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WHAT'S NEW IN PATHOLOGY?

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THE LATEST NEWS IN GI

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The 5th Edition of the WHO Classification of Tumours: Digestive System Tumours "blue book" was released in mid-2019. Key updates are below.

General updates

• The classification of digestive neuroendocrine neoplasms is revised. They are categorized as neuroendocrine tumors (NETs, formerly "carcinoids") or neuroendocrine carcinomas (NECs) based primarily on histology.
• NETs can be grade 1, 2 or 3, with a Ki67 of less than 3% qualifying as grade 1 (formerly 0 - 2%). Mitotic rate is counted per 2 mm^2, not per 10 high power fields.
• NECs are always high grade and therefore do not require numerical grading. Mixed adenoneuroendocrine carcinoma (MANEC) has been replaced with the more inclusive conceptual term of mixed neuroendocrine-nonneuroendocrine neoplasm (MiNEN); the actual diagnosis should indicate the lesion's components.
• Carcinoma grading is generally now two tier (low grade and high grade).
• Poorly cohesive carcinoma is a diagnostic term incorporated into most organ system chapters, with signet ring cell carcinoma considered a subtype.
• Hematolymphoid lesions, mesenchymal lesions and syndromes have been separated into their own respective chapters.
• There is now a separate chapter on "other tumors" covering mucosal melanoma, germ cell tumors and metastases.

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Esophagus

• Gastroesophageal junction carcinomas have been incorporated into the esophagus chapter.
• Undifferentiated carcinoma is separated into its own entity rather than a squamous cell carcinoma subtype. Lymphoepithelioma-like carcinoma is considered a subtype of this entity.

Stomach

• Undifferentiated carcinoma is now its own separate entity with many subtypes (large cell carcinoma with rhabdoid phenotype, pleomorphic carcinoma, sarcomatoid carcinoma and carcinoma with osteoclast-like giant cells).
• Micropapillary adenocarcinoma is added as an aggressive subtype of adenocarcinoma.
• Gastroblastoma is added as an entity.

Small bowel / Ampulla

• Ampullary carcinomas have been incorporated into the small bowel chapter, though the chapter distinguishes between ampullary and nonampullary carcinomas.
• Intra-ampullary papillary-tubular neoplasm has been added as a subtype of ampullary adenoma.

Appendix

• Low grade appendiceal mucinous neoplasm (LAMN) is formalized as a separate entity rather than a form of appendiceal adenocarcinoma.
• High grade appendiceal mucinous neoplasm (HAMN) is added as a diagnostic entity similar to LAMN but showing high grade dysplasia.
• Goblet cell carcinoid is renamed goblet cell adenocarcinoma, with a new grading system. High grade examples represent what was previously termed "adenocarcinoma ex goblet cell carcinoid" (Figure 1).

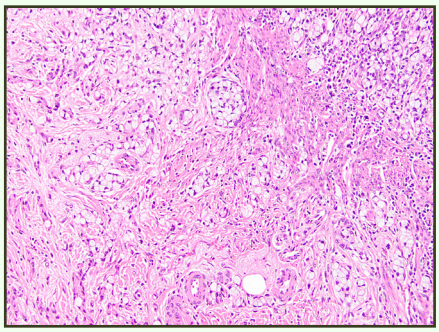

***Figure 1**: Goblet cell carcinoid of the appendix is renamed goblet cell adenocarcinoma.*

• Tubular carcinoid and L-cell carcinoid are renamed tubular NET and L-cell NET, respectively.

Colorectum

• Sessile serrated adenoma / polyp is renamed to sessile serrated lesion, with the reasoning that they are not always polypoid on colonoscopy. Only one unequivocally distorted crypt is now needed to make this diagnosis.
• Adenoma-like adenocarcinoma is added as a subtype of colorectal carcinoma (CRC) with a good prognosis. Adenosquamous carcinoma is also now considered a CRC subtype.
• Cribriform-comedo type adenocarcinoma is removed as a CRC subtype.
• Spindle cell carcinoma is renamed to carcinoma with sarcomatoid components.
• Rather than grading CRC based on the predominant component,

the WHO now recommends grading based on the least differentiated component, regardless of amount.

Liver / Intrahepatic bile ducts

- Several subtypes of hepatocellular carcinoma (HCC) have been added: steatohepatitic, clear cell (formerly a "cytological variant"), macrotrabecular-massive, chromophobe and neutrophil-rich. The lymphoepithelioma-like subtype is renamed to lymphocyte-rich.
- Molecular features of HCC subtypes are emphasized, particularly the *DNAJB1-PRKACA* translocation of fibrolamellar HCC.
- Emphasis is placed on categorizing intrahepatic cholangiocarcinoma into large and small duct types.
- Hepatoblastoma subtypes have been reorganized, and calcifying nested stromal-epithelial tumor is separated out as a distinct entity rather than a variant / related neoplasm.
- The subtypes of combined HCC-cholangiocarcinoma are less strictly defined. Cholangiolocarcinoma is moved from this classification scheme and is now considered a type of small duct cholangiocarcinoma instead.
- Primary neuroendocrine neoplasms of the liver have been formally added.

Gallbladder / Extrahepatic bile ducts

- Grading of biliary intraepithelial neoplasia (BilIN) is now two tier (low and high grade) rather than three tier.

Pancreas

- Acinar cystadenoma is officially renamed acinar cystic transformation.
- Pancreatic intraepithelial neoplasia (PanIN) is now two tier. Numerical grading (PanIN-1A, etc.) is no longer used.
- Intraductal oncocytic papillary neoplasm (IOPN) is established as a distinct entity separate from intraductal papillary mucinous neoplasm (IPMN), due to a different mutational profile (Figure 2).

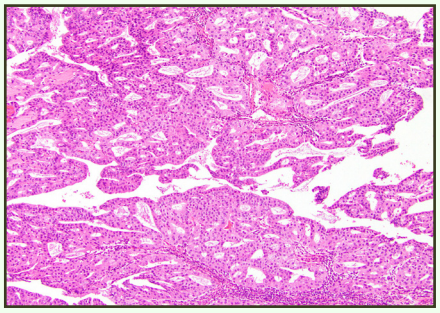

***Figure 2**: IOPN of pancreas is officially distinct from IPMN.*

- The neuroendocrine section is markedly expanded, including discussion of each hormone producing subtype and emphasis on new molecular data.

Lymphoma

- Duodenal-type follicular lymphoma, intestinal T cell lymphoma NOS, indolent T cell proliferative disorder of the gastrointestinal tract and EBV positive inflammatory follicular dendritic cell sarcoma are added as distinct entities.
- Monomorphic CD56+ intestinal T cell lymphoma is renamed to monomorphic epitheliotrophic intestinal T cell lymphoma.

Mesenchymal

- Malignant gastrointestinal neuroectodermal tumor is added as a distinct entity. It may represent the same entity as clear cell sarcoma-like tumor of the gastrointestinal tract or a subtype.
- Molecular information on gastrointestinal stromal tumors (GISTs) is added, in particular the succinate dehydrogenase (SDH) deficient subtype.
- Epithelioid inflammatory myofibroblastic sarcoma is added as an aggressive subtype of inflammatory myofibroblastic tumor with *RANBP2* rearrangement.
- New hemangioma subtypes are specified: anastomosing hemangioma, diffuse hepatic hemangiomatosis and hepatic small vessel neoplasm.
- Molecular data is added to epithelioid hemangioendothelioma, namely the characteristic *WWTR1-CAMTA1* and *YAP1-TFE3* translocations.

Genetics

- Several new polyposis syndromes are added, including gastric adenocarcinoma and proximal polyposis syndrome (GAPPS), *NTHL1* associated polyposis, polymerase proofreading associated polyposis (caused by *POLD1* or *POLE* mutation), *AXIN2* associated polyposis and immune deficiency associated polyposis.
- Familial pancreatic cancer (caused by many potential germline mutations) is added.
- Criteria for serrated polyposis have been modified: either (1) ≥ 5 serrated lesions ≥ 5 mm in size proximal to the rectum, with at least 2 ≥ 10 mm, or (2) > 20 serrated lesions throughout the colorectum, with ≥ 5 proximal to the rectum.

Meet the Author

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