Diagnostic Algorithm for Pancreatic Tumors

**Gross/Radiographic Appearance?**

- **Solid**
  - **Epithelium/Stroma?**
    - Individual glands
    - Desmoplastic stroma
    - Mucin production
  - **Predominant cellular differentiation?**
    - Acinar
      - Stains: (+) chymotrypsin, trypsin
    - Neuroendocrine
      - Stains: (+) synaptophysin, chromogranin
    - Unknown
      - Stains: (+) β-catenin (nuclear), CD10, CD56, E-Cadherin shows lost membranous staining
  - Squamoid nests?
    - Yes
    - No

- **Cystic**
  - **Degenerative?**
    - (No epithelium lining cysts)

**Epithelium Lined Cysts**

- **Serous**
  - Cuboidal, clear cells, glycogen-rich (PAS +; PASd -)
  - Stains: (+) Inhibin
- **Mucinous**
  - Columnar, often mucin-filled

- **Ovarian-type stroma, separate from ducts**
  - Yes
  - No

**Pancreatoblastoma**
- Most common in children
- Prominent nucleoli, granular cytoplasm, Lipase secretion
  → Subcutaneous fat necrosis

**Acinar Cell Carcinoma**
- Prominent nucleoli, granular cytoplasm, Lipase secretion
- Subcutaneous fat necrosis
- See back

**Pancreatic Neuroendocrine Neoplasm (SPPN)**
- Usu. young woman, Low malignant potential
- See back

**Solid-Pseudopapillary Neoplasm (SPPN)**
- Usu. young woman, Low malignant potential
- Usu. Cystic, but can be solid

**Serous Cystadenoma**
- Characteristic radiology, Benign, Usu. Cystic, but can be solid
- Usu. Body or Tail, Almost exclusively in women

**Mucinous Cystic Neoplasm (MCN)**
- Papillary architecture, Grossly visible (>1 cm), if tubular consider ITPN

Adapted from WHO by Kurt Schaberg
Pancreatic Ductal Adenocarcinoma

85% of Pancreatic tumors, Often unresectable at time of diagnosis, Poor Prognosis (often < 1 year)
Majority arise in the head
Precursor lesions: IPMN, MCN, PanIN

Genetics:
>90% show KRAS activation point mutations (also in PanIN)
Also often present are inactivating mutations in the tumor suppressors: TP53, P16, and/or SMAD4

Subtypes:
If squamous differentiation → adenosquamous carcinoma (poorer prognosis)
If >80% of tumor has abundant extracellular mucin → Colloid Carcinoma (better prognosis)
If pleomorphic, no gland formation, +/- osteoclast-like giant cells → Undifferentiated (anaplastic) carcinoma (with osteoclast-like giant cells)

Pancreatic Neuroendocrine Tumors

<table>
<thead>
<tr>
<th>Classification/Grade</th>
<th>Ki67 Proliferation Index</th>
<th>Mitotic index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well-differentiated PanNET</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 1</td>
<td>&lt;3%</td>
<td>&lt;2</td>
</tr>
<tr>
<td>Grade 2</td>
<td>3-20%</td>
<td>2-20</td>
</tr>
<tr>
<td>Grade 3</td>
<td>&gt;20%</td>
<td>&gt;20</td>
</tr>
<tr>
<td>Poorly-differentiated PanNET</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small cell type</td>
<td>&gt;20%</td>
<td>&gt;20</td>
</tr>
<tr>
<td>Large Cell type</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Ki67 Proliferation index baed on evaluation of ≥ 500 cells in a “hot spot.” Mitotic count based on evaluating 50 Hpfs, but reported per 10 Hpfs.

Can occur anywhere in the pancreas. All tumors have malignant potential. Associated with MEN1 and VHL
Carcinoid syndrome → Flushing, diarrhea, bronchoconstriction. Usu. Only if mets. Elevated serum 5-HT and/or urine 5-HIAA
Insulinoma → Usu. Small, present with hypoglycemia
VIPoma → Watery diarrhea with hypokalemia and achlorhydria
Glucagonoma → Necrolytic migratory erythema, stomatitis
Gastrinoma → ZE syndrome