and high-risk groups, making the addition of genetic testing very important in potentially identifying high-risk cysts.[32]

The "PaN-High" category is dominated by high-grade IPMN, which is a grossly visible cystic lesion involving the main and/or branch pancreatic ducts. The primary differential diagnosis is with high-grade MCN.

Ancillary testing support for "PaN-High" category includes molecular analysis showing late mutations in the adenoma-carcinoma progression, including *TP53*,[32–34,66] *SMAD4*,[33,34,66] and *CDKN2A* (p16).[33,34] Immunohistochemical stains on cell blocks include mutant p53 expression demonstrated by strong nuclear staining or no expression (null pattern),[67,68] and loss of nuclear *SMAD4*[69,70] or p16.[71] These stains should be interpreted with caution on scant specimens.

Surgical resection warrants careful clinical consideration with a PaN-high diagnosis. Conservative observation is a reasonable option in a poor surgical candidate with low-risk imaging features.

CATEGORY: SUSPICIOUS FOR MALIGNANCY

A specimen characterized as "Suspicious for Malignancy" demonstrates some cytopathologic features suggestive of malignancy but with insufficient features either in number or quality to make an unequivocal diagnosis of malignancy. The "Suspicious for Malignancy" category represents approximately 4.7% to 16% of cases.[24,72,73] This and the "Atypical"

category provide indeterminate categories that help to optimize the accuracy and predictive values of the "Benign" and "Malignant" categories. Reported ROMs for the "Suspicious for Malignancy" category for pancreatic FNAB range from 80% to 100%.[8,9,15,17,74] Malignancy risk for BDB specimens ranges from 74% to 100%.[23–26,28,43,75,76]

The "Suspicious for Malignancy" category indicates that the cytopathologic findings are highly concerning for but not diagnostic of a malignancy. Factors contributing to the "Suspicious for Malignancy" category include scant cellularity, technical limitations of specimen staining or preparation, cytomorphologic features lacking for a definitive diagnosis of malignancy, and caution on the part of the cytopathologist. Contributing factors resulting in a "Suspicious for Malignancy" rather than a "Malignant" diagnosis include caution in the setting of concurrent pancreatitis, stent placement, stones, inflammatory conditions such as sclerosing cholangitis, and sampling of subclinical high-grade premalignant lesions of the pancreas.[15,77–79]

Categorization of a specimen as "Suspicious for Malignancy" is not equivalent to a "Malignant" diagnosis and should not by itself result in neoadjuvant therapy or radical surgery. In all cases, further patient management and clinical decisions require correlation with clinical and imaging findings.

CATEGORY: MALIGNANT

A specimen categorized as "Malignant" demonstrates unequivocal cytopathologic features of malignancy. Tumors in this category include both primary and secondary malignancies, with pancreatic ductal adenocarcinoma (PDAC) and cholangiocarcinoma accounting for most primary malignancies.[80] As in the PSC System,[3] pancreatic acinar cell carcinoma, neuroendocrine carcinomas, pancreatoblastoma, primary and secondary hematopoietic malignancies, and sarcomas are also included in this category. A change from the PSC System is the inclusion of PanNET and SPN in this category to make this system consistent with the classification of pancreatic tumors in the 5th edition of the WHO Classification of Tumours, *Digestive System Tumours*.[14] In the PSC System, these were included in the "Neoplastic: Other" category.

The ROM of a "Malignant" pancreatic FNAB specimen ranges from 97% to 100%[8,9,15,45,81]; the ROM of a "Malignant" BDB sample ranges from 88% to 100% with a mean of 96%.[8,9,15,45,81]

Most malignancies in the pancreas are PDACs, which can be quite challenging to diagnose owing to bland cytomorphology resembling benign glandular cells. Criteria include glandular cells with a loss of the normal honeycomb pattern, nuclear enlargement with anisonucleosis greater than 4: 1, chromatin clearing, nuclear membrane irregularities, and cytoplasmic mucin[82–86] (Figure 4).

Surgical management is usually the first-line treatment for malignancies of the pancreaticobiliary tract.[87] An exception is for patients with a PanNET smaller than 2 cm and a Ki-67 less than 3%, who may be managed with surveillance.[88] Patients presenting with borderline or locally advanced PDAC may be treated with neoadjuvant therapies in an attempt to convert the PDAC to resectable disease.[89] Patients with unresectable disease are treated with a combination of chemotherapeutic agents and radiation therapy if indicated.

CONCLUSIONS

As with all reporting systems involving categorization of cytopathology specimens, the new WHO Reporting System for Pancreaticobiliary Cytopathology is designed to improve communication between clinicians and cytopathologists about their patient's biopsy results. Each category has a calculated ROM that aims to assist the clinical care team in patient management.

The WHO Reporting System for Pancreaticobiliary Cytopathology raises the profile and use of cytopathology by increasing awareness of its current role in diagnosis and management of patients with pancreaticobiliary disease.

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