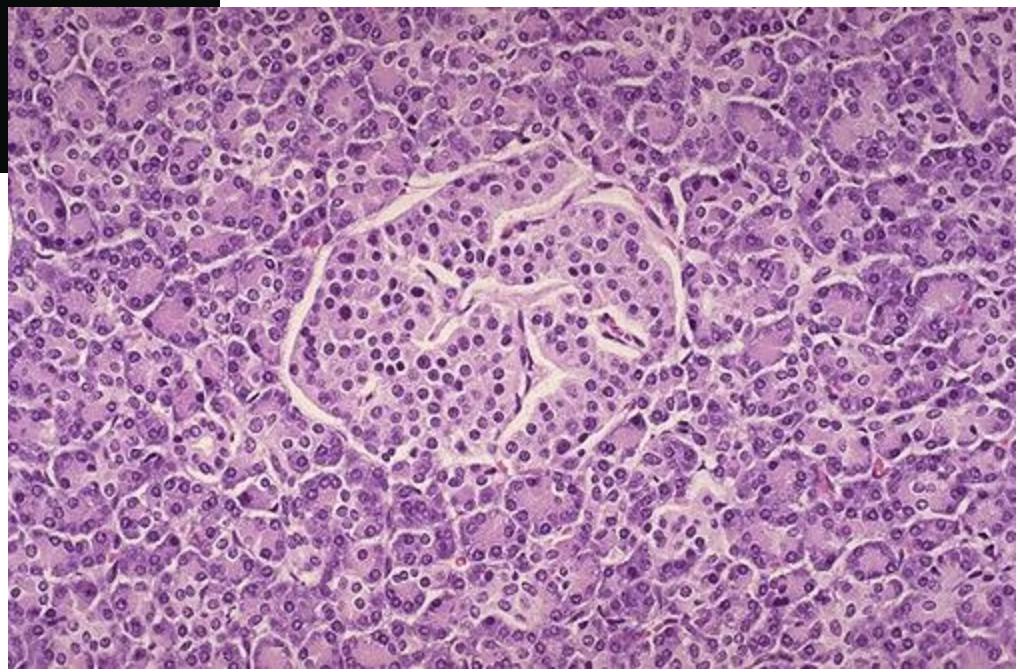
5. Practice

The pathology of pancreas

2017/2018. – 2nd semester

MACROSCOPY- MICROSCOPY



THE STRUCTURE OF PANCREAS

- **Exocrine**: 80-85%
  - Enzymes in the zymogenic granules of acinar cells: trypsin, chymotrypsin, aminopeptidase, elastase, amylase, lipase, phospholipase, nuclease
  - Bicarbonate production in the ductular epithelium
- **Endocrine**: 1-2%
  - Langerhans islets: hormones

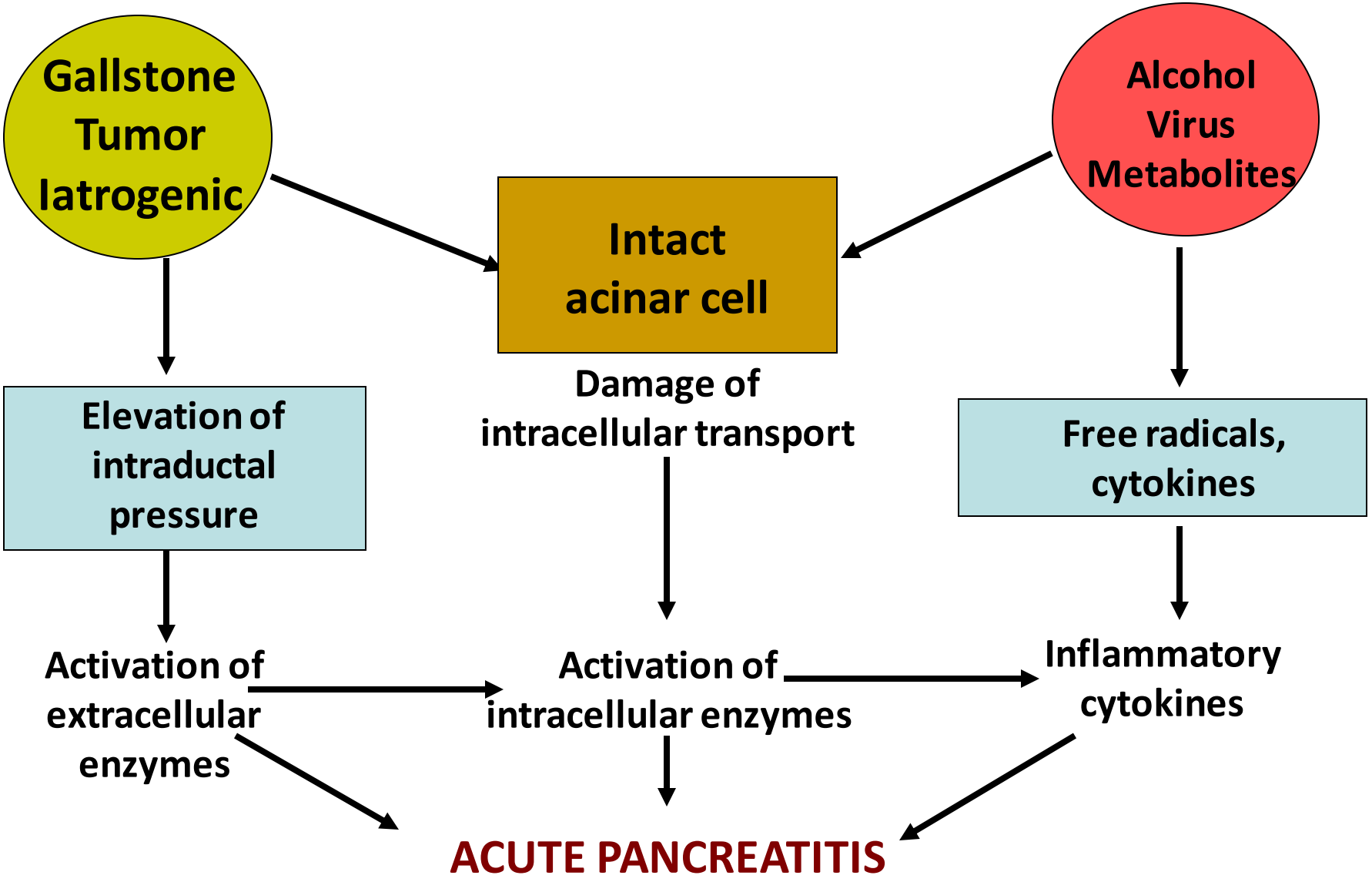
INFLAMMATION – PANCREATITIS

It can be classified according to…

- **Course of disease**: acute or chronic

- **Cause of disease**: autoimmune, infection (Mumps, Cytomegalovirus, Coxsackie, Hepatitis, Scarlet fever), alcohol, biliary, metabolic, mechanic, vascular, hereditary …

ACUTE PANCREATITIS - PATHOGENESIS



ACUTE PANCREATITIS
CLINICOPATHOLOGIC CLASSIFICATION

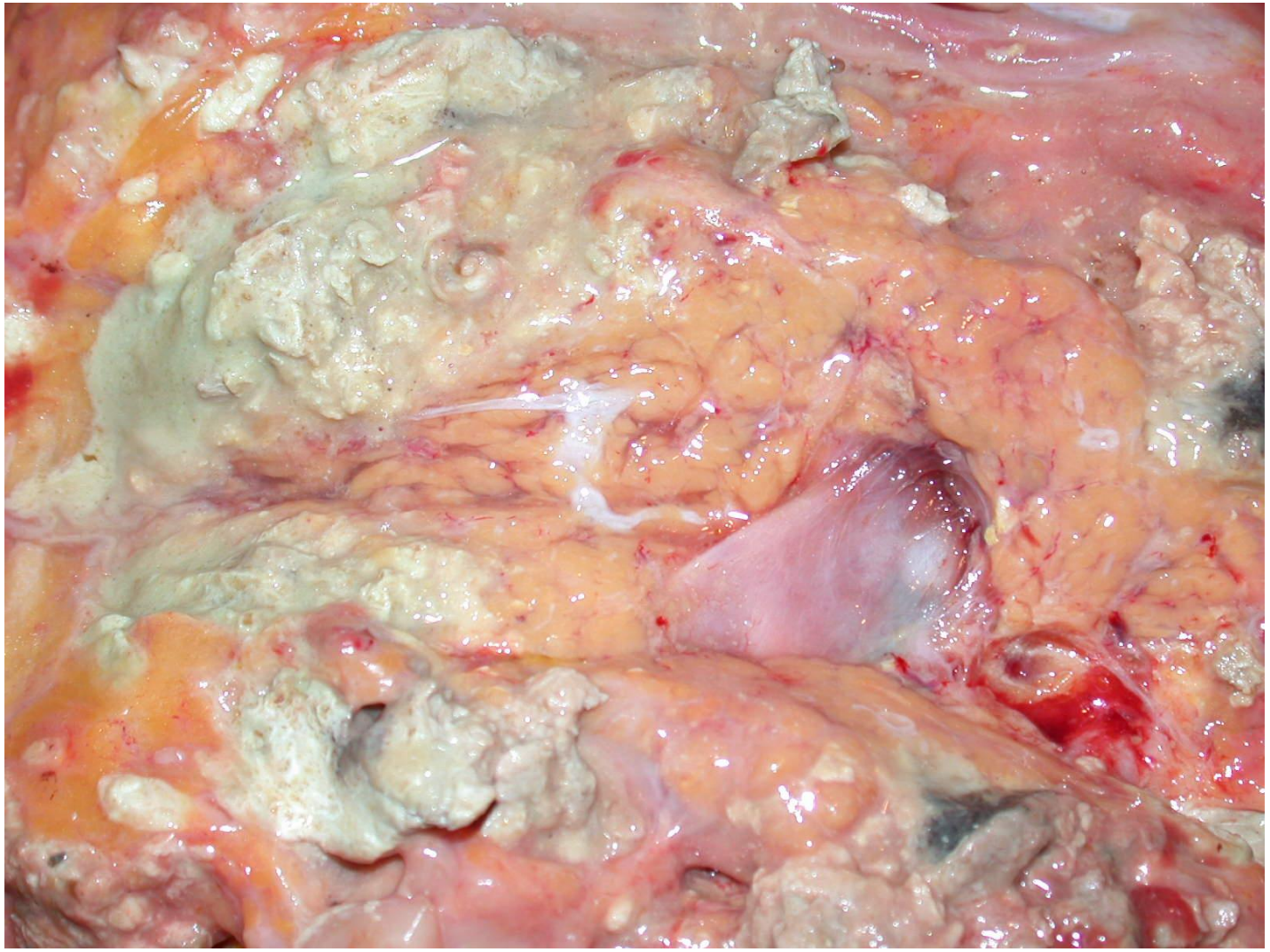
1. **Acute edematous (interstitial) pancreatitis** – 80-90%

   - morphology: interstitial edema and mild acute inflammatory infiltration, focal, peripancreatic fat necrosis

2. **Acute hemorrhagic necrotizing pancreatitis** – 10-15%

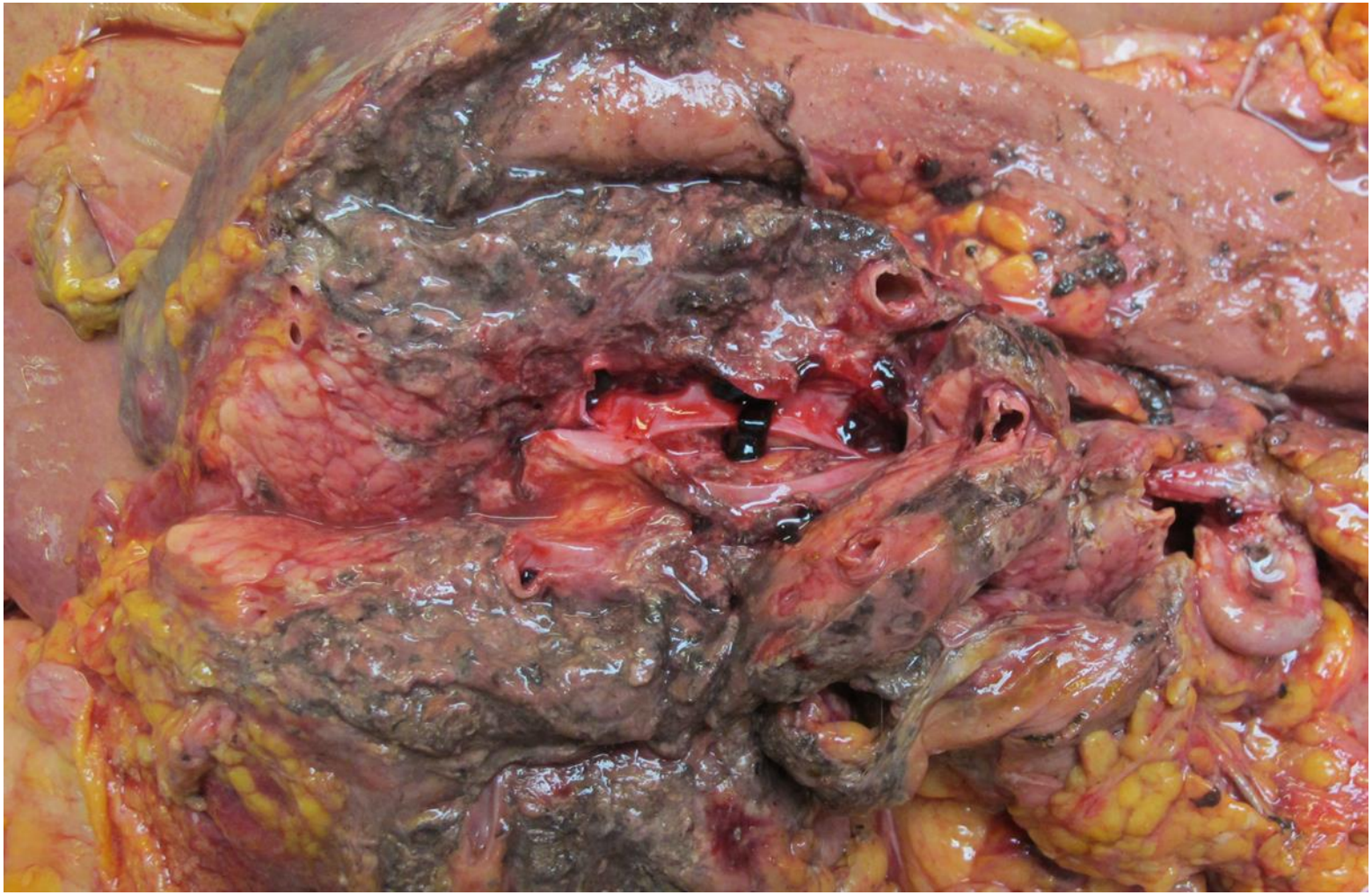
   - morphology: parenchymal and vascular destruction (enzymatic and inflammatory), hemorrhage and necrosis (fat necrosis), expansive destruction of parenchyma, pronounced acute inflammatory infiltration, high mortality rate

Acute pancreatitis

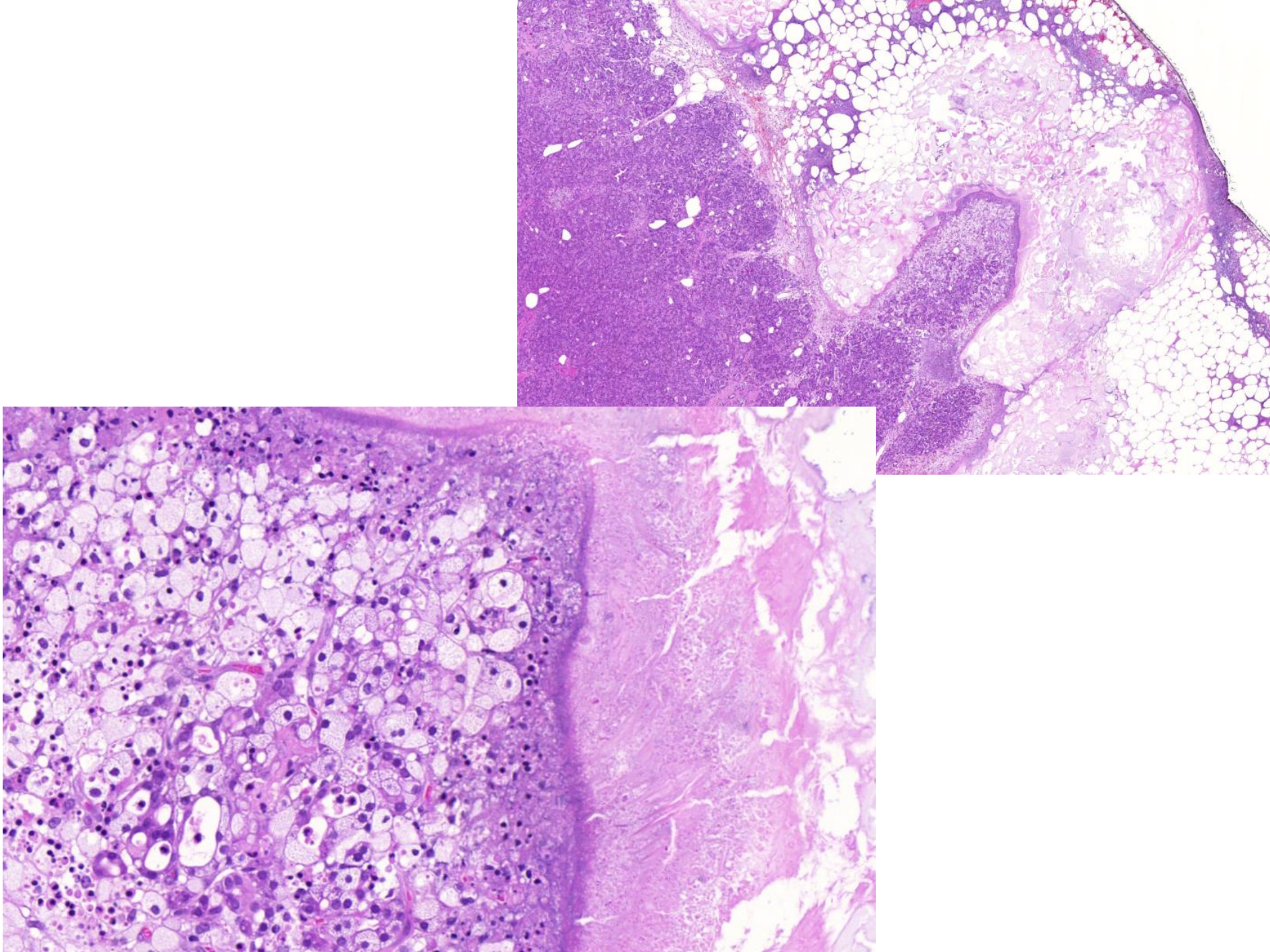


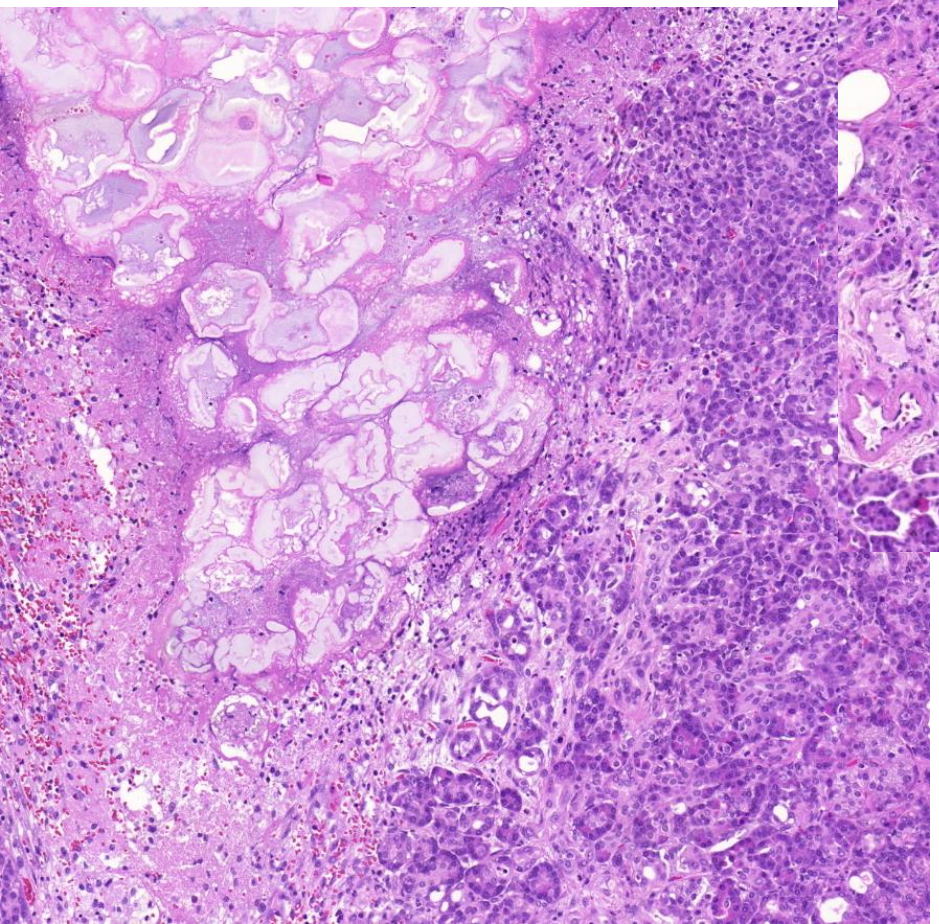
Archive picture of SE-2nd Department of Pathology

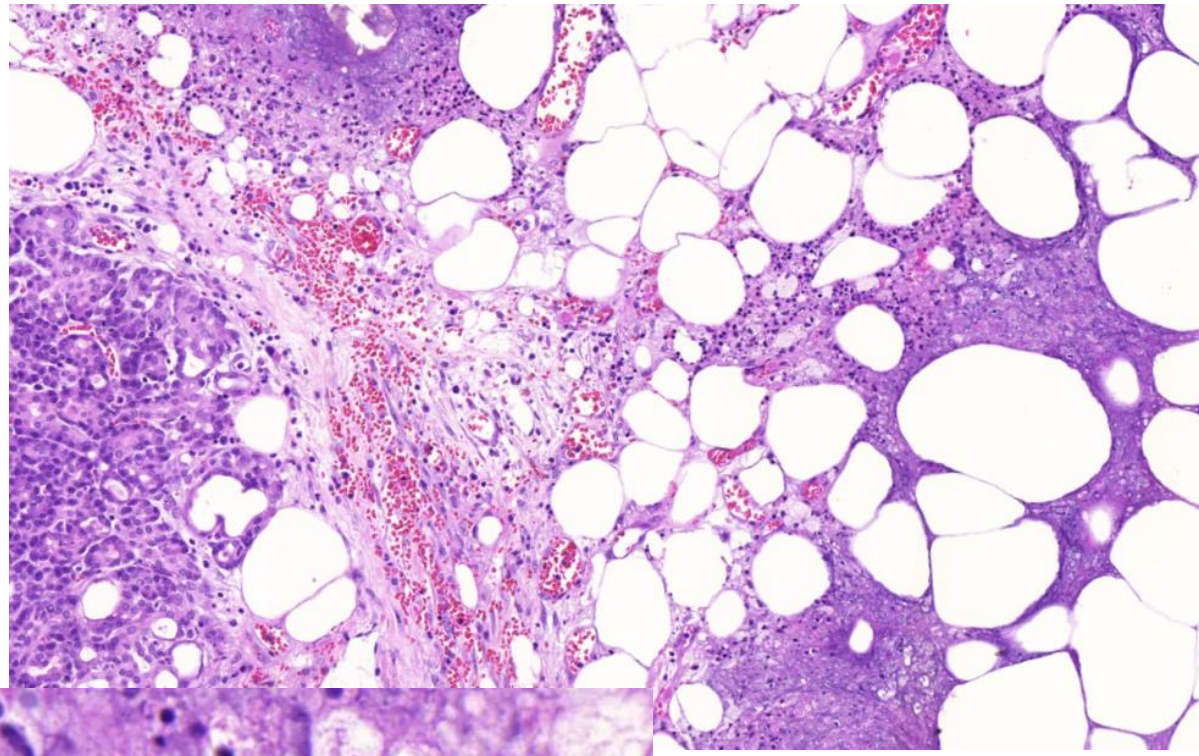
Acute pancreatitis

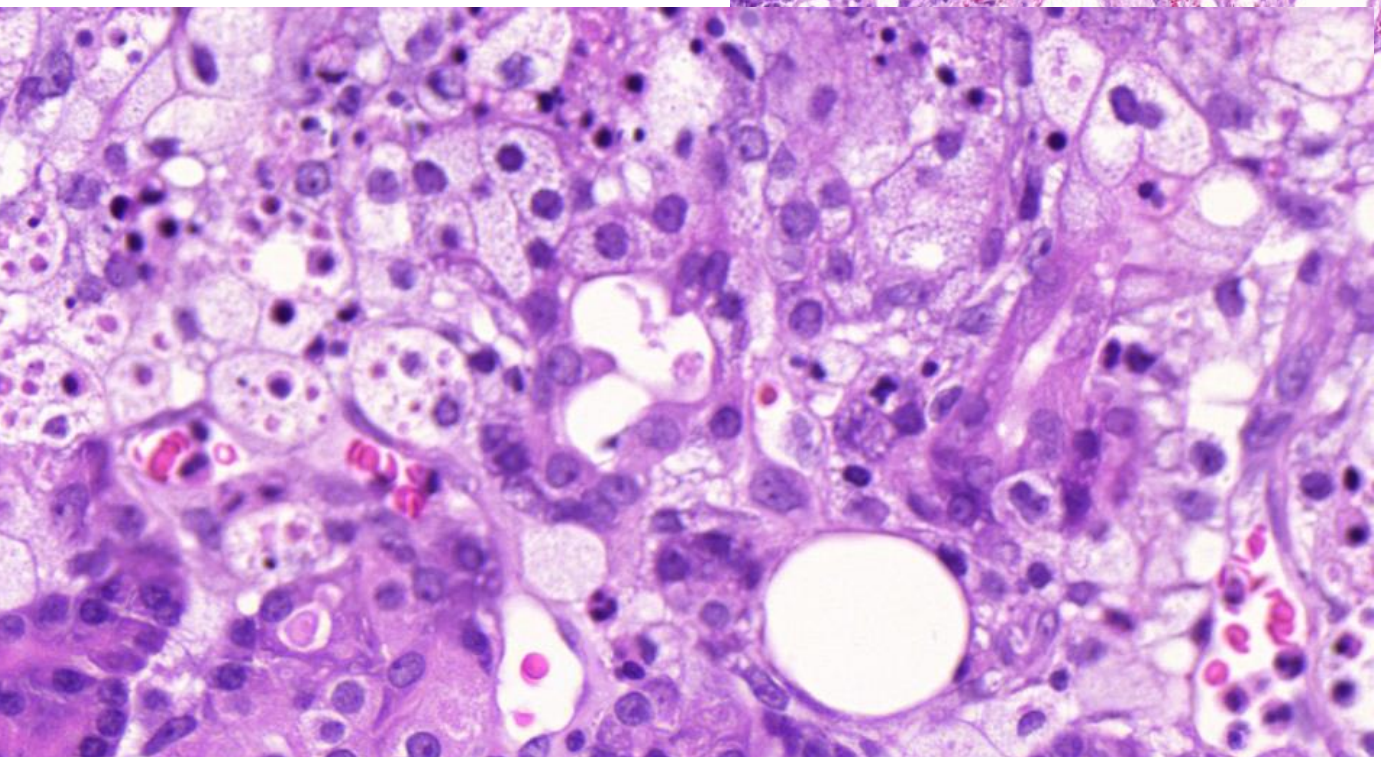


Archive picture of SE-2nd Department of Pathology









CONSEQUENCES

- **Local**:

  Peripancreatic edema, necrosis of pancreas

  abscess, pseudocyst

- **Extrapancreatic consequences**

  circulatory collapse, GI hemorrhage, coagulopathy (DIC)

  encephalopathy, respiratory failure (ARDS), endocrine failure (diabetes), acute renal failure, SIRS, MOF, hypocalcemic tetany, peritonitis, ileus, fat necrosis (metastatic)

DIFFERENTIAL DIAGNOSIS

- Perforation of gastric or duodenal ulcer
- Mechanic ileus
- Mesenteric infarction
- Posterior myocardial infarction
- Aortic aneurysm
- Thrombosis of mesenteric vein, splenic infarction, extrauterine gravidity, biliary colic, porphyria, angioedema, heroin abuse, intoxication (paraquat, thallium), mumps, diverticulitis, macroamylasemia

CHRONIC PANCREATITIS

- Recurring inflammation with mild symptoms

- **Clinical features**: belt-like radiation of abdominal pain, symptoms of pancreatic insufficiency: obstipation, diarrhea, diabetes mellitus, steatorrhea

CHRONIC PANCREATITIS

- Alcoholic chronic pancreatitis – ACP
- Hereditary pancreatitis – HP
- Autoimmune pancreatitis – AIP
- Obstructive chronic pancreatitis – OCP

CHRONIC PANCREATITIS

- **Causes**: **alcohol**, biliary obstruction (**gall stone**), pancreas divisum, genetic (cystic fibrosis), malnutrition, autoimmune (ulcerative colitis, PSC), unknown
- **Development:**

  a. obstruction of pancreatic duct

  b. pathologic ratio and secretion of proteins

  c. accumulation of free radicals

MORPHOLOGY

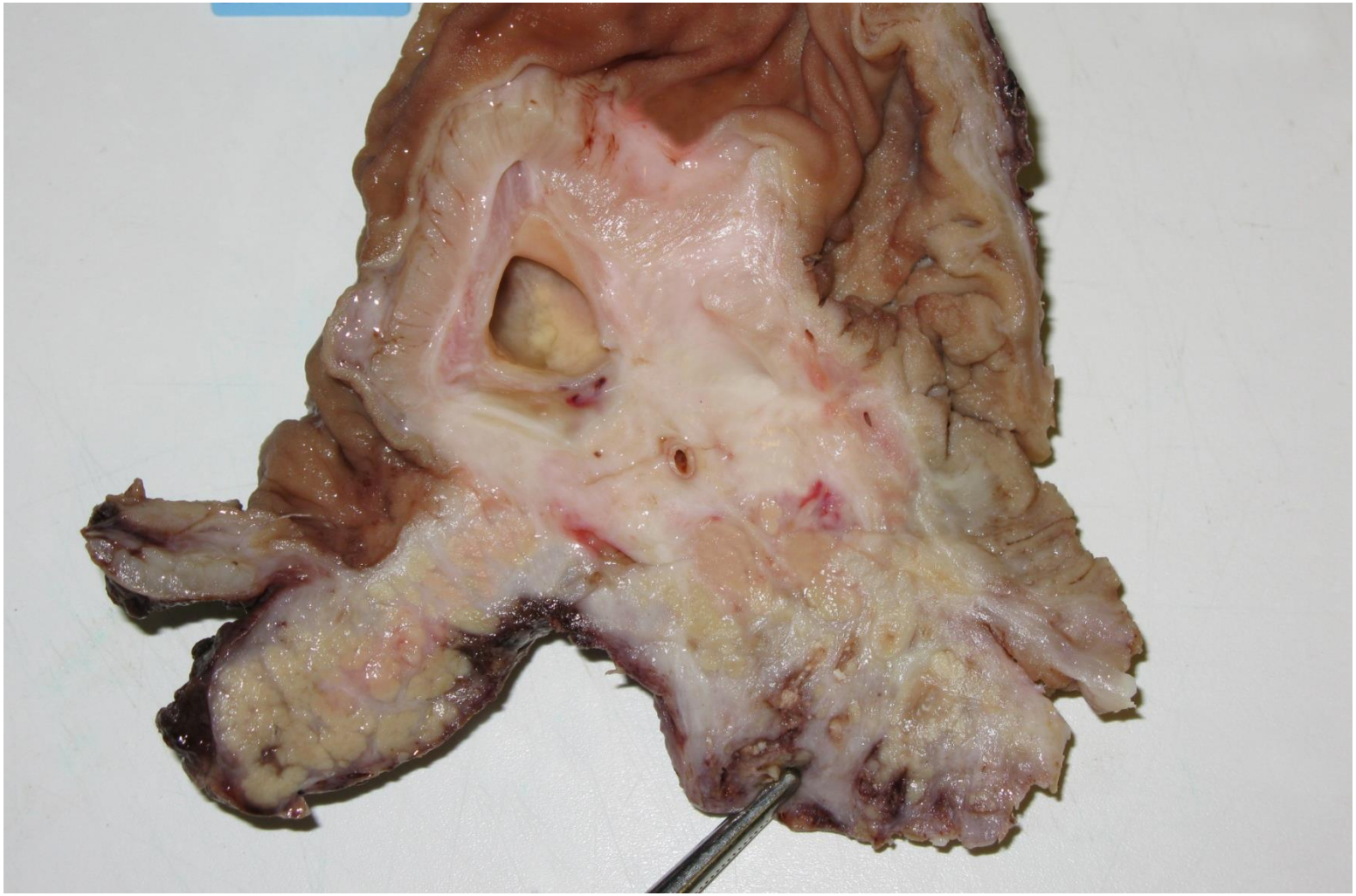
- **Macroscopy**: firm parenchyma dissected by septa of connective tissue, calcification (calcified secreted substance in the dilated ductus)

- **Microscopy**: loss of parenchyma (atrophy), chronic inflammatory infiltration, proliferation of ductus, fibrosis (even perineural), calcification, pseudocyst formation, mucinous metaplasia (PanIN IA - low grade)

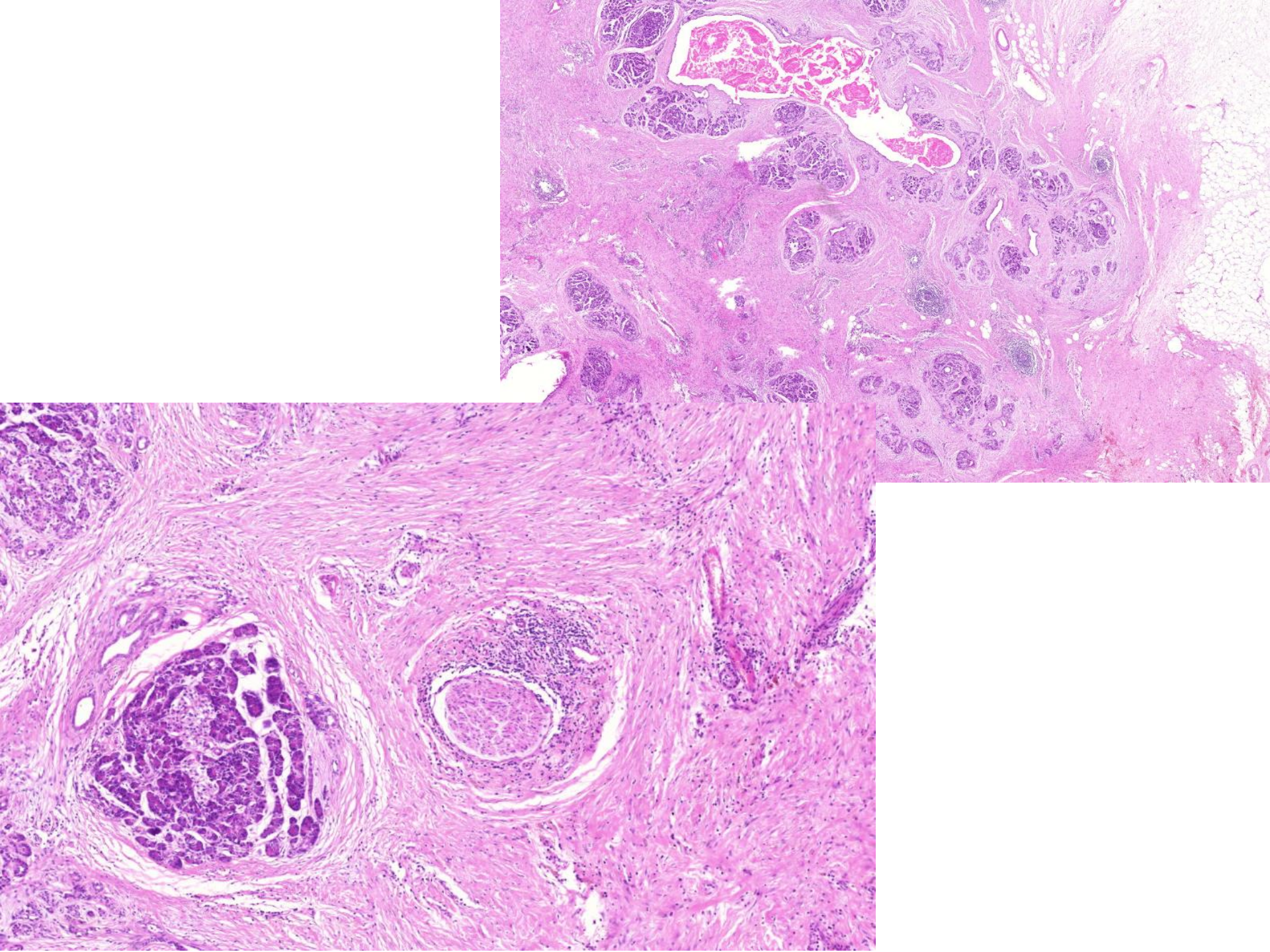
CONSEQUENCES

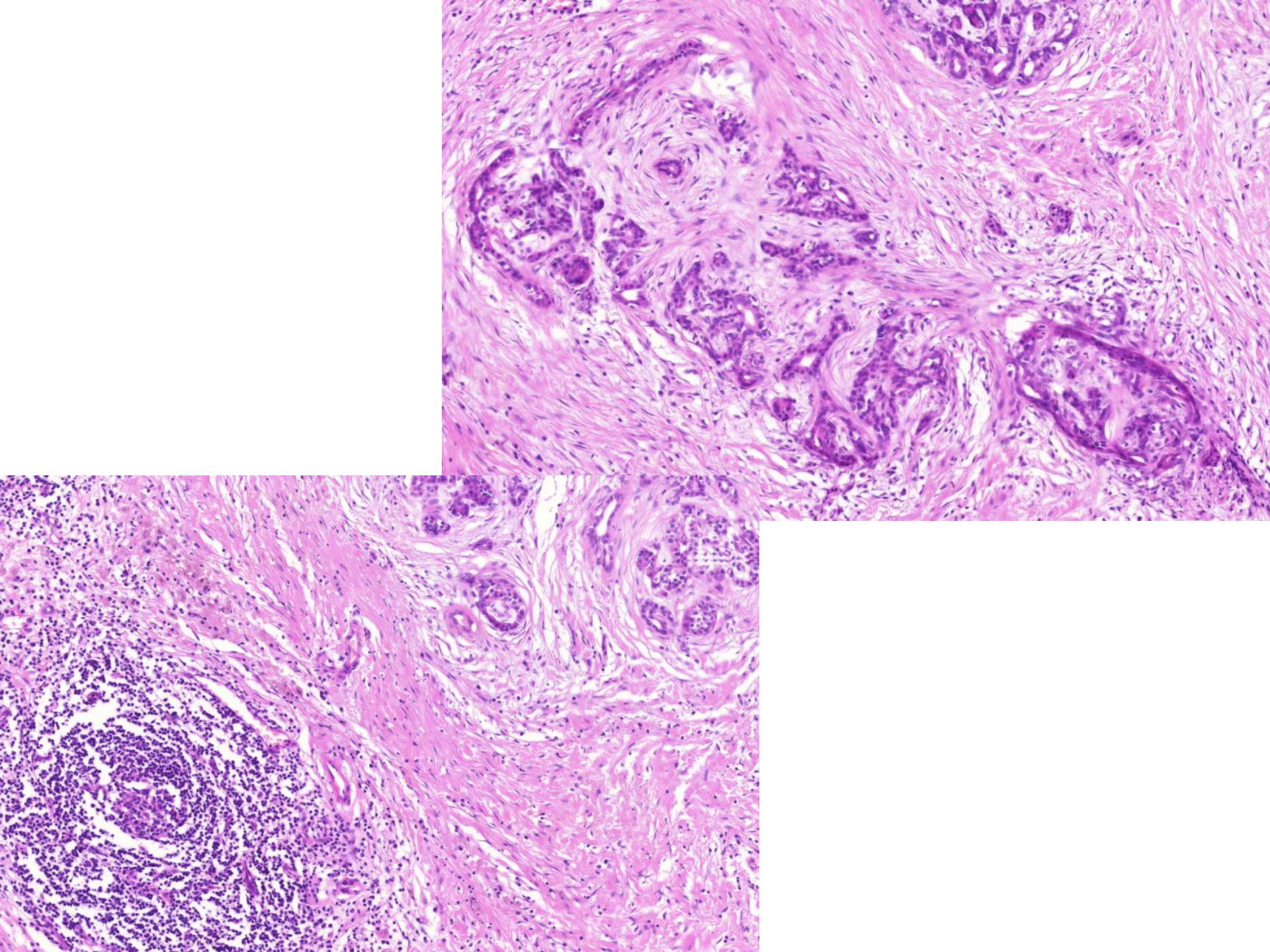
- pseudocyst
- stenosis of ductal lumen
- stones
- obstruction
- stenosis of common bile duct
- duodenal stenosis
- steatorrhea
- sec. diabetes mellitus
- perineural fibrosis
- fat necrosis (metastatic)

Chronic pancreatitis with pseudocyst



Archive picture of SE-2nd Department of Pathology





TUMORS OF PANCREAS

ductal epithelium, acinar cells, NE cells, stromal cells

- **Exocrine** tumors

  every 20th abdominal tumor

  it can be detected during 1 % of autopsies

  deriving: **ductal epithelium**, acinar cells
- **Endocrine** tumors
- **Mesenchymal** tumors - rare
- **Lymphoma** - rare

EXOCRINE MALIGNANT TUMORS

WHO classification

- **Ductal adenocarcinoma**
- Adenosquamous carcinoma
- Mucinous adenocarcinoma
- Hepatoid carcinoma
- Medullary carcinoma, NOS
- Signet ring cell carcinoma
- Undifferentiated carcinoma Undifferentiated carcinoma with osteoclast-like cells
- **Acinar cell carcinoma**
- Acinar cell cystadenocarcinoma
- **Intraductal papillary mucinous carcinoma (IPMN) with an associated invasive carcinoma**
- Mixed acinar-ductal carcinoma
- Mixed acinar-neuroendocrine carcinoma
- Mixed acinar-neuroendocrine-ductal carcinoma
- Mixed ductal-neuroendocrine carcinoma
- **Mucinous cystic neoplasm (MCN) with an associated invasive carcinoma**
- Pancreatoblastoma
- Serous cystadenocarcinoma, NOS
- **Solid-pseudopapillary neoplasma**

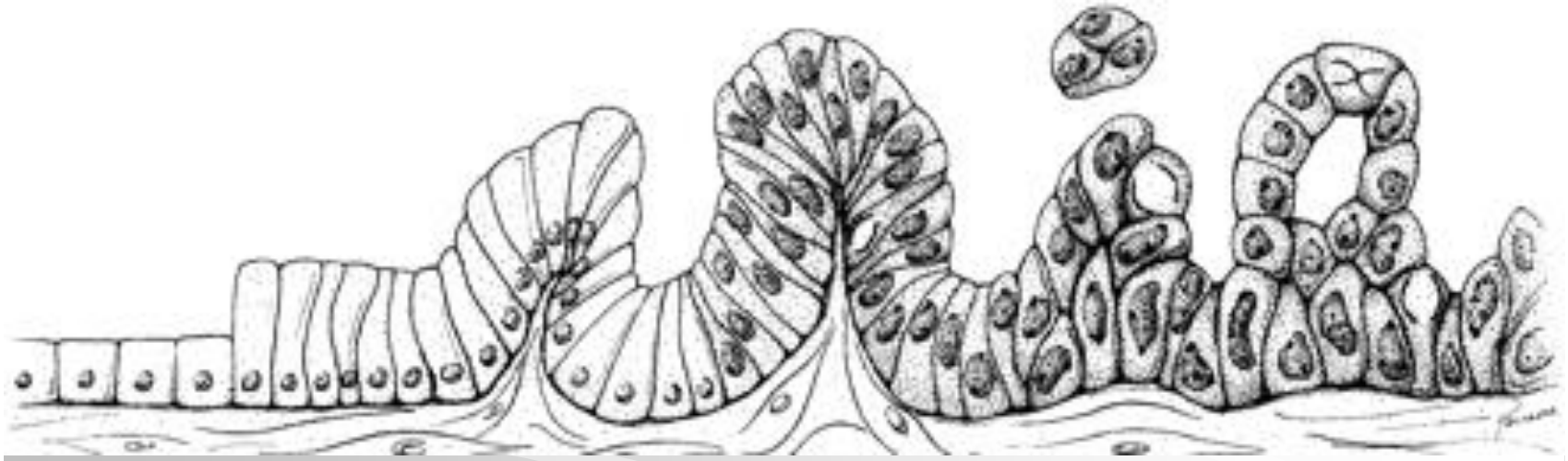
DUCTAL ADENOCARCINOMA
Clinical features

- 50 years, male:female - 1,5:1
- Belt-like radiation of abdominal pain
- Icterus
- Elevation of pancreatic enzyme levels: alkaline phosphatase, amylase
- Courvoisier sign
- Trousseau sign: migrating thrombophlebitis (paraneoplastic syndrome)
- Elevation of tumor marker levels: CEA, SPan-1, CA 19-9

MACROSCOPY

- 66% -Head region
- 33% -Body and tail region: occult cc. (metastasis)
- Greyish-white, firm tumor (desmoplastic stroma)

Carcinogenesis



Normál PanIN-1a PanIN-1b PanIN-2 PanIN-3

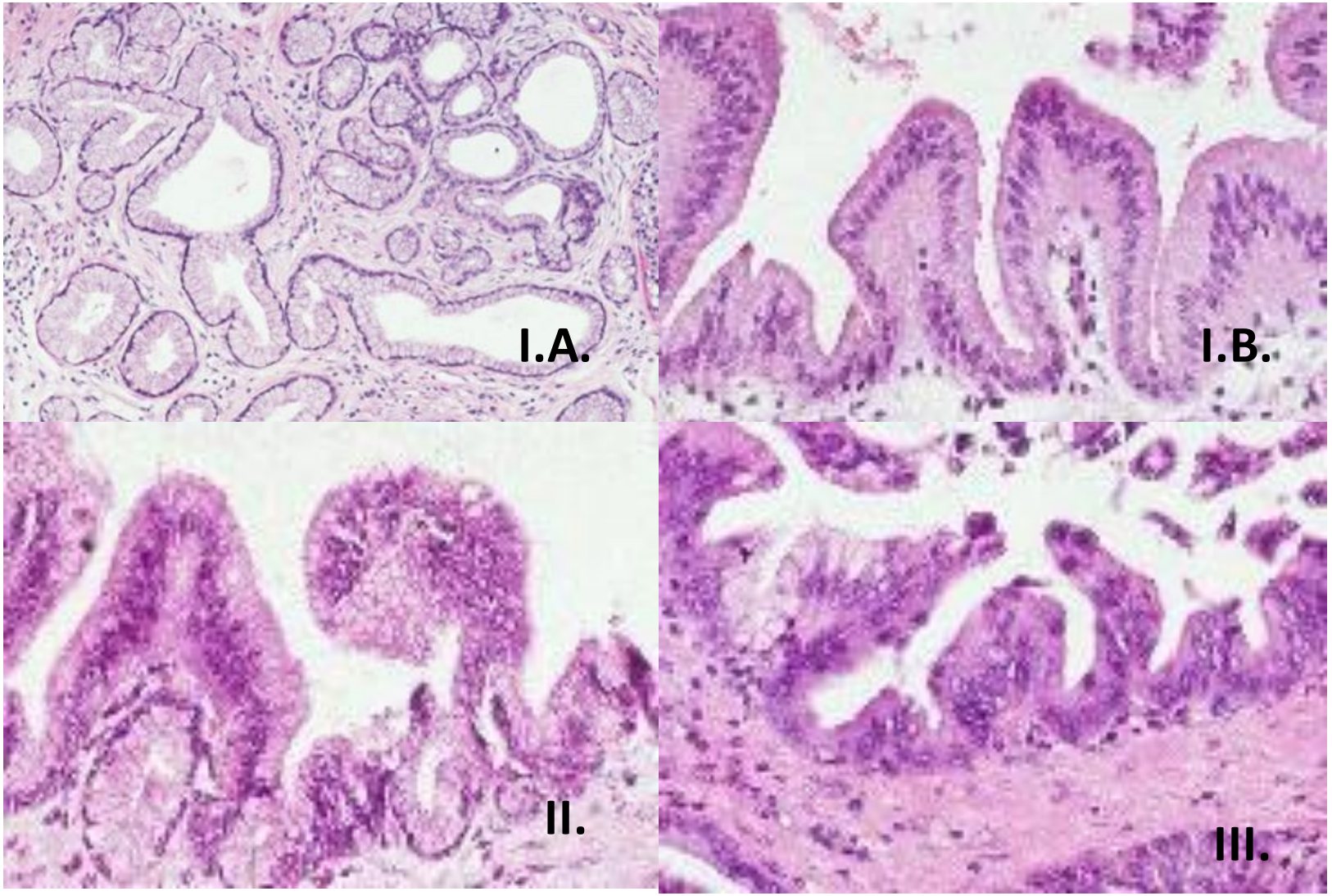
Her2/neuK
-ras

p16
LOH 9p

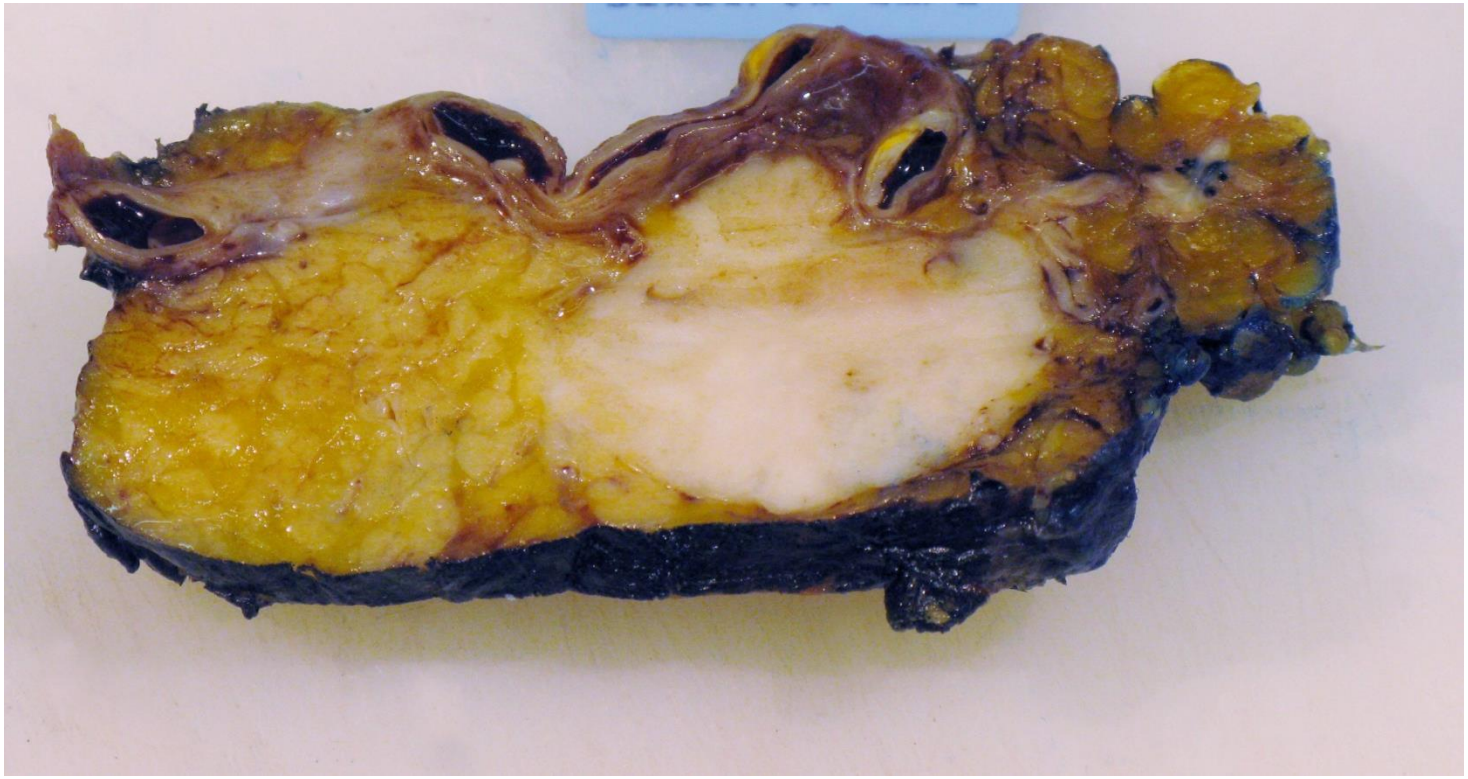
p53
DPC4
BRCA2
LOH18q,17p 6q

Pancreatic **I**ntraepithelial **N**eoplasia

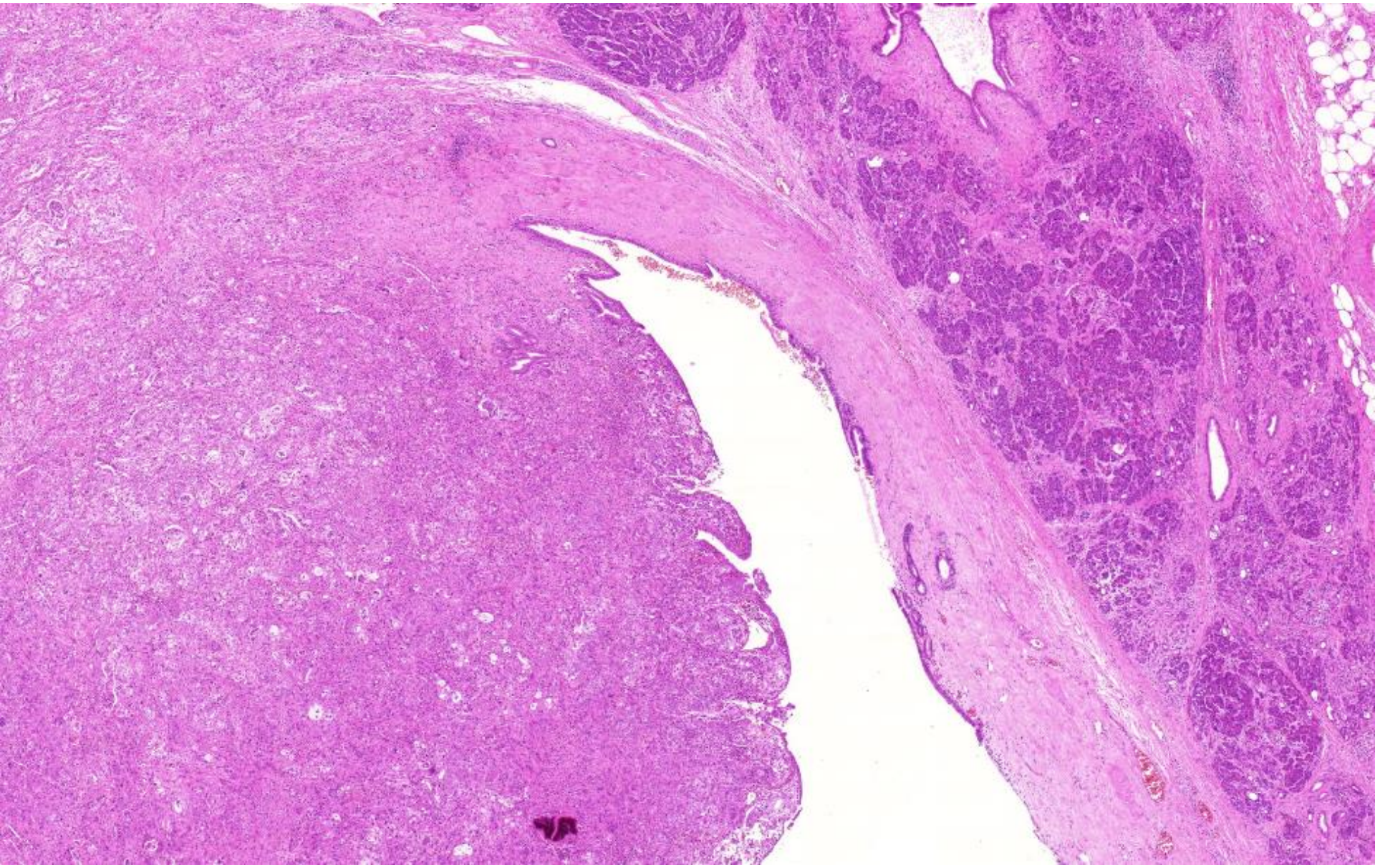
PanIN

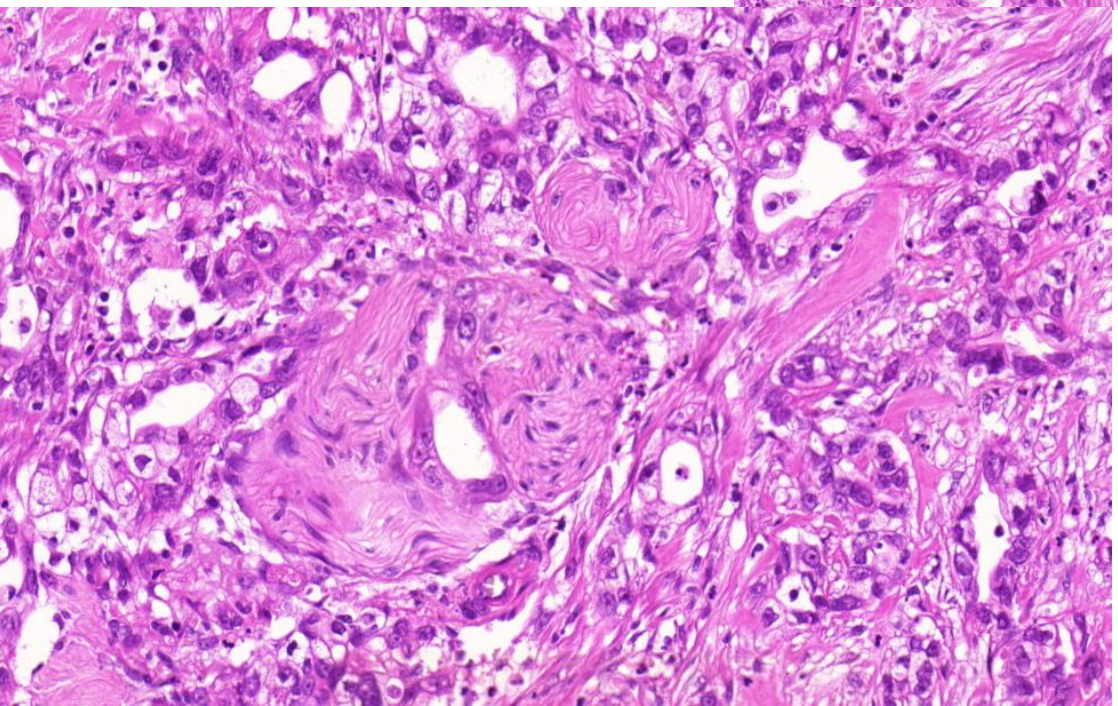


Pancreatic adenocarcinoma



Archive picture of SE-2nd Department of Pathology





Metastases

- **Lymphogenic**: regional lymph node
- **Haematogenic:** liver, lung, pleura, bones

- **Treatment**: surgical (Whipple procedure, PPPD), chemoradiotherapy

Pancreatic **N**euro**E**ndocrine **T**umors **(PNET)**

- Derive from the neuroendocrine cells of pancreas
- Functioning (hormone producing) and non-functioning tumors
- ***All tumors have malignant potential***
- Often associated with multiplex endocrine neoplasia syndrome I (MEN-I syndrome)

MORPHOLOGY OF NEUROENDOCRONE TUMORS

- **Macroscopy**:
  - Generally well circumscribed, surrounded by pseudocapsule, small in size (insulinoma), but they can be large and infiltrative as well
- **Microscopy**:
  - Dispersity of chromatin (salt and pepper), granulated (EM: dens core granulum) cytoplasm
  - Small and medium size cells forming bands, nests and tubules
  - In the stroma amyloid and calcification can present

Types of hormone producing neuroendocrine tumors

- **Insulinoma** – most common, derives from β cells, usually has good prognosis, hyperinsulinemia (life threatening hypoglycemic shock can occur)
- **Glucagonoma** – derives from α cells, usually aggressive, often metastatic, glucagon sy. (DM, necrotizing migrating skin lesions, stomatitis, weight loss, anemia)
- **Somatostatinoma** – poor prognosis, steatorrhea, DM, cholelithiasis, diarrhea, hypochlorhydria, weight loss, anemia
- **VIPoma** – poor prognosis, Verner-Morrison sy. (Watery Diarrhea, Hypokalemia, Achlorhydria - WDHA)
- **Gastrinoma** – poor prognosis, often secondary (usually small size tumor presenting in the stomach or duodenum), Zollinger-Ellison sy. – gastric parietal cell hyperplasia, increased HCl production, multiple peptic ulcers
- **Carcinoid** – derives from enterochromaffin cells, it causes carcinoid sy. (serotonin, histamine)

CARCINOID SYNDROME

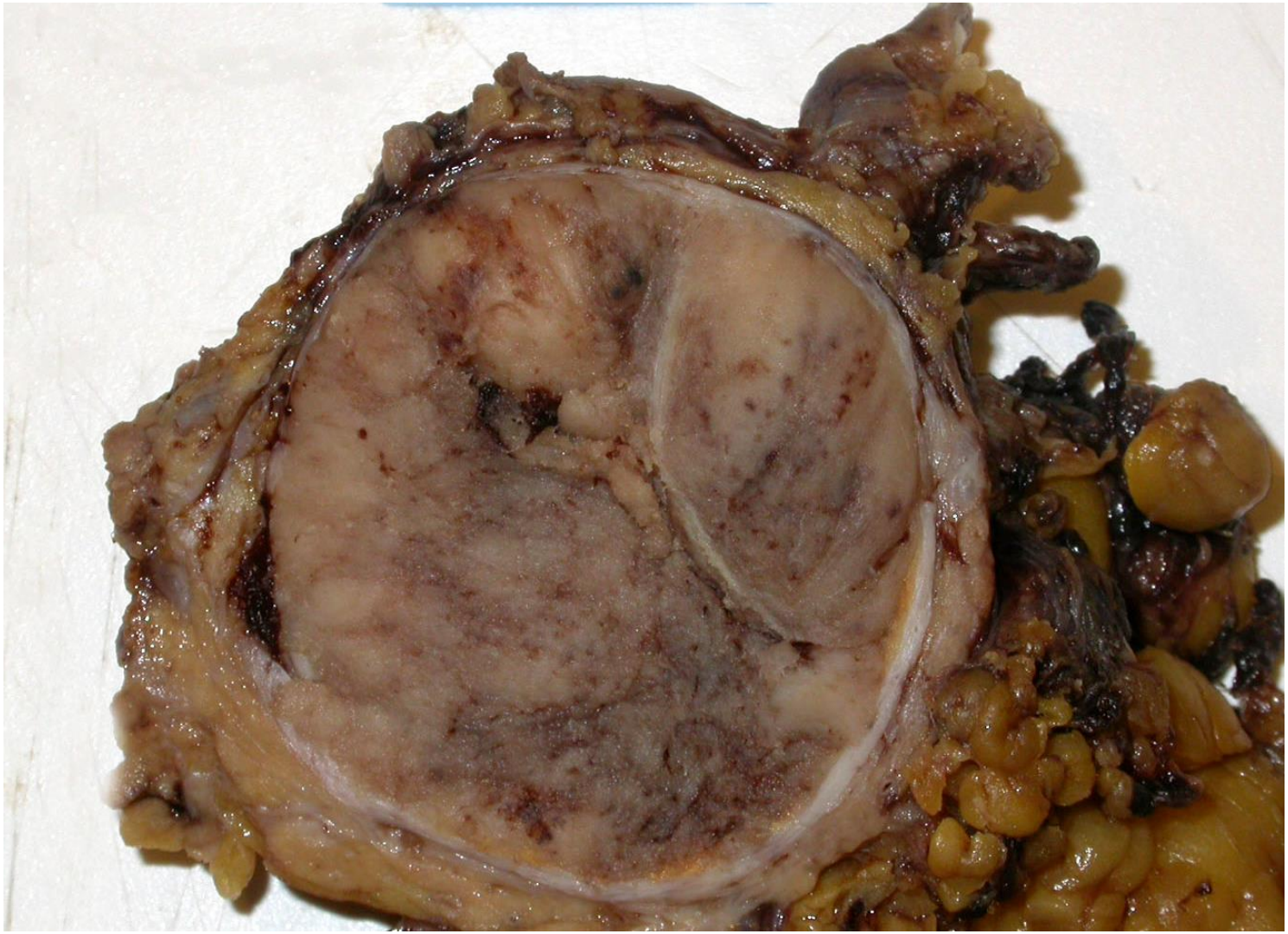
- The tumor cells produce serotonin, that is transformed to 5-HIAA in the liver, this appears in the urine→ diagnosis
- If there are liver metastases serotonin can get into the systemic circulation
  → clinical symptoms - **carcinoid syndrome**
  - Flush, bronchospasm, diarrhea
  - Endocardial fibrosis in the right side of the heart (consequential pulmonary stenosis, tricusp. insuff, right-sided heart failure)

Potentially malignant tumors → Grade, TNM
Grade: WHO – 2017 (Number of mitoses, Ki-67 index)

Well differentiated neuroendocrine neoplasms	**Ki-67 index**	**Number of mitoses**
Neuroendocrine tumor NET G1	<3 %	<2/10 NNL
Neuroendocrine tumor NET G2	3-20%	2-20/10 NNL
Neuroendocrine tumor NET G3	>20 %	>20/10 NNL
Poorly differentiated neuroendocrine neoplasms		
Neuroendocrine carcinoma (NEC) G3	>20 %	>20/10 NNL
Small-cell		
Large-cell		

Mixed Neuroendocrine-Nonneuroendocrine Neoplasms (MiNENs)

Pancreatic neuroendocrine tumor



Archive picture of SE-2nd Department of Pathology