

# Pathology of pancreas

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MARKÉTA HERMANOVÁ

# Exocrine pancreas

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The exocrine pancreas produces trypsin, lipase, phospholipase, amylase, elastase. These enzymes, with the exception of lipase, are in a form of inactive proenzymes and they are activated in the duodenum

Most of the proenzymes are activated by trypsin, which itself is activated from inactive trypsinogen by enteropeptidase in the duodenum

Acinar and ductal cells produce protease inhibitors

# Congenital anomalies of pancreas

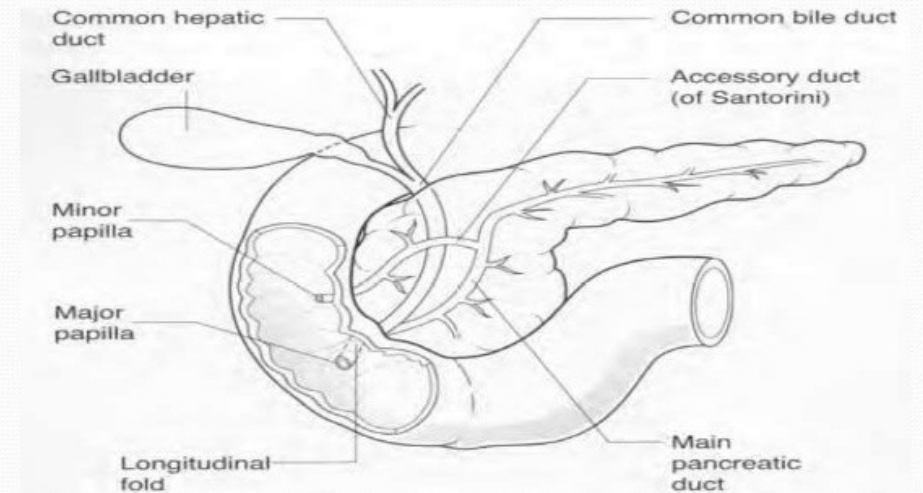
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Usually as a result of failure of migration and fusion of dorsal and ventral parts of the pancreas

May cause stenosis of duodenum, increase the risk of pancreatitis

- Annular pancreas
- Pancreas divisum
- Ectopic pancreas (stomach, duodenum, jejunum,...)
- Congenital/dysgenetic cysts of pancreas

## Ductal anatomy



# Cystic fibrosis (mucoviscidosis)

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- AR inherited disease caused by the presence of mutations in the *CFTR* gene (7q 31.2)
- *CFTR* gene encodes the chloride channel protein, it also participates in the regulation of other ion channels (Na, K) and cellular processes (transport of ATP, bicarbonate and mucus secretion)
- Leads to abnormal transport of ions and water through membranes
- Effect of *CFTR* is tissue-specific:
  - *Sweat glands*: chloride and sodium reabsorption; loss of *CFTR* function → hypertonic sweat (with excessive NaCl – „children with salty-tasting skin“)
  - *Respiratory and intestinal epithelium*: *CFTR* ensures active luminal chloride secretion; loss of *CFTR* function → reduction of luminal chloride secretion and increased reabsorption of sodium and water from the lumen → dense viscous mucus which obstructs ducts of the glands

# Cystic fibrosis (mucoviscidosis)

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Disorder with a wide degree of phenotypic variation

5 classes of mutations of *CFTR* gene:

- combination of 2 „severe mutations“ → severe („classic“) phenotype of CF
- combination of less severe mutations → mild phenotype of CF

+ modifier genes

(e.g. polymorphisms in genes, whose products modulate neutrophil function in response to bacterial infections)

# Cystic fibrosis (mucoviscidosis): pathological features in organs

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## Pancreas

- viscous mucus obstructs ducts, which leads to dilatation of ducts, atrophy of the parenchyma and fibrosis
- exocrine pancreatic insufficiency (fat malabsorption and avitaminosis A,D,E,K)
- endocrine pancreatic insufficiency (diabetes associated with cystic fibrosis)

## Lungs

- airway obstruction, recurrent and persistent infections
- bronchitis, bronchiectasis, bronchopneumonia, abscess
- *Pseudomonas aeruginosa*, *Haemophilus influenzae*, *Staphylococcus aureus*, *Burkholderia cepacia*, *Strenotrophomonas maltophilia*, atypical mycobacteria

## Meconium ileus

Bile ducts obstruction (with the development of biliary cirrhosis)

Impairment of salivary glands (analogical to pancreatic impairment)

Azoospermia and infertility (resulting from congenital bilateral absence of vas deferens)

Impairment of sweat glands

# Pancreatitis

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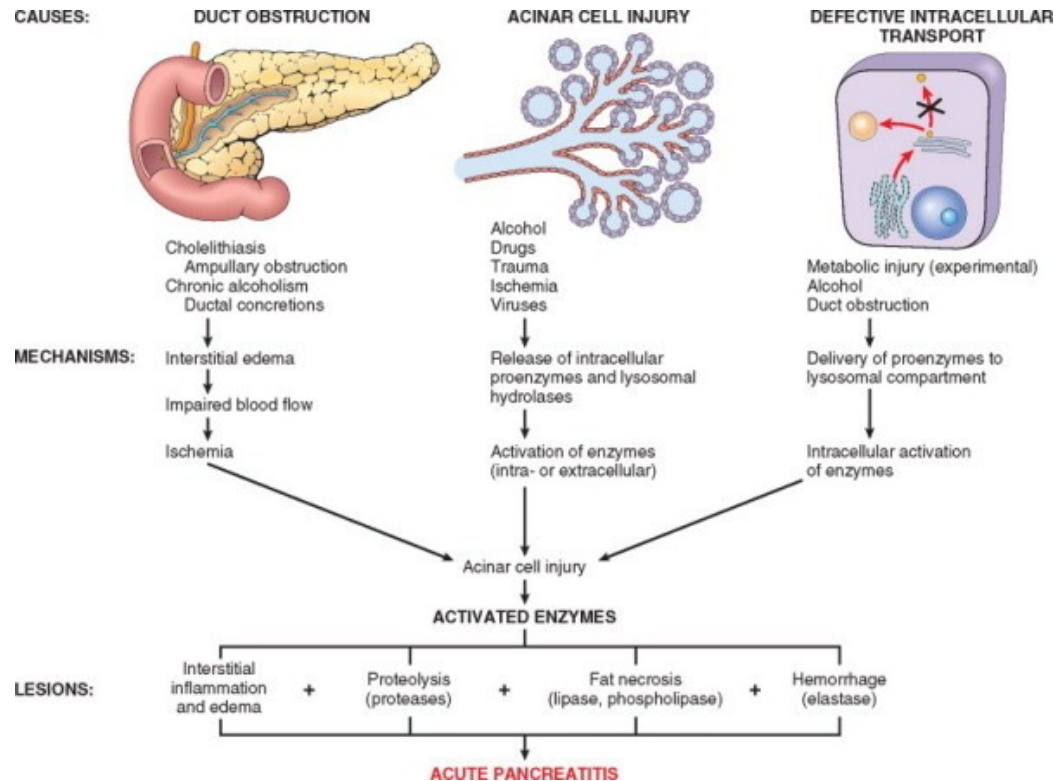
- Acute (AP)

Systemic inflammatory response to **autodigestion of the pancreas and peripancreatic tissue** by inappropriate release and activation of its own enzymes.

- Chronic (CP)

Prolonged inflammation of the pancreas, during which functional parenchyma is gradually replaced by fibrotic tissue with the development of irreversible destruction of exocrine, later endocrine pancreas.

# Etiology of acute pancreatitis



## Initiation of AP:

Inappropriate and massive activation of trypsinogen

Activation of elastase and phospholipase → damage of cell membranes and hemorrhage, ARDS (phospholipases interact with the surfactant)

Activation of other enzymes, activation of complement, kallikrein-kinin system, coagulation and fibrinolytic system → DIC, shock (with mortality of 2-4 %)

## Main pathways of pathogenesis of AP:

- duct obstruction
- primary acinar cell injury
- primary defective intracellular transport of proenzymes

The most common causes of AP are **alcoholism and biliary tract disease**



# Acute pancreatitis – etiologic factors

80 % of acute pancreatitis is associated with alcoholism and disorders of bile ducts

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## Metabolic

- Alcoholism
- Hyperlipoproteinemia (type I a V)
- Hypercalcemia (hyperparathyroidism etc.)
- Drugs (thiazide diuretics, azathioprine, estrogens, sulfonamides, furosemide, metyldopa, pentamidine, procainamide)
- Genetic

## Mechanical

- Trauma
- Obstruction (gallstones, pancreas divisum, tumors, parasites(*Ascaris lumbricoides*)), spasms
- Iatrogenic injury (perioperative injury, ERCP)

## Vascular, ischaemic

- Shock, thrombosis, embolism
- Vasculitis – polyarteriitis nodosa

## Infectious

- Mumps
- Coxsackievirus
- *Mycoplasma pneumoniae*

+ idiopathic AP (10-20 %)

Focal oedema and necrosis of fat tissue → Diffuse necrosis of pancreatic parenchyma and hemorrhage

# Acute pancreatitis

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The basic alterations of morphology of the pancreas include:

- **Interstitial oedema** caused by microvascular leakage
- **Necrosis of fat** caused by lipolytic enzymes
- **Acute inflammatory reaction**
- **Protelolytic destruction of pancreatic parenchyma**
- **Destruction of blood vessels** caused by elastase with **interstitial hemorrhage**

## Clinical features

Pain in the upper abdomen, anorexia, nausea, emesis; severe cases cause acute abdomen

DIC, ARDS, shock

Hypocalcemia, elevated levels of amylase and lipase in plasma

Postnecrotic pseudocysts, secondary infections, abscess

# Clinical-pathological subtypes of AP

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- **Acute interstitial pancreatitis**

moderate inflammation, interstitial oedema and focal necrosis of fat tissue of pancreas and peripancreatic tissue

- **Acute necrotizing pancreatitis**

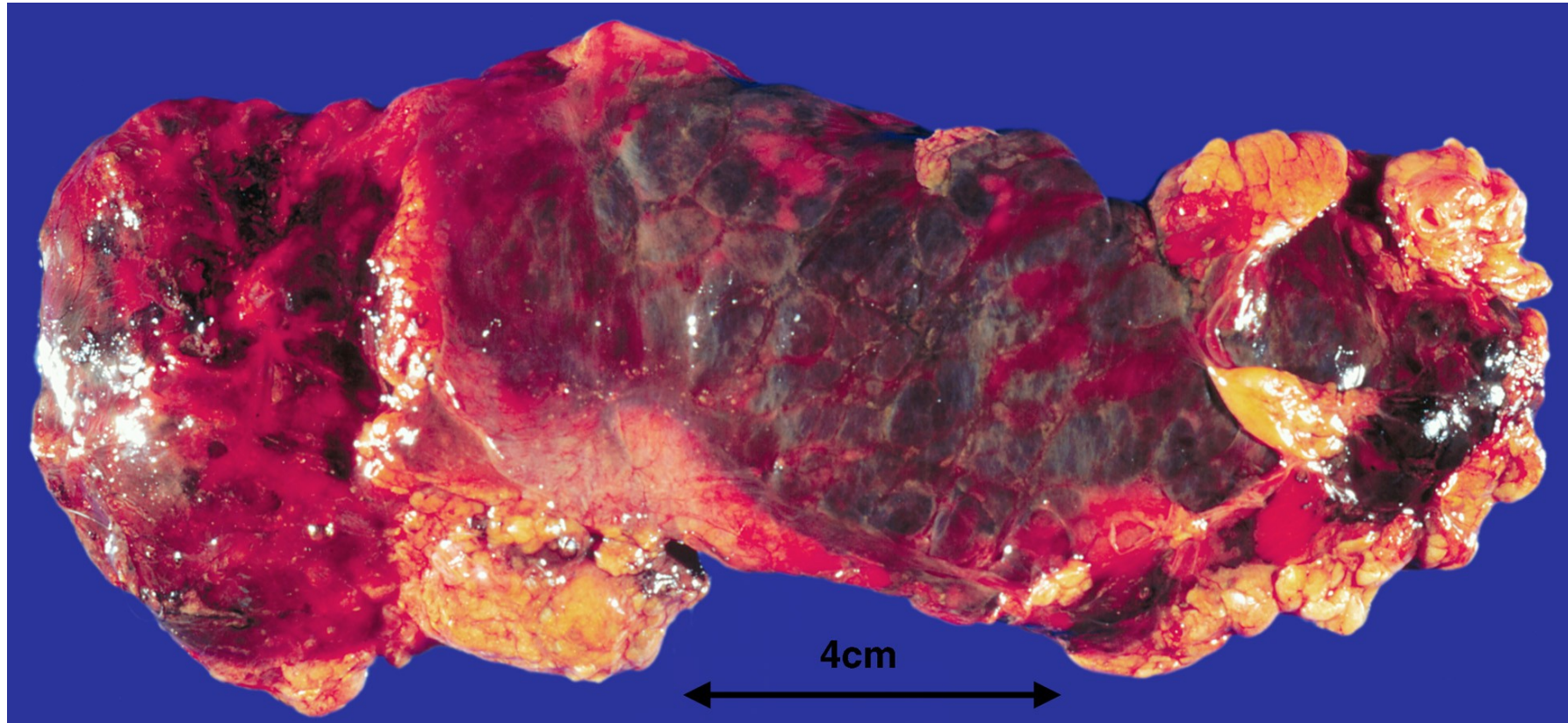
necrosis of fat tissue of pancreas and peripancreatic tissue (Balsler's fatty necrosis, Ca bound to necrotic tissues, hypocalcemia of blood), colliquation of necrotic areas, destruction of structures of exocrine and endocrine pancreas, interstitial hemorrhage

- **Hemorrhagic pancreatitis**

Extensive necrosis of pancreatic parenchyma, hemorrhage

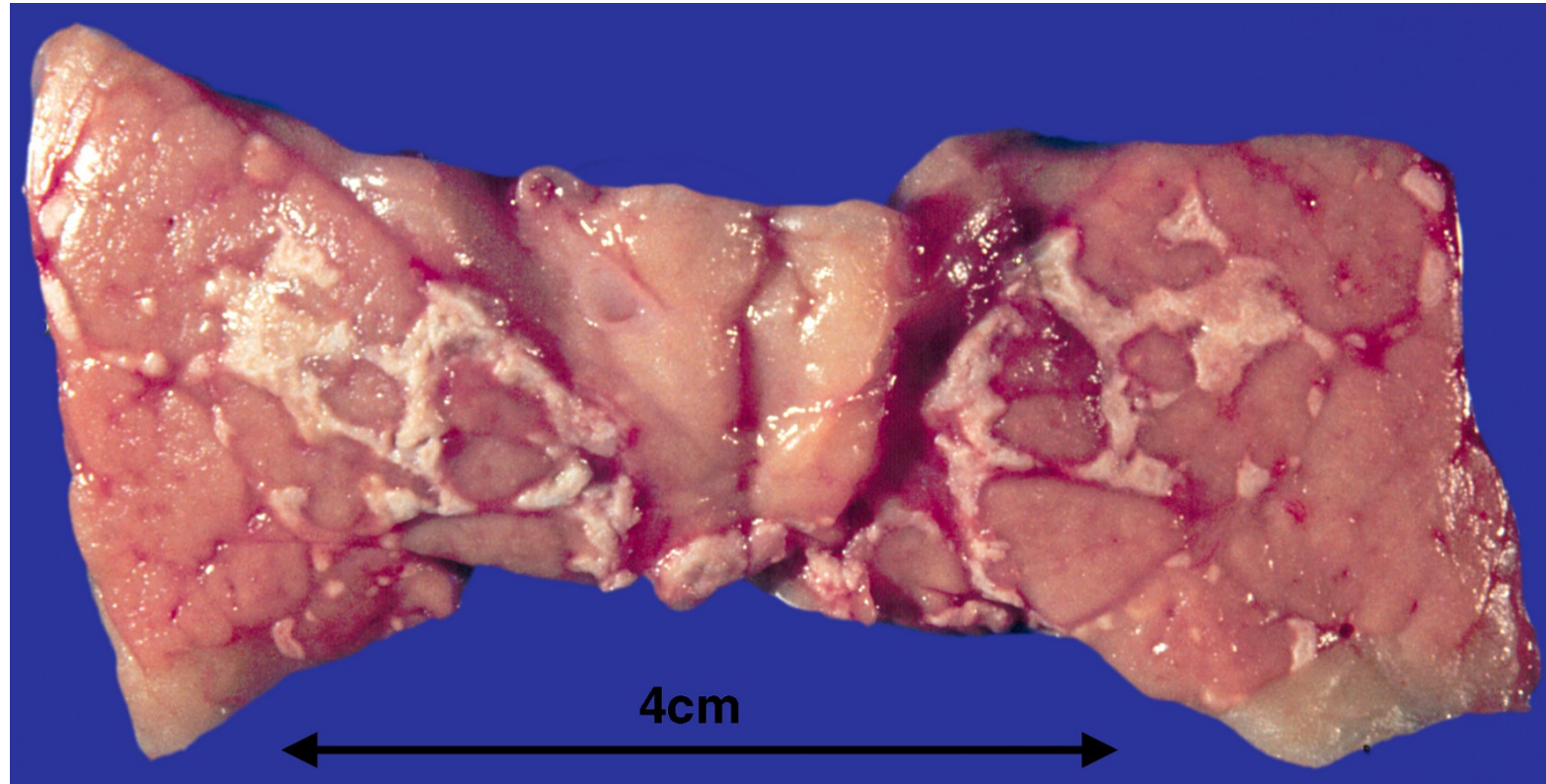
# Acute pancreatitis

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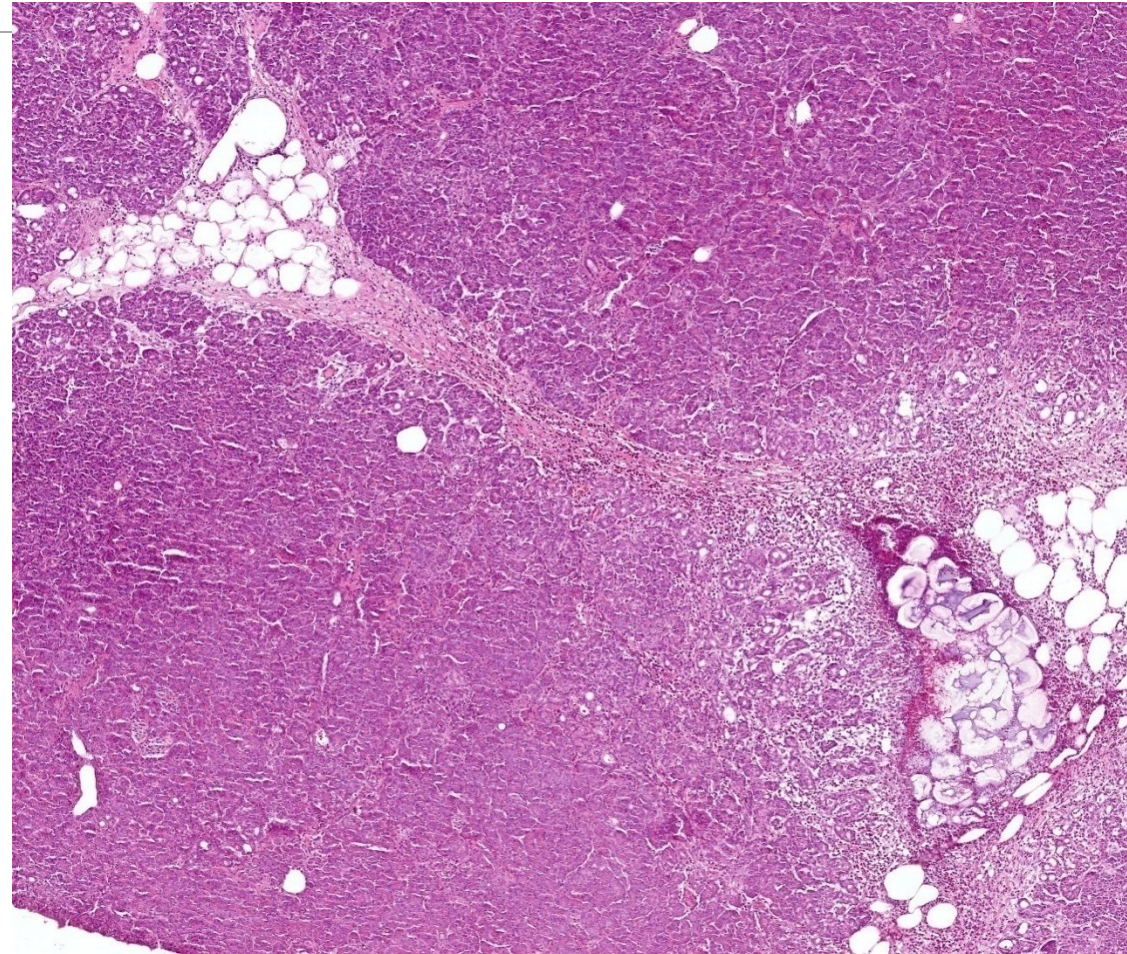
# Necrotizing acute pancreatitis

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# Necrotizing acute pancreatitis

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# Necrosis adipose tissue of omentum

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# Chronic pancreatitis (CP)

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# Pathogenesis of CP

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Obstructive causes

Toxic-metabolic causes

Oxidative stress

Necrosis-fibrosis

# Etiology of chronic pancreatitis– classification TIGARO

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**Toxic-metabolic** (alcohol (alcoholic CP), nicotine, hyperlipidemia, drugs, uremia, toxins...)

**Idiopathic**

**Genetic**

- hereditary pancreatitis, AD (mutation in gene *PRSS1* (trypsinogen 1)), high risk of development of pancreatic carcinoma

- genetically induced pancreatitis (alterations in genes *CFTR*, *SPINK1* (trypsin inhibitor),...)

- alpha-1 antitrypsin deficiency

**Autoimmune** (imitates carcinoma!)

**Recurrent** (repeated episodes of acute pancreatitis)

**Obstructive** (gallstone obstruction, tumor,...)

## **Clinical features and aftermath:**

Atrophy and insufficiency of exocrine and endocrine pancreas, fibrosis.

Chronic pain in the upper abdomen, weight loss, icterus

Pancreatogenic malabsorption syndrome

An increased risk of cancer (pancreatic ductal adenocarcinoma (PDAC))

# Chronic pancreatitis (CP)

**Associated with extensive architectonical and cytological alterations of pancreas**

**Destruction of acinar cells**

**Perilobular and intralobular fibrosis**

**Distortion of persistent ductal elements → morphologically looks like well-differentiated pancreatic ductal adenocarcinoma (PDAC) – diff. dg. PDAC x CP!!!**

**Reactive cytonuclear changes of epithelium**

**Dysplastic ductal lesions – pancreatic intraepithelial neoplasia (PanINs) in CP**

# Clinical diff. dg. of CP and pancreatic ductal adenocarcinoma (PDAC)

Age (PDAC is rare in younger age (<40 years))

Long-term history of clinical problems of patient with CP

Chronic alcoholic, hereditary and so-called paroduodenal pancreatitis → development on the bases of recurrent acute pancreatitis; formation of pseudocyst

Icterus

- CP - usually after years of progressive CP
- PDAC - sudden manifestation of icterus

PDAC: disease of older adults (>50 years), without history of CP or alcoholism

\* Different in autoimmune pancreatitis!

# Gross description (CP in surgical material)

**Unevenly distributed fibrosis with foci of fibrotization and lobular parenchyma in CP (alcoholic and hereditary)**

**Consistency is more elastic in CP, impairment of pancreas is more diffuse**

**Pseudocyst in CP**

**Calcificated mucoprotein plugs in CP**

**Progression of stenosis of major pancreatic duct in CP**

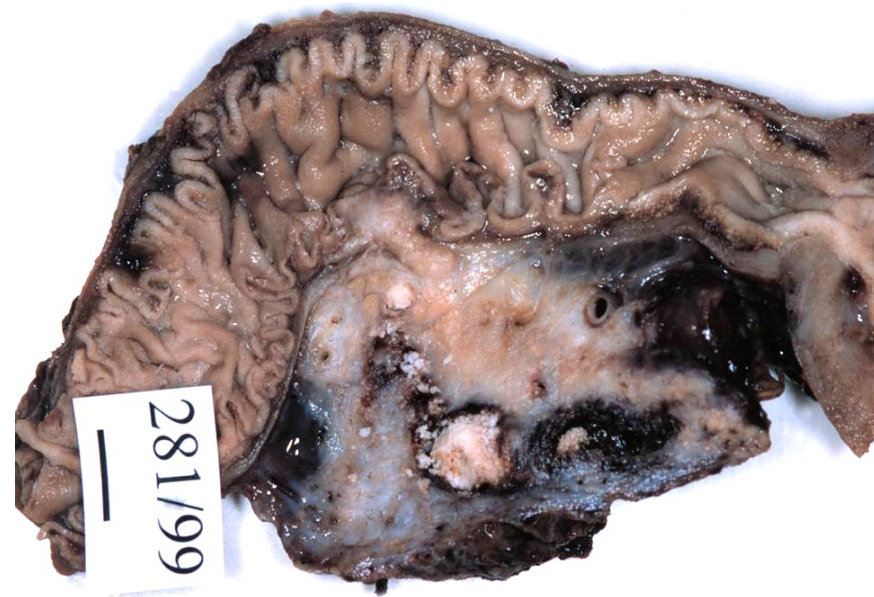
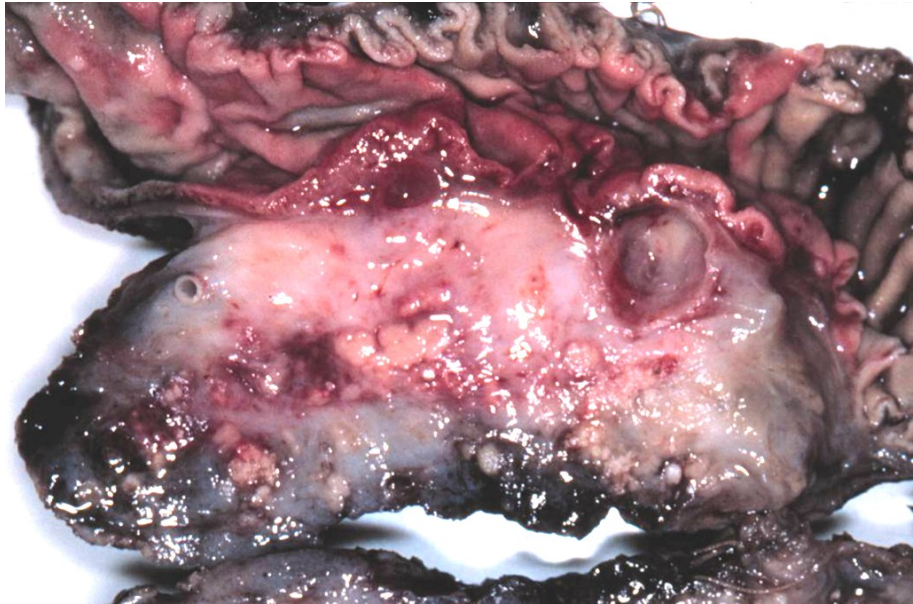
**Paraduodenal pancreatitis**

(inflammatory, fibrous and cystic changes in loci of predilection)

**Autoimmune pancreatitis**

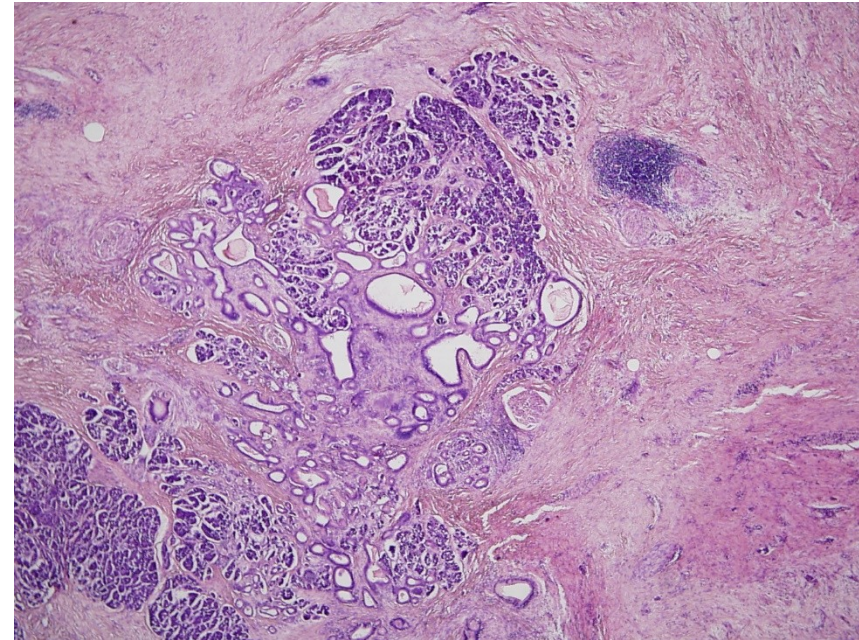
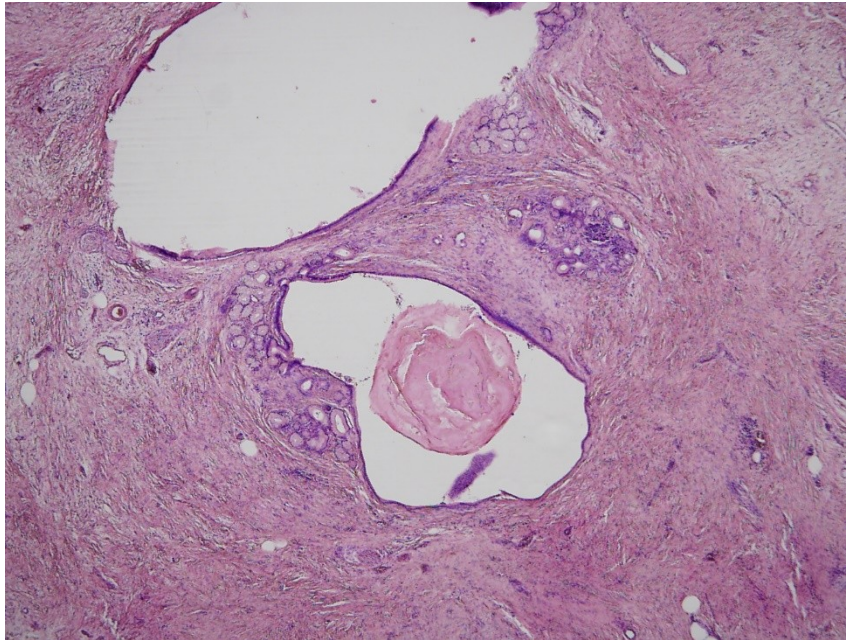
(grossly looks like PDAC, predominantly in pancreatic head, diffuse impairment, stenosis of the major pancreatic duct and damage of extrahepatic bile ducts)

# Alcoholic chronic pancreatitis in resection specimen



# Alcoholic chronic pancreatitis

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# Hereditary pancreatitis

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**Mutations in genes encoding pancreatic enzymes or their inhibitors → increased autoactivation of trypsinogen or resistance to inactivation → autodigestion of pancreatic tissue, recurrent pancreatitis**

*PRSS1* (cationic trypsinogen gene), AD

*SPINK1* (serum protease inhibitor), AR

Fibrosis - perilobular, periductal, sometimes intralobular; diffuse X focal

Dilatation of ducts, inspissation of luminal mucus, calcification (similarity with ACP), hyperplasia, metaplasia and dysplasia of ductal epithelium.

**50-70x increased risk of development of pancreatic carcinoma (vs 2-5x increased risk in sporadic CP)**



# Autoimmune pancreatitis

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## 2 clinicopathologic subtypes of autoimmune pancreatitis:

- **lymphoplasmacytic sclerosing pancreatitis (LPSP, type 1)**
  - often associated with other IgG4-related sclerosing lesions
- **idiopathic ductocentric pancreatitis (IDCP, type 2)**
  - also known as AIP with granulocytic epithelial lesion
  - usually occurs solitary
    - rarely associated with ulcerative colitis
  - dense periductal inflammation with neutrophilic infiltration and destruction of ductal epithelium
  - absence or low IgG4+ plasmocyte count

	<b>LPSP (AIP w/o GEL)</b>	<b>IDCP (AIP with GEL)</b>	<b>Alcoholic CP</b>
<b>Infiltration</b>	Lymphoplasmacytic + eosinophilic + neutrophilic	Lymphoplasmacytic + neutrophilic (ducts, acinar cells)	Few chronic inflammatory cells
<b>Ducts</b>	Dense periductal infiltration w/o destruction	Dense periductal infiltration + GEL	Distortion of ducts, dilatation, w/o infiltration
<b>Mucoprotein plugs and Ca</b>	No	No	Often
<b>Lobuli</b>	Infiltration of acinar cells with destruction	Focal infiltration with neutrophils	Focal lobular atrophy and fibrosis
<b>Veins</b>	Phlebitis obliterans	Rarely phlebitis obliterans	W/o phlebitis obliterans
<b>Arteries</b>	Rarely intensive arterial impairment	Usually w/o arterial impairment	W/o arterial impairment
<b>Pseudocysts</b>	No	No	Yes
<b>Involvement of peripancreatic adipose tissue</b>	Common	Minimal, inflammation restricted to pancreatic tissue	Loci of necrosis
<b>IgG4 IHC</b>	>10 IgG4+ plasmocytes/HPF	few or none IgG4+ plasmocytes	few or none IgG4+ plasmocytes
<b>Clinical features</b>	M > F IgG4 sclerosing lesions	M=F, younger AIP+UC	

# Clinical features of AIP

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Obstructive icterus

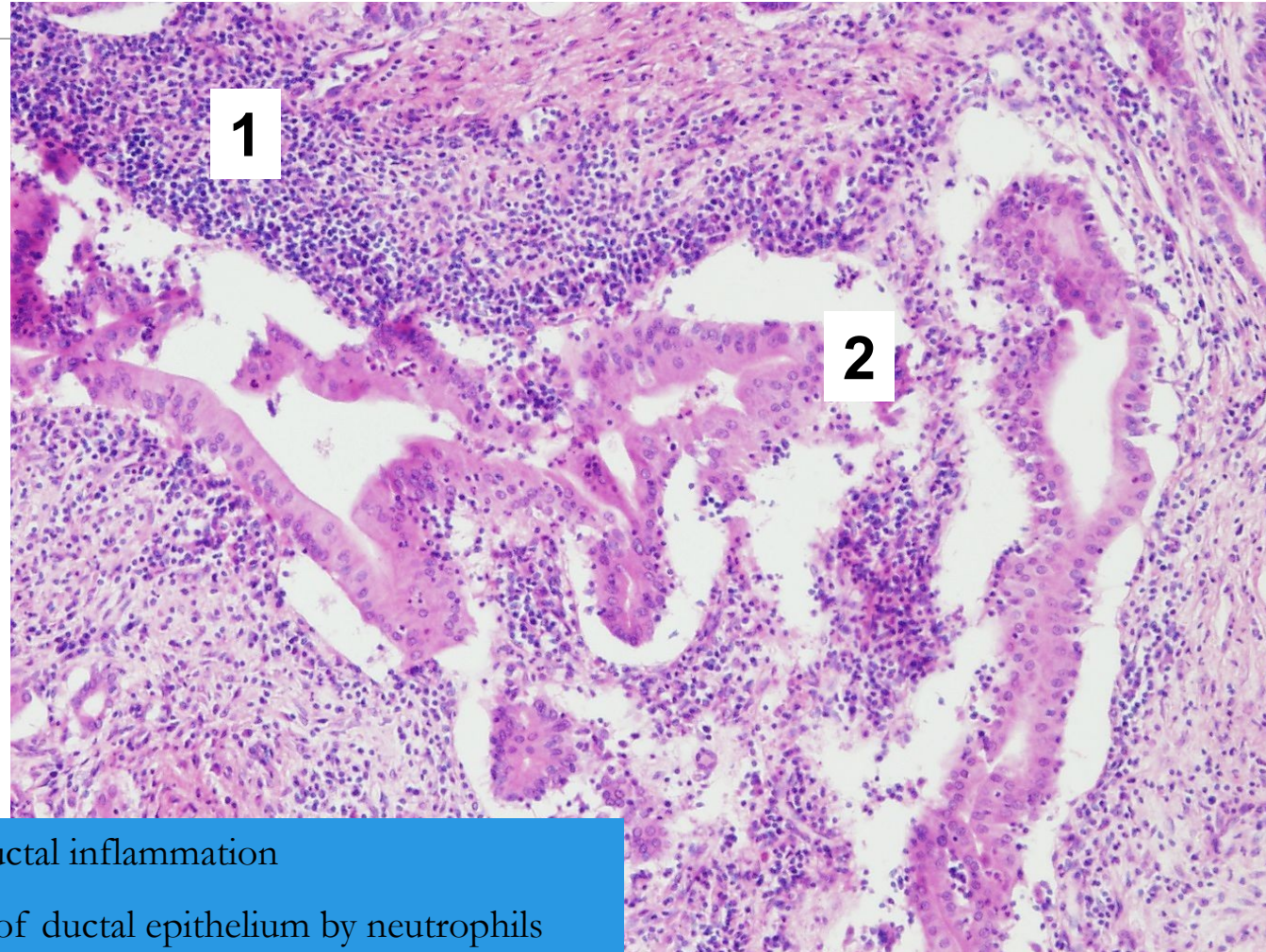
Abdominal pain

Imaging methods – diffuse/focal enlargement of pancreas

ERCP – diffuse irregular major pancreatic duct with stenosis and stenosis of ductus choledochus

Responds to steroid therapy

## Autoimmune pancreatitis (IDCP, type 2)



1. Dense periductal inflammation
2. Destruction of ductal epithelium by neutrophils

# IgG4-related sclerosing lesions

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## Autoimmune pancreatitis

Sclerosing cholangitis

Lymphoplasmacytic sclerosing cholecystitis

Sclerosing sialadenitis (Küttner tumor)

Idiopathic retroperitoneal fibrosis (M. Ormond)

Inflammatory pseudotumor of liver, lungs and pituitary gland

IgG4-related tubulointerstitial nephritis

IgG4-related interstitial pneumonia

Sclerosing prostatitis

Sclerosing thyroiditis

Hypophysitis

Pachymeningitis

Sclerosing dacryoadenitis (Mikulicz disease).....

- M>F; respond to steroid therapy, lymphadenopathy; mimic neoplastic lesions

- sclerosing lesions with diffuse lymphoplasmacytic infiltration, irregular fibrotisation

- may be present: eosinophils, phlebitis obliterans, dense infiltration of IgG4+ plasmacytes

- increased risk of development of malignant lymphoma

# Obstructive pancreatitis

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diffuse perilobular and intralobular fibrosis

dilatation of ducts w/o obstruction, irregularity or signs of destruction of ductal epithelium

w/o signs of inspissation of luminal mucus and calcifications in ducts

hyperplasia of ductal epithelium

necrosis and pseudocysts not present

# Paraduodenal pancreatitis

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Also known as: cystic dystrophy of heterotopic pancreas (the residue of the dorsal part of pancreas in duodenal wall), periampullary duodenal wall cyst, „groove“ pancreatitis, pancreatic hamartoma of duodenal wall,...

Alcohol consumption

Clinical features associated with duodenal stenosis, loss of weight, icterus in 20 % of cases

Changes in region of **minor duodenal papilla** (obstruction, pancreas divisum) + impairment of pancreatic head + paraduodenal cystic changes (between the duodenal wall and the pancreas)

Prolong inflammation in submucosa and wall of the duodenum and the adjacent pancreas, foci of necrosis, myofibroblast proliferation, pseudocystic lesions, granulation tissue, granulomatous response, Brunner gland hyperplasia

# „Idiopathic chronic pancreatitis“

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3-9 % of all case of CP

Mutation in *CFTR* gene

(cystic fibrosis transmembrane conductance regulator gene)

Mutation v *SPINK1* gene

(PSTI – pancreatic secretory trypsin inhibitor)

+ external factors (smoking, alcohol)

Dysfunction of sphincter of Oddi

Pancreas divisum



# Cysts of pancreas

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## Congenital cysts

- unilocular
- multilocular (AD polycystic disease (cysts of kidney, liver, pancreas), syndrome von Hippel-Lindau)
- (dermoid (mature teratoma))

## Benign lymphoepithelial cyst

**Mucinous non-neoplastic cyst** (v.s. mucinous cystic neoplasm (MCN)??)

**Periampullary duodenal wall cyst** (in heterotopic pancreas)

**Enterogenous cyst**

**Retention cyst**

**Endometrial cyst - endometriosis**

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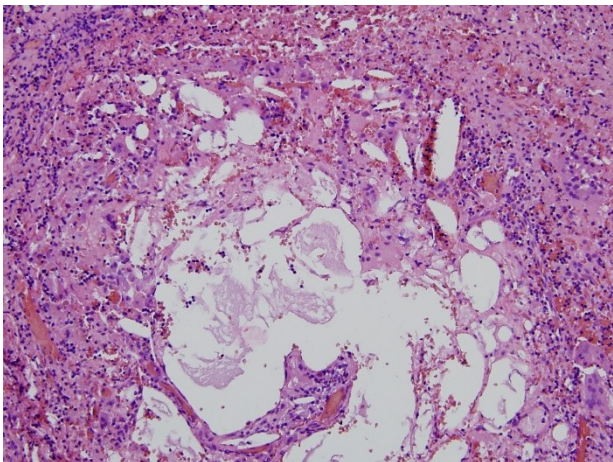
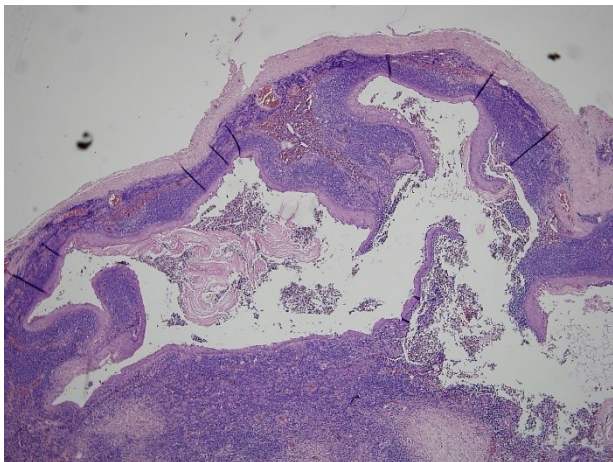
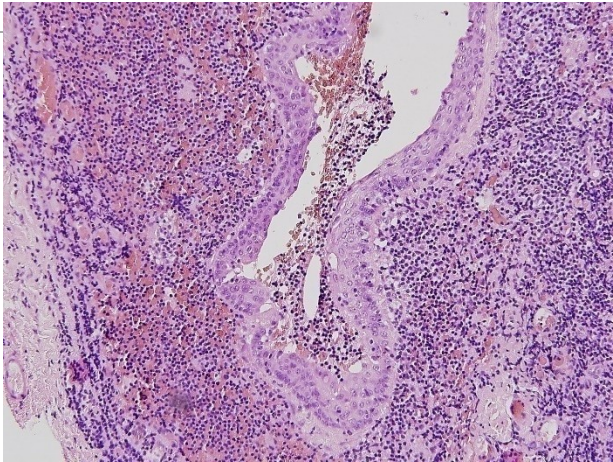
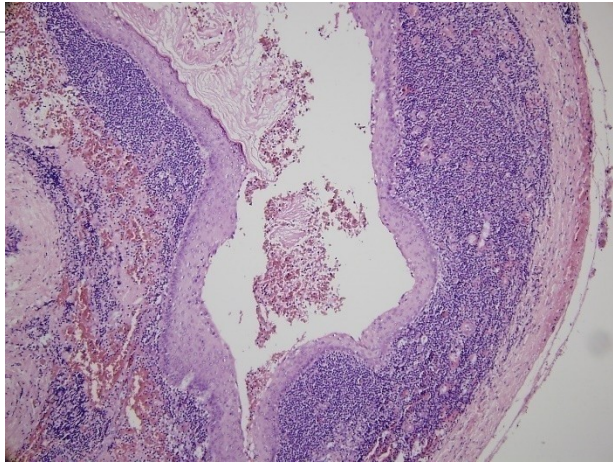
## Parasitic cysts (*Ecchinococcus granulosus*)

### Pseudocysts

- associated with pancreatitis
- the result of trauma

### -Abscesses

# Benign lymphoepithelial cyst of pancreas



# Pancreatic tumors

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**Epithelial**

Non-epithelial

Secondary (metastatic) tumors

Type of neoplasm	Incidence	Location	Features
<b>Ductal adenocarcinoma (PDAC)</b>	<b>85-90 %</b>	<b>H&gt;T</b>	<b>solid, poorly defined masses, desmoplastic stroma</b> <b>Highly aggressive</b>
<b>Intraductal papillary-mucinous carcinoma</b>	3-5 %	H>T	Cystic, intraductal, progression into carcinoma
<b>Neuroendocrine neoplasia (NEN)/ Tumors of the endocrine pancreas</b>	1-2 %	H=T	Solid, pseudocystic*, different degrees of malignancy, see classification of NEN GIT; hormonally active
<b>Mucinous cystic neoplasm</b>	1-2 %	T>>H	Cystic, absence of communication with ducts, , progression into carcinoma, female predominance
<b>Serous cystic neoplasm</b>	1-2 %	H=T	Cystic, absence of communication with ducts, benign
<b>Acinar cell carcinoma</b>	1-2 %	H=T	Solid, pseudocystic*, aggressive
<b>Solid pseudopapillary neoplasm</b>	1-2 %	H=T	Solid, pseudocystic*, young women, low malignant potential
<b>Pancreatoblastoma</b>	<1 %	H=T	Solid, in children, malignant

H - head; T - tail; \* often with pseudocystic degeneration

## **Risk factors**

### **Exogenous risk factors**

**Age**

**Smoking**

**Alcohol\***

**Diet (especially high-fat), obesity**

**Exposition to organic substances or radiation**

### **Endogenous risk factors**

**Familial occurrence**

**Hereditary syndromes**

**Chronic pancreatitis**

**Diabetes mellitus**

\* Indirect impact by induced chronic pancreatitis

# Genetic syndromes associated with PDAC

Syndrome	Type of inheritance	Gene
Lynch sy (hereditary nonpolyposis colorectal cancer)	AD	<i>MSH2, MLH1,...</i>
Familial breast cancer; genes of Fanconi anemia	AD	<i>BRCA2, PALB2, FANCC, PANCG, (BRCA1)</i>
Familial pancreatic cancer	AD	Unknown
Familial Atypical Multiple Mole Melanoma syndrome (FAMMM)	AD	<i>CDKN2A</i> (p16)
Hereditary pancreatitis	AD ( <i>PRSS1</i> ) AR ( <i>SPINK1</i> )	<i>PRSS1</i> <i>SPINK1</i>
Peutz-Jeghers sy	AD	<i>STK11</i>

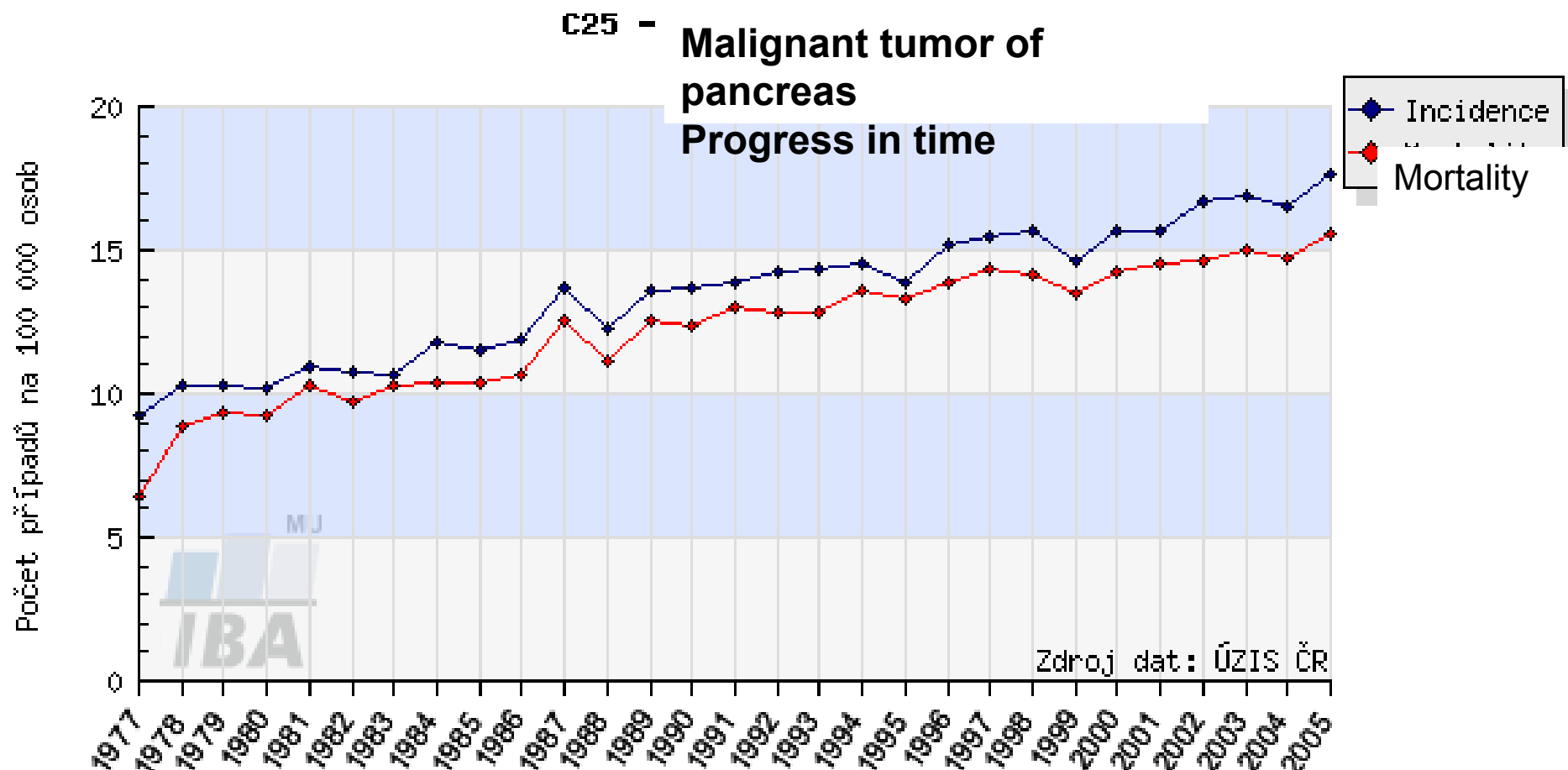
# Features of PDAC

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- 85-90% of all pancreatic neoplasms
- very poor prognosis, the five-year relative survival rate is about 5 %, mortality almost equals to incidence
- incidence is increasing, the highest incidence of pancreatic cancer in Czech republic
- 5th leading cause of cancer related death in Western countries (2nd among GIT malignancies)
- causes of this unfavorable state:
  - absence of effective screening
  - diagnosis often made in advanced stage of the disease due to lack of symptoms
  - molecular-biologic characteristics of PDAC
- radical resection – favourably increases survival rate of patients; at time of diagnosis only 10-15 % patients with PDAC meet criteria for resection; 70 % of patients are presented with metastases in regional lymph nodes. Despite radical resection, recurrence of PDAC in about 90 % of patients within two years after surgery.



# Pancreatic cancer



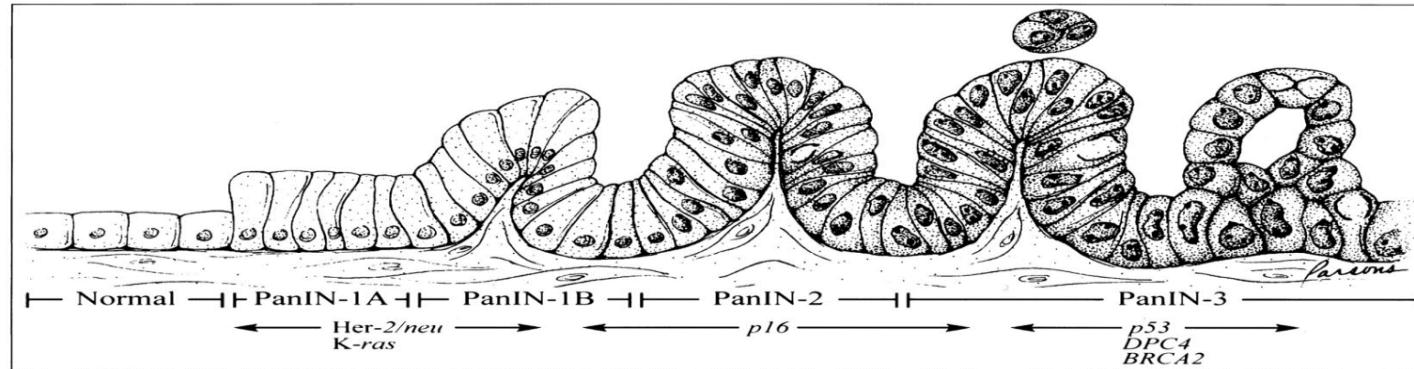
Analyzovaná data: N(inc)=40309, N(mor)=36479

<http://www.svod.cz>

source: NOR ČR

# Precursor lesions of pancreatic cancer

## Pancreatic intraepithelial neoplasms (PanIN) – precursor of PDAC



## Mucinous cystic neoplasms (MCN)

## Intraductal papillary-mucinous neoplasms (IPMN)

- multistage process of histologic and genetic progress into invasive cancer
- different clinico-pathological and genetic features

# Pancreatic cancer

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Disease induced by germline or acquired mutations of germ or somatic cells

Multiple alterations of numerous genes responsible for progression of pancreatic cancer

Knowledge of molecular basis of the disease – revelation of effective marker for early diagnosis + potential target for therapy

Precursor lesions: helpful tool for study of molecular basis of pancreatic cancer

Potentially successful therapeutic strategy: combination of drugs targeted for pancreatic tumor stem cells and their microenvironment and conventional chemotherapeutic agents ???

# Microenvironment of pancreatic cancer – role of fibrogenesis in pancreatic cancer

**Tumor stroma – integral component of cancerogenesis; provides communication between tumor and stroma cells**

**Role of activated pancreatic stellate cells (stromal cells with similar behaviour as myofibroblasts):**

- Production of extracellular matrix proteins and matrix metalloproteinases (MMPs)
- Source of cytokines and growth factors
- Effect on tumor and other cells favouring tumor progression and fibrosis

**Role of proteases produced by stromal cells in DM and ↓BMI**

- Biopeptides of glucose homeostasis (+ neuropeptide Y, peptide YY, proline) substrates of these proteases
- Fusion products ↓active/inactive → induction of diabetes associated with pancreatic cancer and loss of body weight (↓BMI)

**Stimulation of pancreatic cancer progression by mediators derived from stromal cells**

- Induction of cell proliferation
- Inhibition of apoptosis
- Chemoresistance
- Invasive growth

**Evolution of therapy targeted on pancreatic stellate cells**

# Signs of PDAC

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**Mostly located in the head of pancreas (2/3)**

**Abdominal pain, loss of weight, suddenly emerged painless icterus, pruritus**

**Thrombophlebitis migrans**

**Signs caused by metastases or by affected surrounding organs**

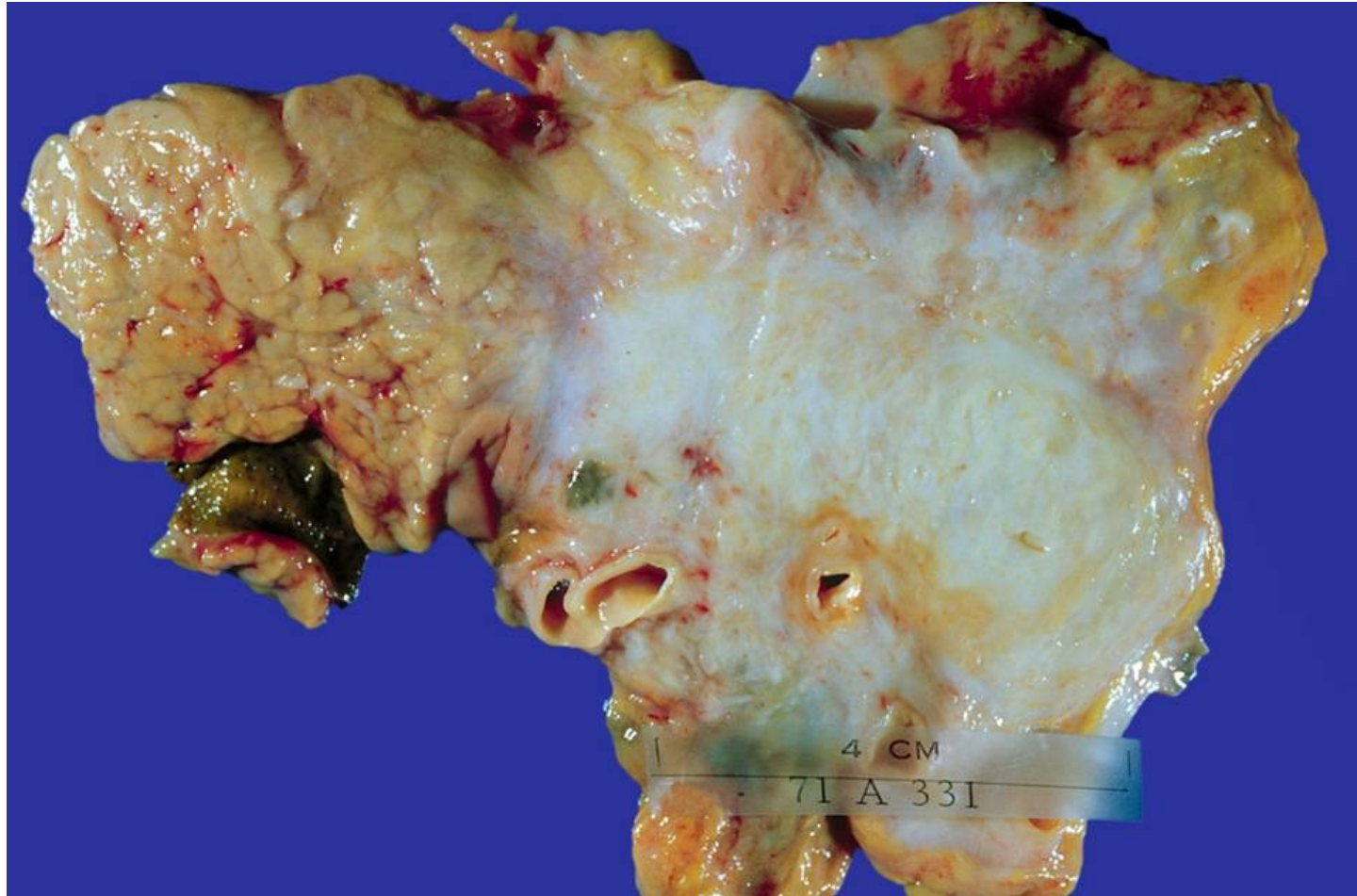
**Oncomarkers (CA 19-9, CEA,...non-specific)**

**DM associated with PDAC (atypical)**

- suddenly in advanced age
- absence of obesity, rapid progression requiring insulin therapy
- recurrence of infections including mycotic
- disbalance of homeostasis with repeated hyperglycemia and tendency towards ketoacidosis and kachexia

# Ductal adenocarcinoma (head of the pancreas)

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# PDAC dissemination

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Lymphatic metastases in regional lymph nodes

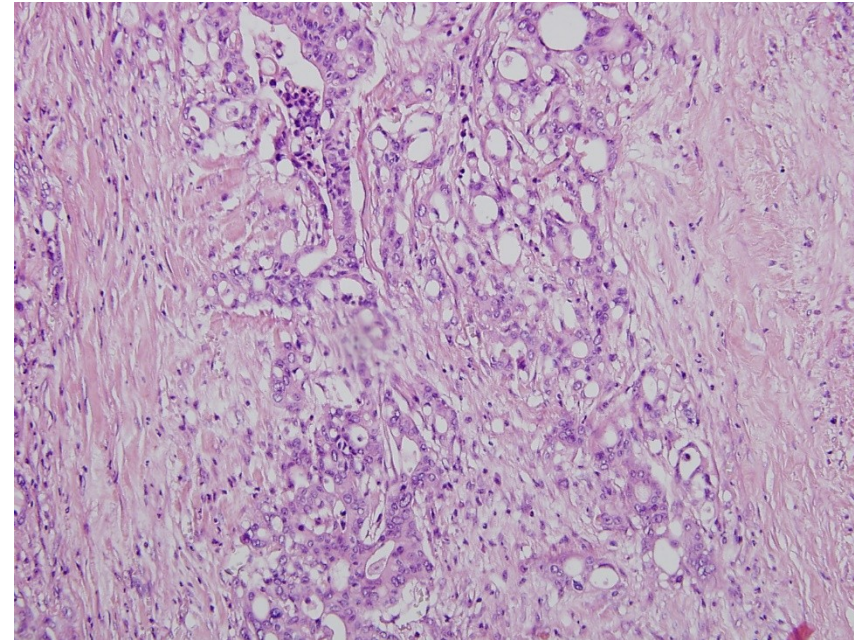
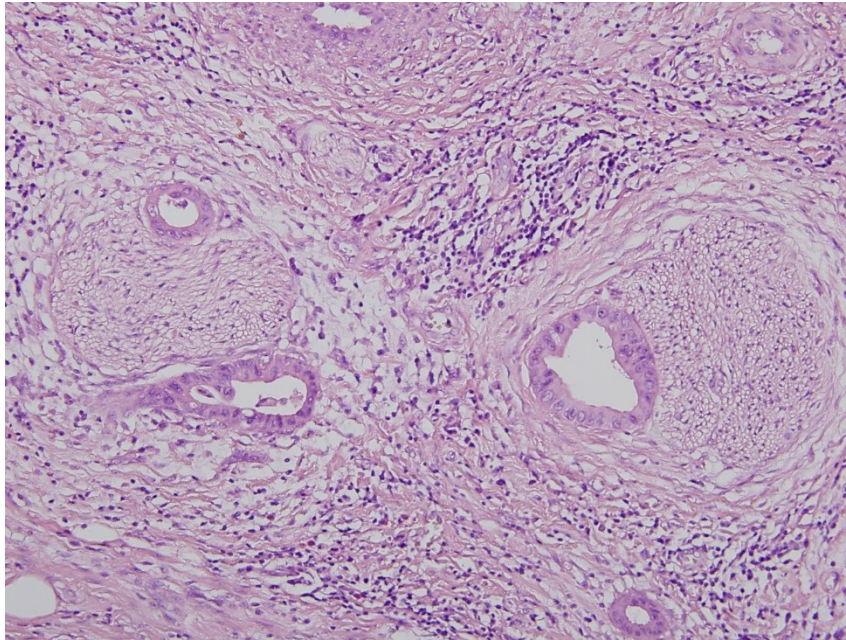
Hematogenous metastases in liver, lungs, bones

Peritoneal carcinomatosis

Perineural invasion

# Ductal adenocarcinoma and perineural invasion

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# Pancreatic Cystic Neoplasms

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## **Mucinous cystic tumors**

Mucinous cystic neoplasm (MCN)

Intraductal papillary-mucinous neoplasm (IPMN)

*Benign, however can progress into carcinoma.*

## **Serous cystic tumors**

*Almost always benign; some might be associated with Von Hippel-Lindau disease.*

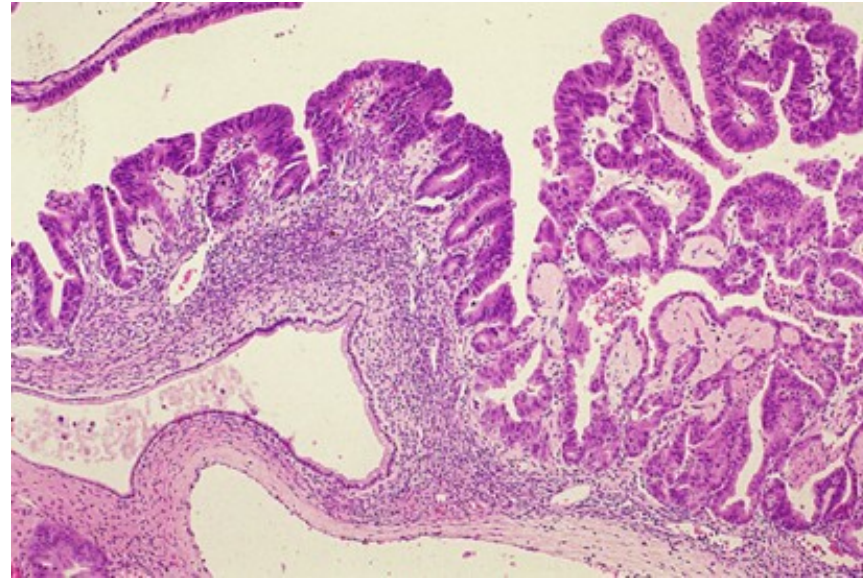
# Mucinous cystic neoplasms (MCN)

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Unilocular or multilocular, no communication with ducts, columnar mucin-producing epithelium supported by ovarian like stroma

90 % in women (5th - 6th decades); body-tale localisation

- Noninvasive  
(excellent prognosis)
- Invasive (60 % five-yers survival rate)



- **Genetic alteration in progression of MCN:**

- Early mutation of oncogene *KRAS*
- Inactivation of TSG *TP53* and *DPC4* in invasive MC carcinomas

# Intraductal papillary mucinous neoplasms (IPMN)

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Mucin producing, growing within the main pancreatic duct or its major branches, papillary architecture

M/F = 60:40; 6th decade

75 % in the head of pancreas; 20 % body and tail + diffuse infiltration

**Precursor lesions: IPMN with mild, moderate and severe dysplasia**

**Malignant lesions: IPMN associated with invasive carcinoma**

**Four morphologic types:**

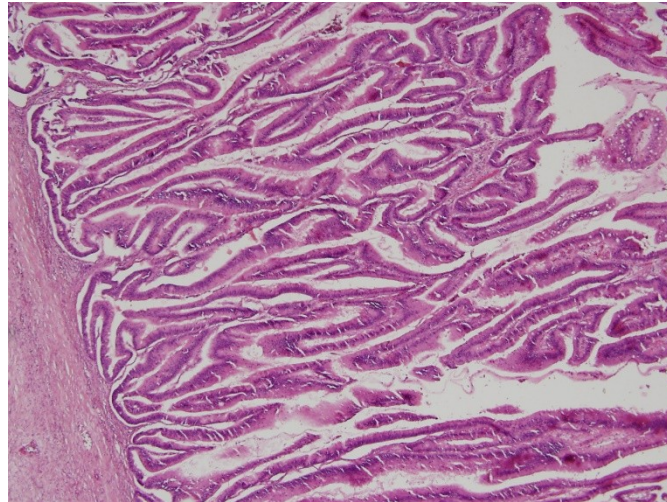
- Intestinal type (MUC2+)
- Pancreatobiliary type (MUC1+)
- Oncocytic type (MUC1+ or MUC2+)
- Gastric type (MUC5AC+; „branch duct type“)

# IPMN

Gastric type IPMN

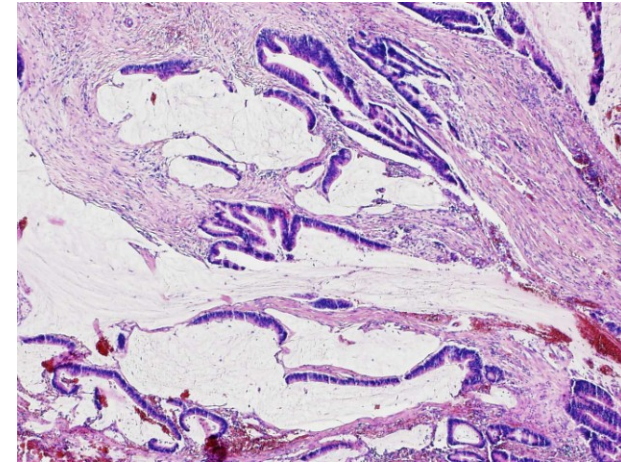
?

Intestinal type IPMN



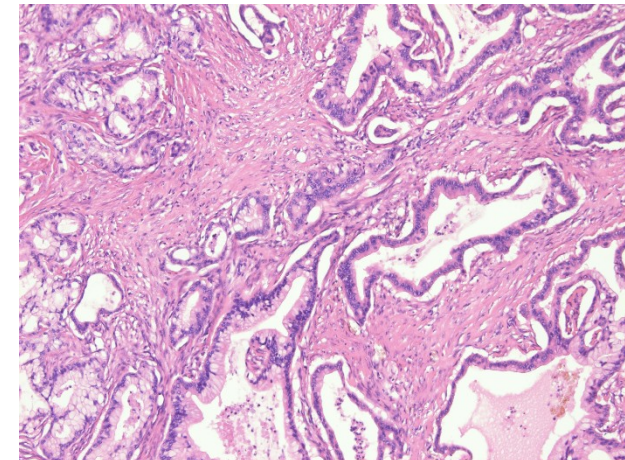
IPMN

Pancreatobiliary type IPMN



Mucinous noncystic carcinoma (2/3)  
Better prognosis

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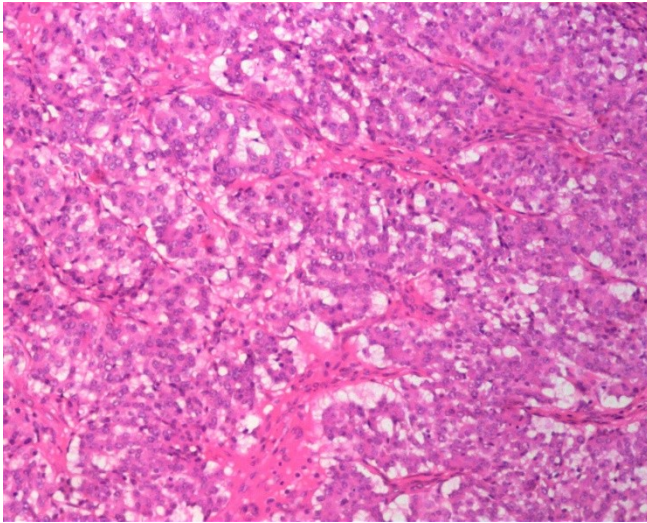


Ductal adenocarcinoma (1/3)  
Poor prognosis

## Genetic alterations in progression of IPMN:

- early mutation of *KRAS*
- late inactivation of *p16* a *TP53*
- inactivation of *DPC4* only in 10 % of IPM invasive carcinomas
- inactivation of *STK11/LKB1* in 1/3 IPMN

# Acinar cell carcinoma, trypsin+



Solid and acinar architecture

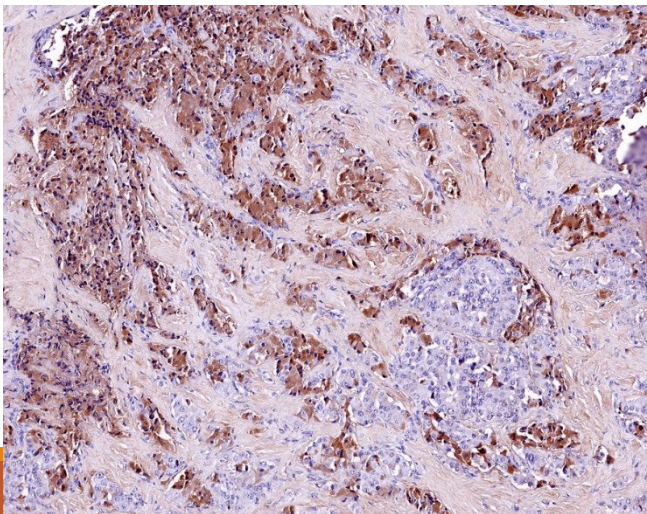
M>F; adults, rare in children

Circumscribed, multinodular, necrosis, cystic degeneration

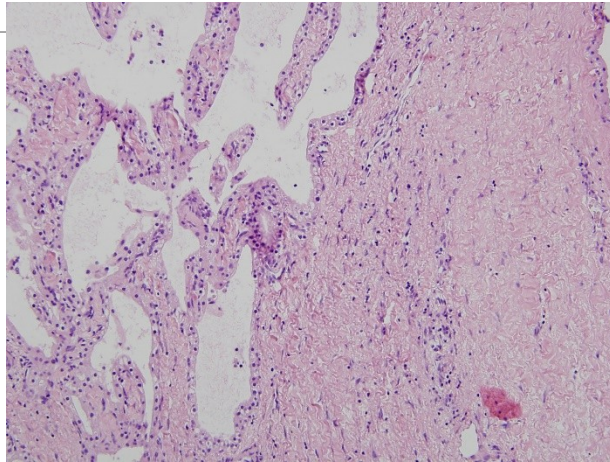
Granular eosinophilic cytoplasm – zymogen granules

Variants:

- acinar cell cystadenocarcinoma
- mixed acinar-endocrine carcinoma (30 % proportion of more than 1 cell type).



# Serous pancreatic neoplasms



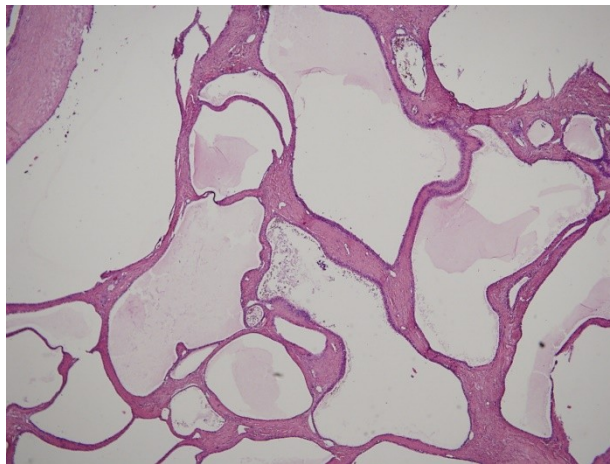
Usually cystic, lined by glycogen-rich, cuboidal type epithelial cells

## **Serous cystadenoma:**

- benign; tail, body > head; central stellate scar; microcystic

## Serous cystadenocarcinoma:

- Extremely rare



+ variants:

- Macrocytic serous cystic neoplasm
- Solid serous neoplasm
- SCN associated with Von Hippel-Lindau sy
- Mixed serous neuroendocrine neoplasm

# Solid pseudopapillary neoplasm

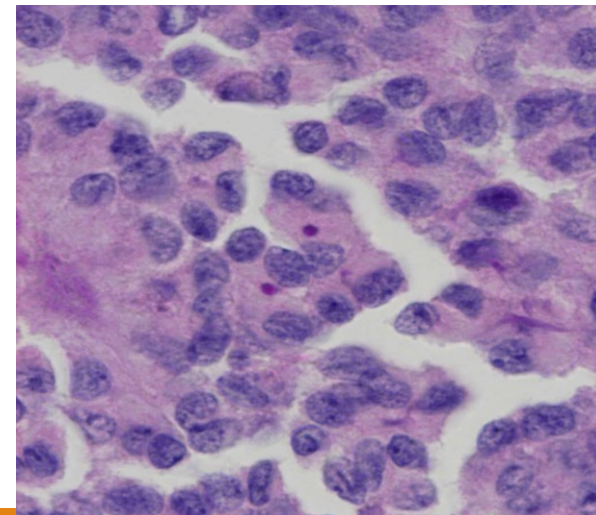
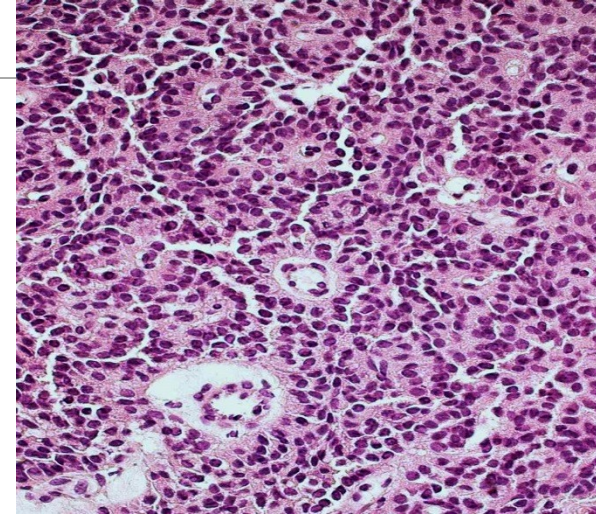
According to WHO 2010 – belongs to malignant lesions (low grade), with favourable biologic behaviour

Young women

Monomorphic cells forming solid and pseudopapillary structures; haemorrhagic-cystic changes

Variable expression of epithelial, mesenchymal and endocrine markers

85-95 % cured with surgical resection



# Pancreatic endocrine tumors

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## Functioning (hormonally active)

- insulinoma
- glucagonoma
- somatostatinoma
- gastrinoma
- VIP-producing tumor
- serotonin-producing tumor
- others – producing ectopic hormones (ACTH, calcitonin,...)

## Non-functioning (clinically asymptomatic without association with hormonal syndrome)

Note: tumors smaller than 0,5 cm – **microadenoma** – usually clinically asymptomatic



# Classification of neuroendocrine neoplasms of GIT valid even for pancreas

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## Neuroendocrine tumor - NET G1/G2/G3

well differentiated neuroendocrine tumor; low grade (G1/G2) and high grade (G3)  
(previously called carcinoids and atypical, malignant carcinoids)

## Neuroendocrine carcinoma - NEC G3

poorly differentiated neuroendocrine neoplasm  
(neuroendocrine carcinomas, high grade malignant tumors)

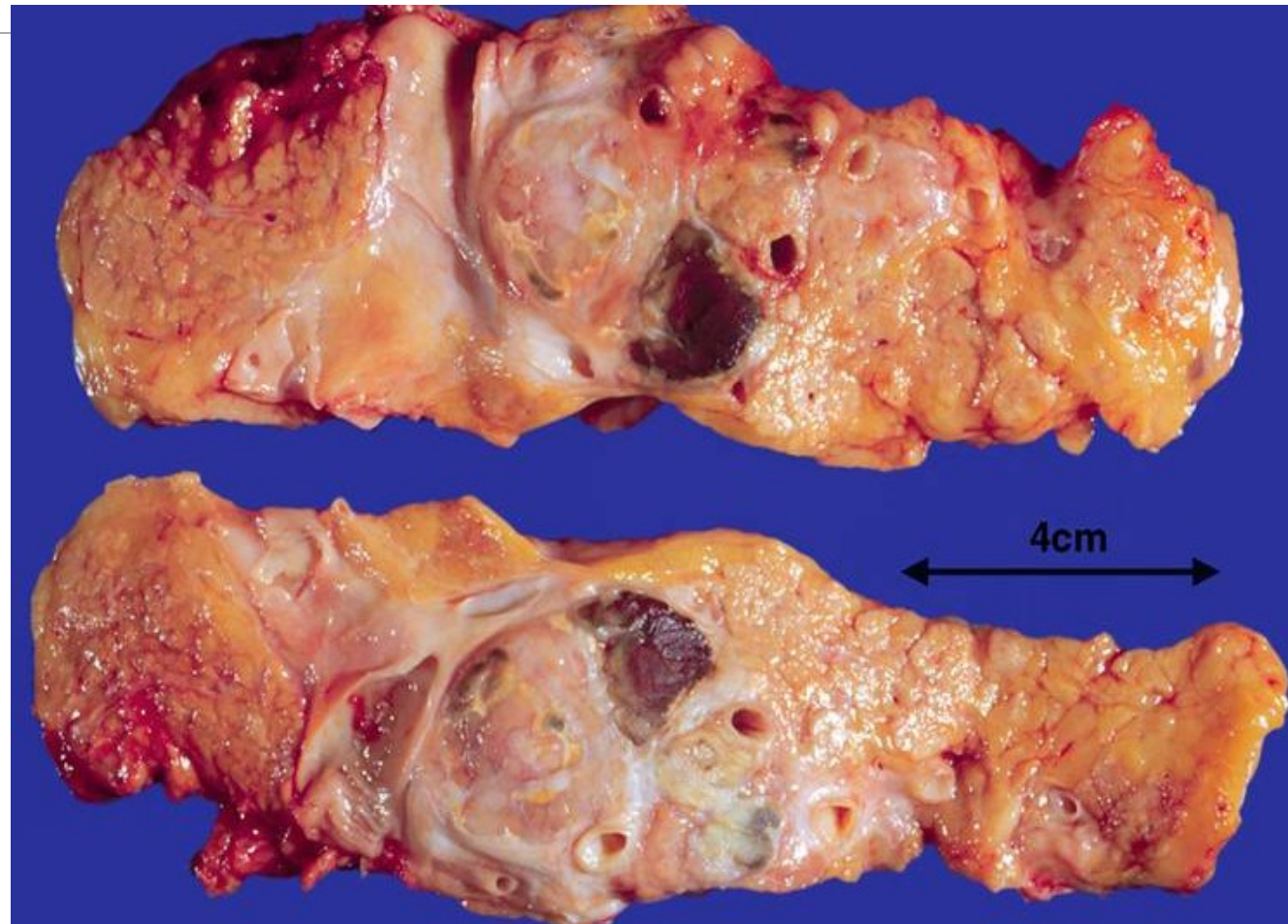
- Small cell neuroendocrine carcinoma
- Large cell neuroendocrine carcinoma

## Mixed neuroendocrine noneuroendocrine neoplasm (MiNEN)

(previously called MANEC)

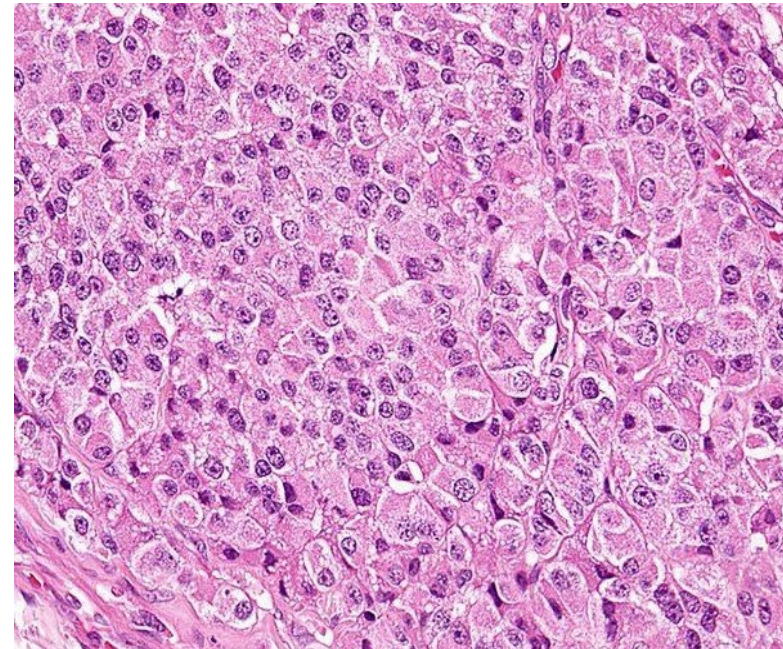
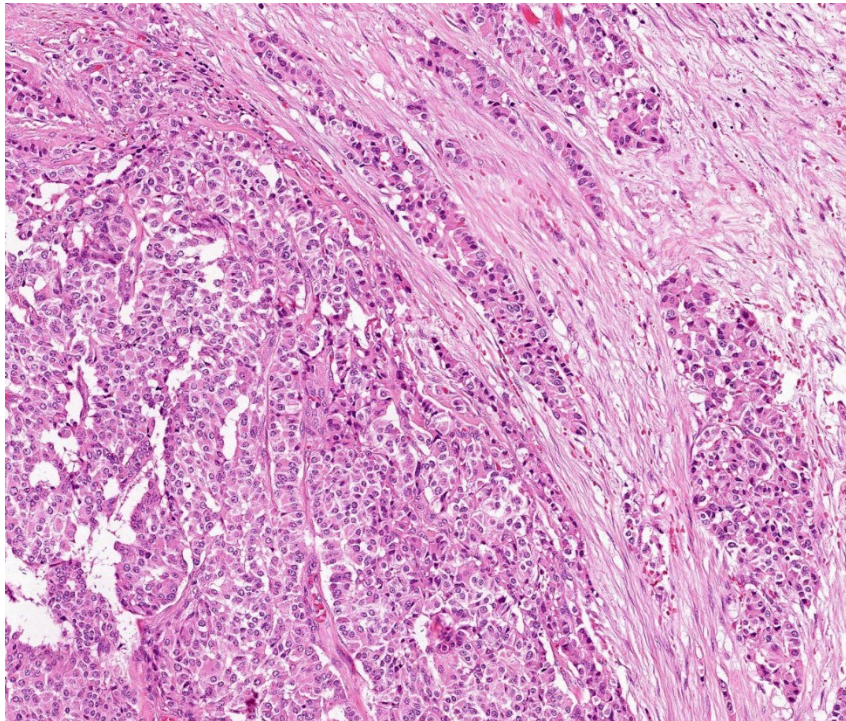
WHO 2010: NET G1/G2; NEC; MANEC)  
WHO 2017: NET G1/G2/G3; NEC; MiNEN)

# Pancreatic endocrine tumor.



# Pancreatic endocrine tumor.

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# Clinical syndromes associated with functioning neuroendocrine tumors

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1) **Insulinoma/hyperinsulinism**.....hypoglycemia

2) **Gastrinoma/Zollinger-Ellison syndrome**.....peptic ulcers in atypical localisations

3) **Glukagonoma**....diabetes, erythema migrans, anemia

4) **Somatostatinoma**...diabetes, cholelithiasis, steatorrhea, hypochlorhydria

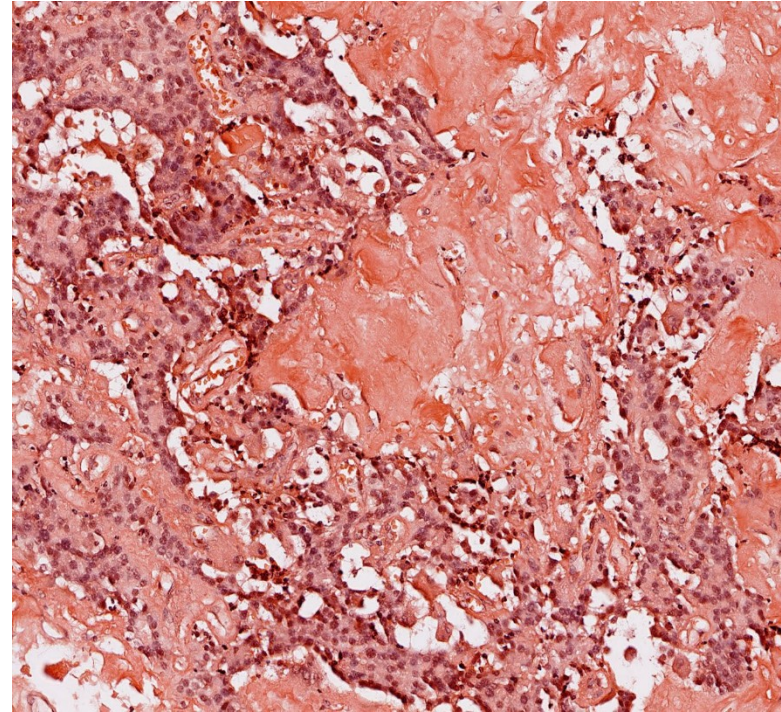
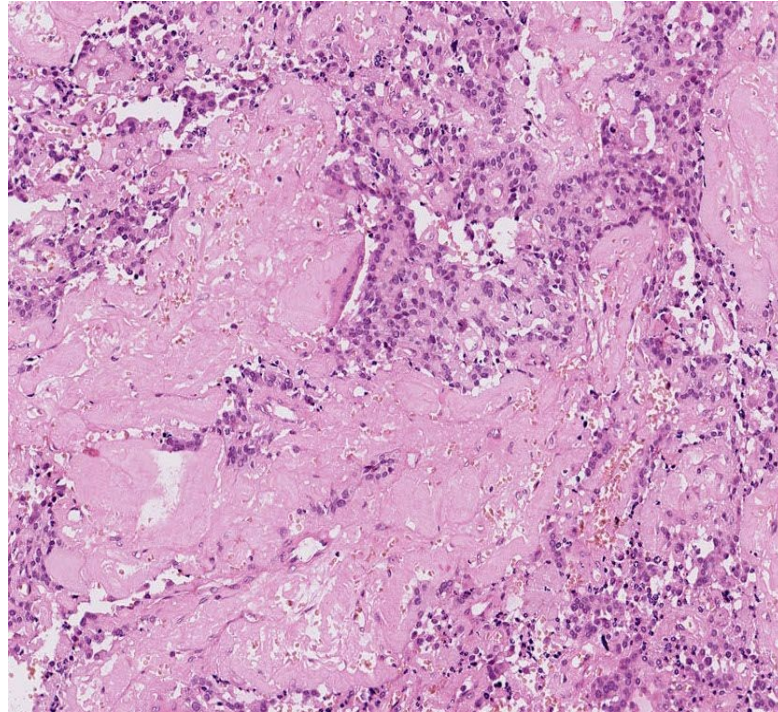
5) **VIPoma/WDHA syndrome**....(„watery diarrhoea, hypokalemia, achlorhydria)

6) **Carcinoid/carcinoid syndrome**

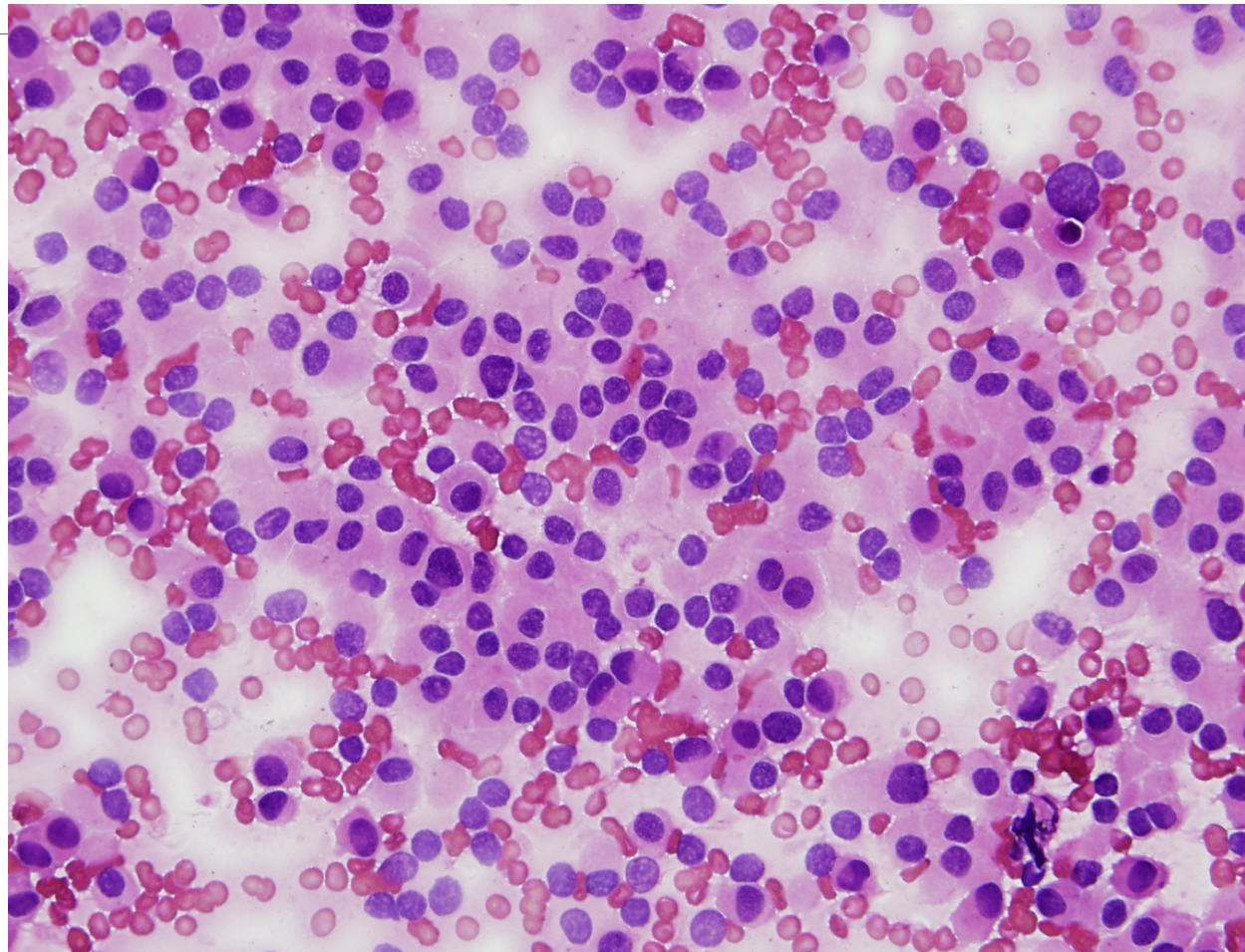
+ tumors with ectopic production of ACTH..Cushing syndrome, MSH..hyperpigmentation, ADH..diabetes insipidus

# Amyloid formation in insulinoma.

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FNAB – cytology of pancreatic endocrine tumor.



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*Thank you for your attention....*

