Pancreatitis

Prof. Dr. A. Driessen
Dept. Pathology
University Hospital Antwerp
University Antwerp

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2. Chronic pancreatitis
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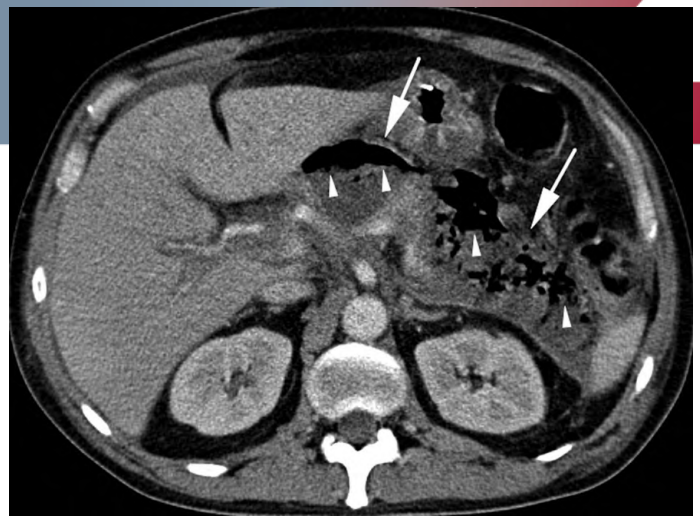
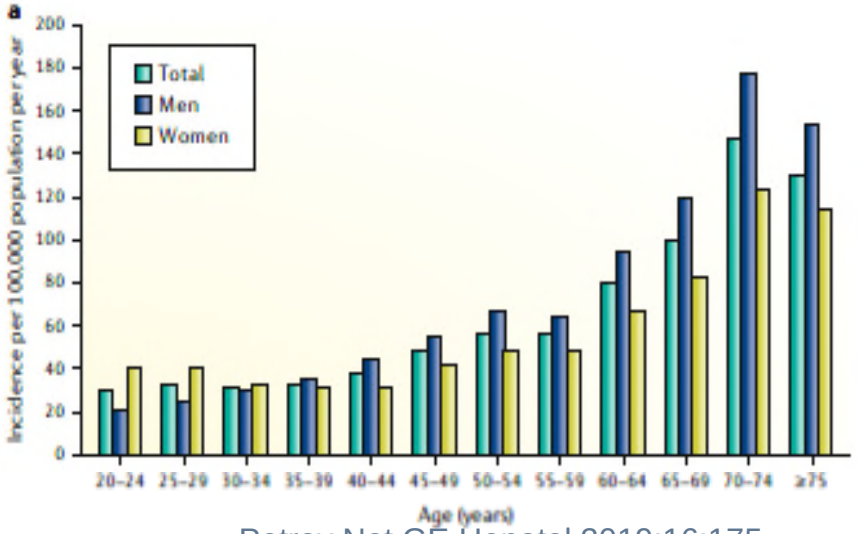
4. Groove pancreatitis

Acute pancreatitis



= Acute inflammatory and primarily sterile disorder of the pancreas (regardless its etiology), with a diverse and often unpredictable course

- Requires two of the three criteria fulfilled:
  - Abdominal pain
  - Elevation of serum amylase or lipase concentrations to ≥ 3x the upper limit of normal
  - Typical findings om imaging (US, CT)
- Most common pancreatic disease:
  - incidence 26-43/100000/yr
  - M ≥ F
  - Frequent hospital admission
  - Mortality 1,6 deaths/100000 person-yrs



Petrov Nat GE Hepatol 2019;16:175

Peter A Banks et al. Gut 2013;62:102-111

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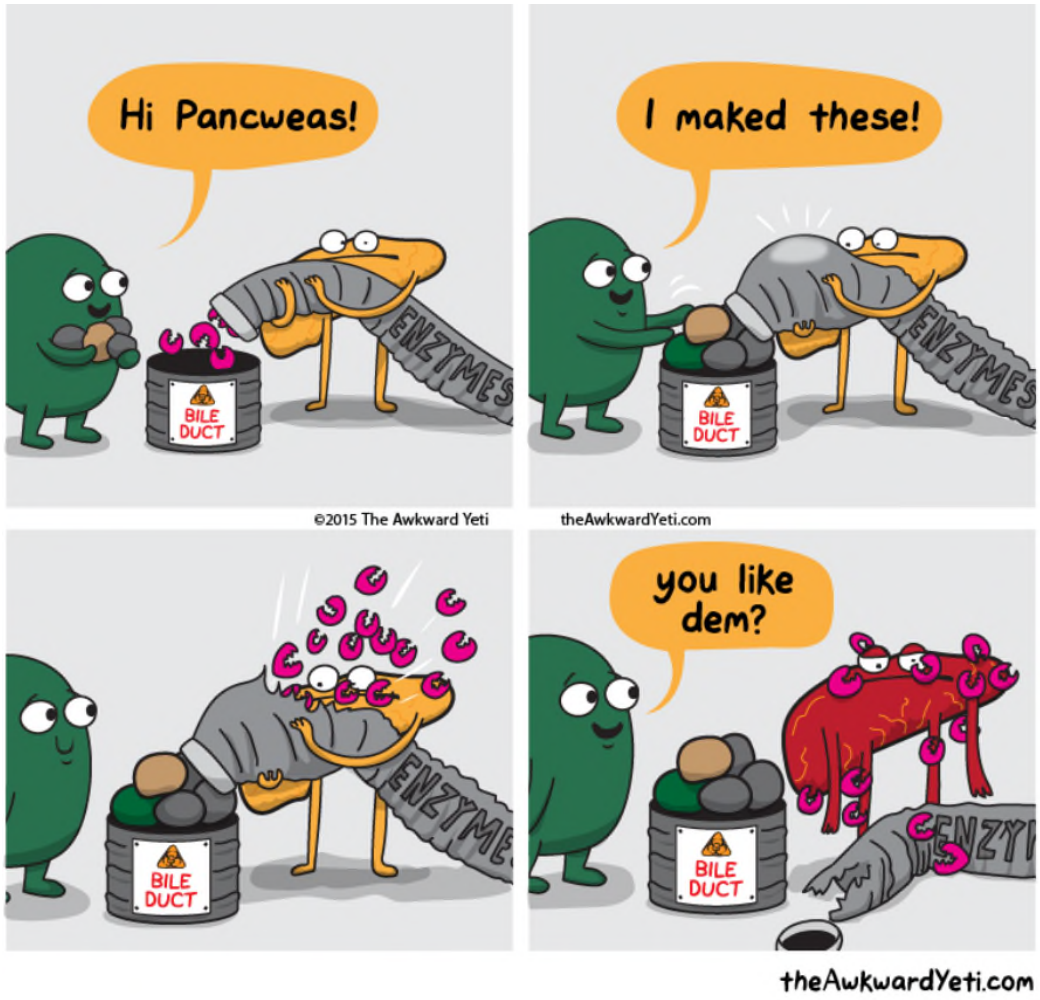
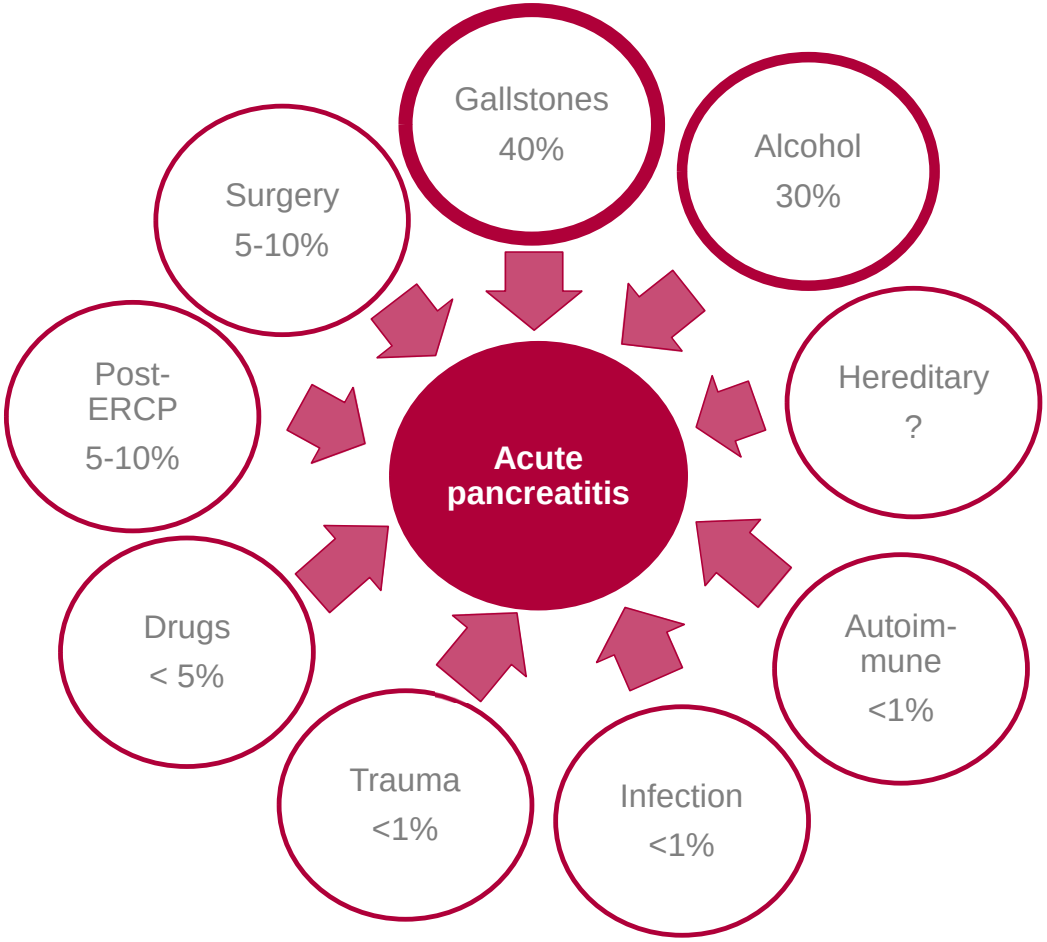
Acute pancreatitis: Etiology



Acute pancreatitis: Etiology



Idiopathic

Forsmark et al. N Engl J Med 2017

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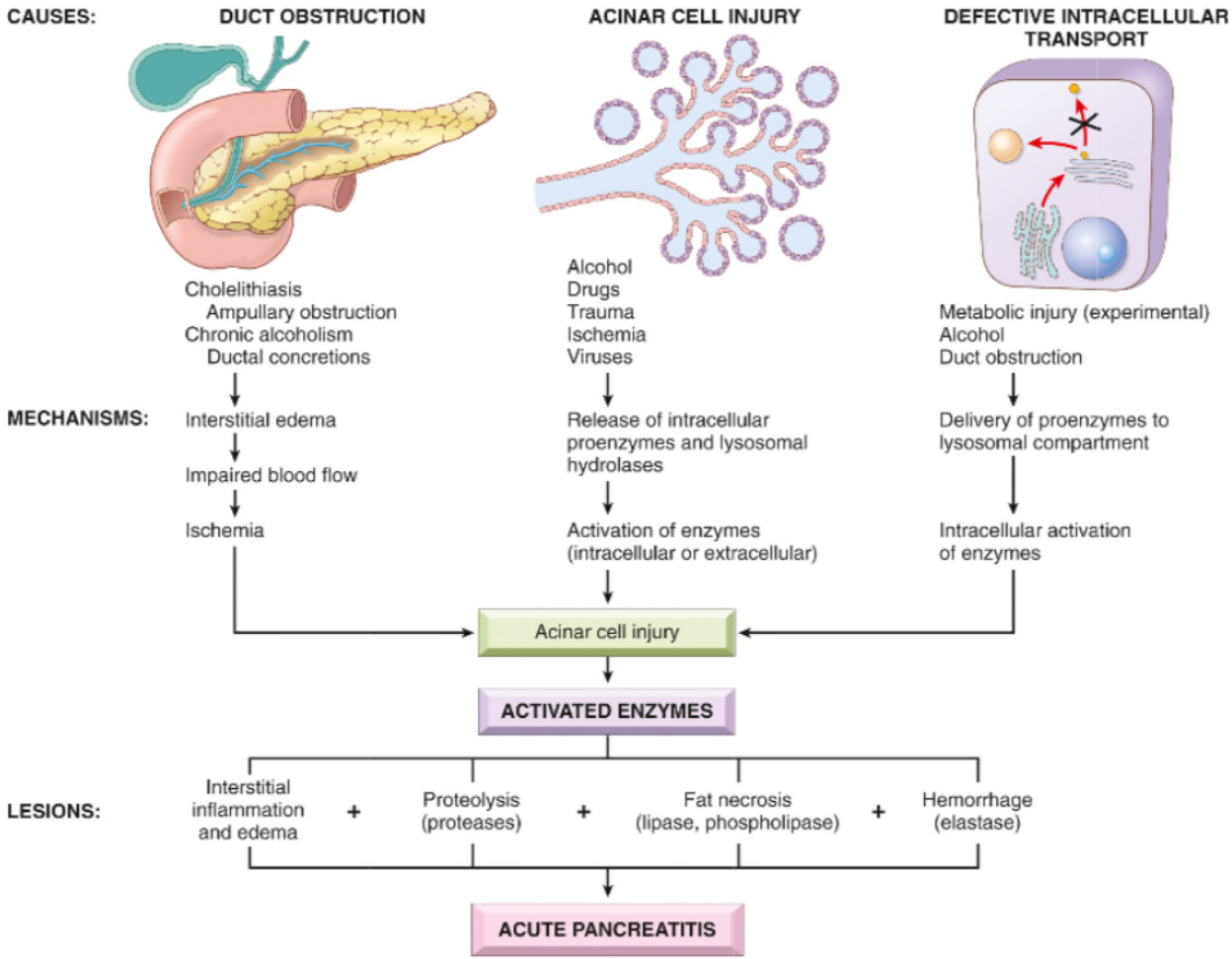
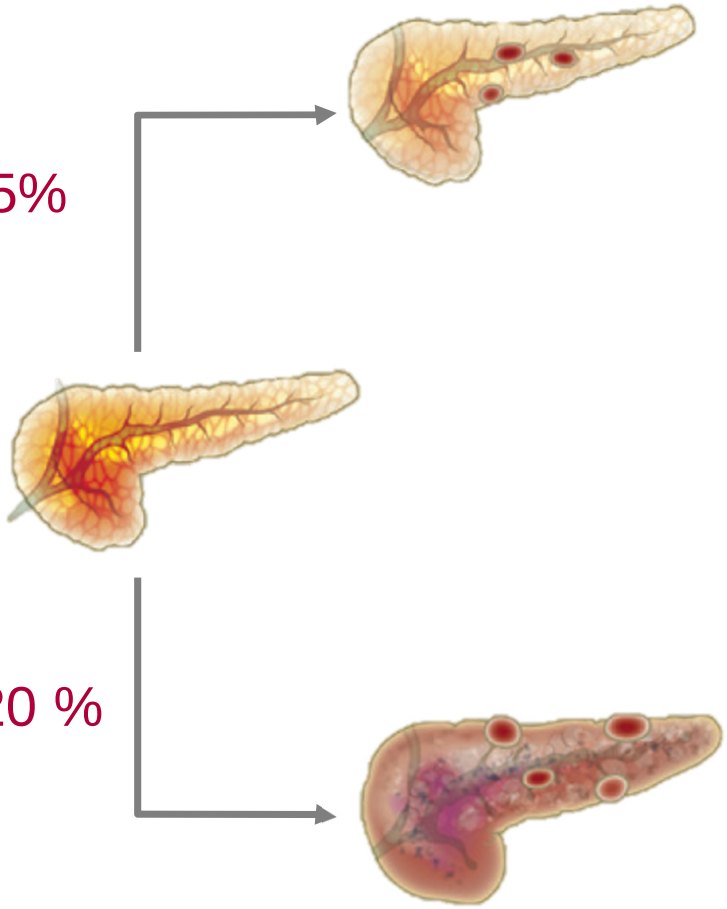
Acute pancreatitis: Pathogenesis



Robbins Pathologic basis of disease 9th Ed.

Acute pancreatitis: Histopathology



80-85%

Interstitial pancreatitis

Acute pancreatitis

15-20 %

Necrotizing pancreatitis

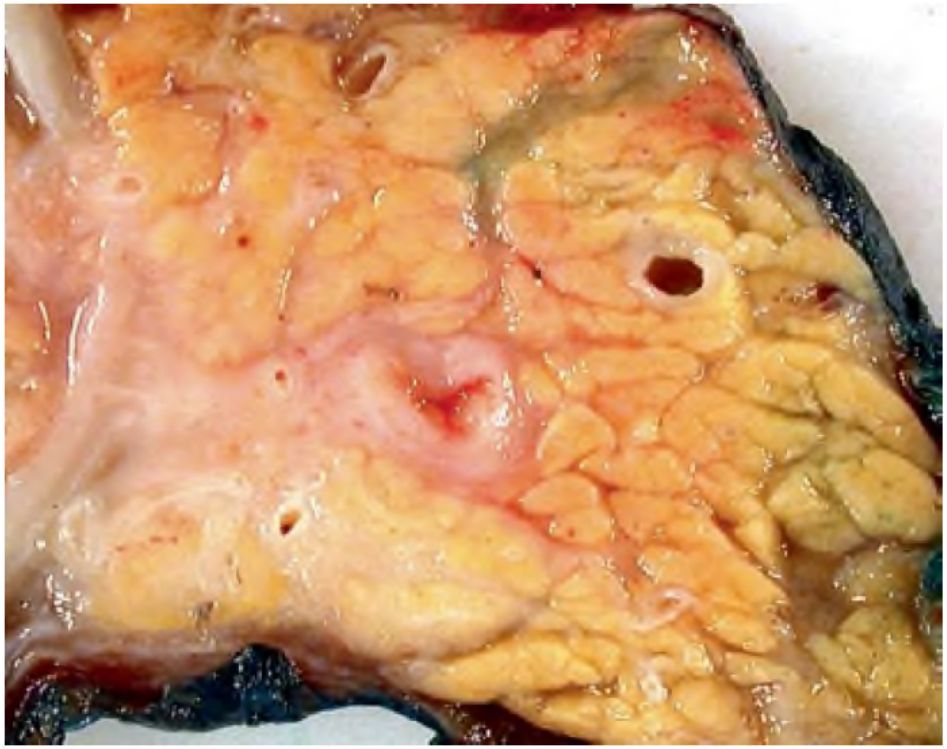
Forsmark et al. N Engl J Med 2017

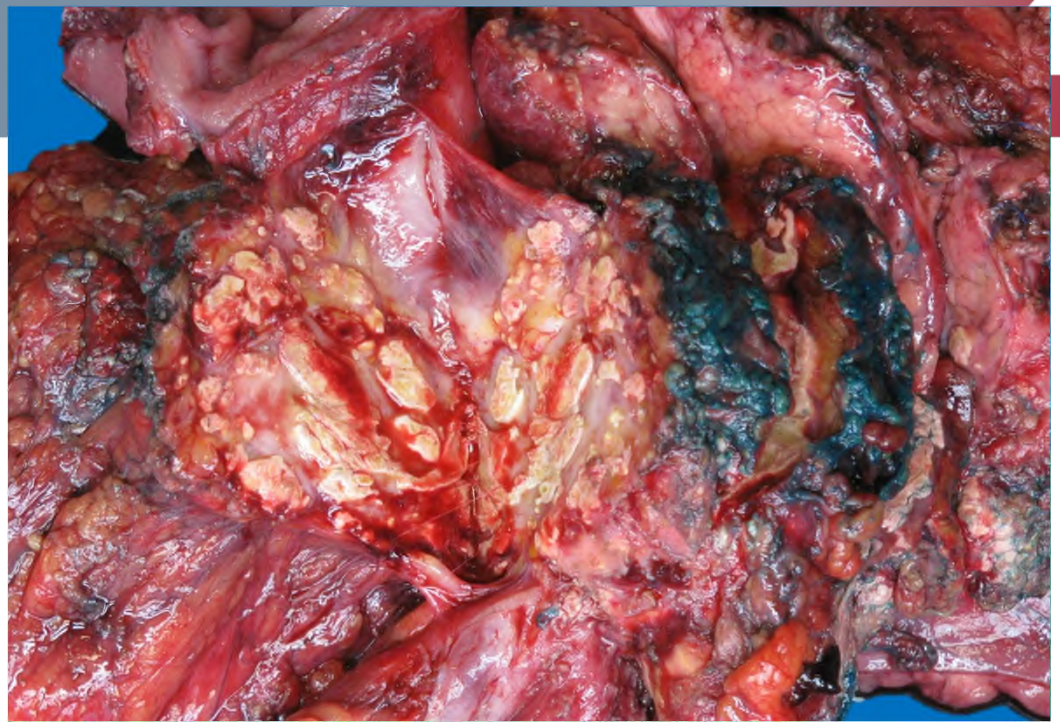
Acute pancreatitis: Histopathology

	Interstitial pancreatitis	Necrotic hemorrhagic pancreatitis
Prevalence	80-85%	15-20%
Macroscopy	Edematous, swollen pancreas	Hemorrhagia, necrosis pancreas, peripancreatic
Necrosis	Rare	Acute necrosis
Fluid accumulation < 4 w after the onset of disease	Acute peripancreatic fluid accumulation, no or incomplete wall on imaging and histologically	Acute necrosis accumulation within the pancreas or peripancreatic, on imaging and histologically no or incomplete wall
Pseudocyst (≥ 4 w)	Extra-pancreatic fluid accumulation with the formation of a complete wall	Extra- and intrapancreatic fluid accumulation with the formation of a complete wall, so-called "walled-off necrosis" (WON)
Mortality	<2%	<20%

Klöppel G Acute pancreatitis ch 22, The Pancreas ISBN 9781119188391
Thoeni RF, Radiol Clin North Am. 2015;53:1189-208.

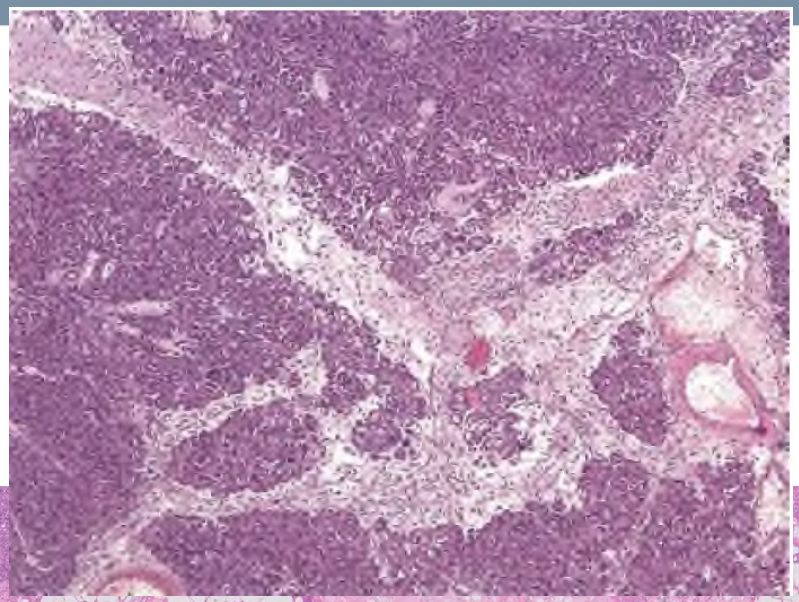
Acute pancreatitis: Macroscopy

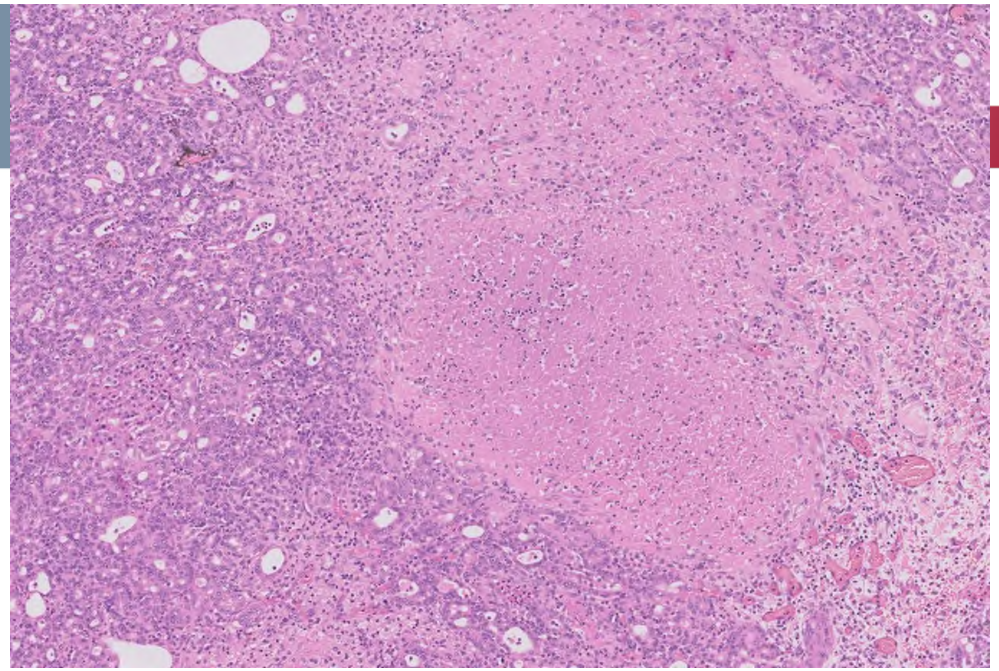


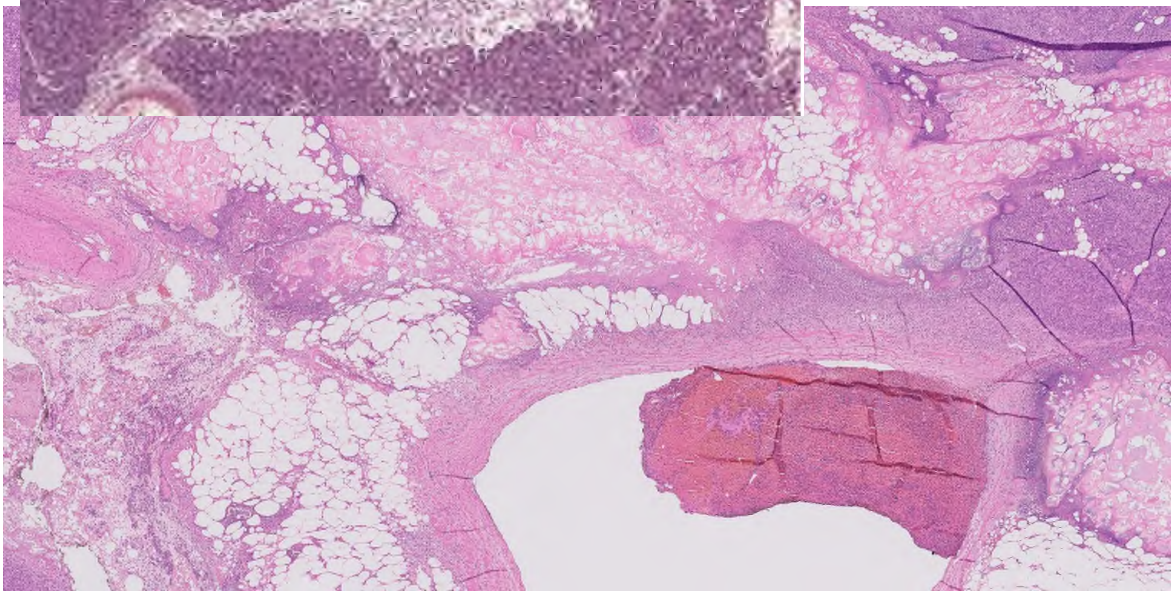


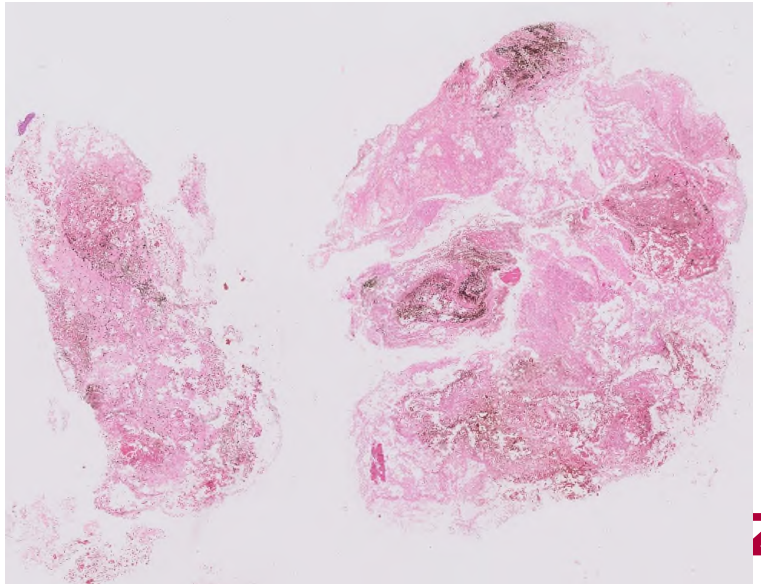
F. Campbell, C.S. Verbeke, Pathology of the pancreas,2021

Acute pancreatitis: Microscopy





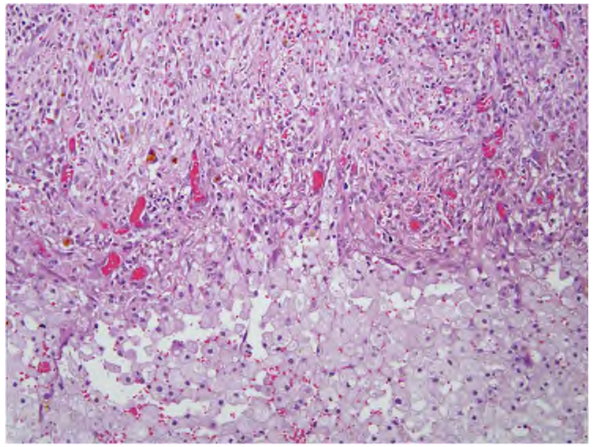


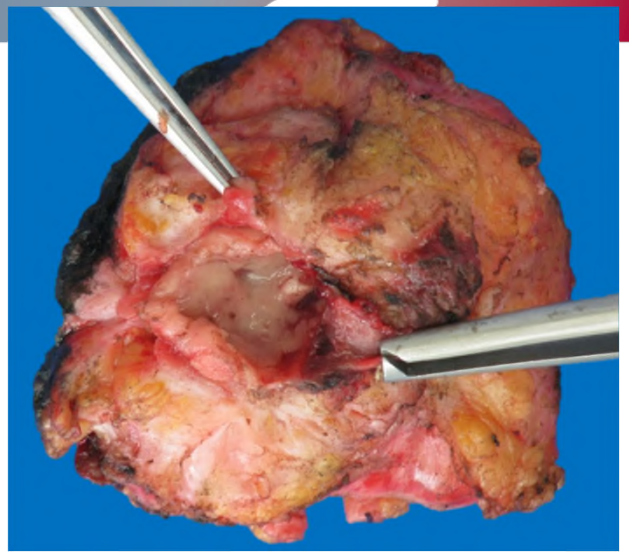


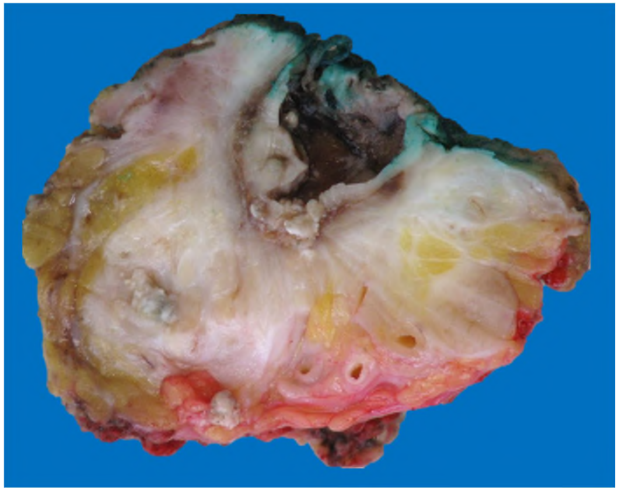
F. Campbell, C.S. Verbeke, Pathology of the pancreas,2021

Complications

- Local complications:
  - Acute peripancreatic fluid collection
  - Acute necrotic collection
  - Pseudocyst
  - Walled-off necrosis with liquid and solid, sticky content
  - Gastric outlet syndrome
  - Colonic necrosis or fistula
  - Splenic and/or portal thrombosis
- Systemic complications
  - Exacerbation of co-morbidity
  - Sepsis
  - Organ failure
- Long term complications
  - Exocrine insufficiency risk dependent on degree necrosis
  - Endocrine insufficiency risk on diabetes after 5 yrs







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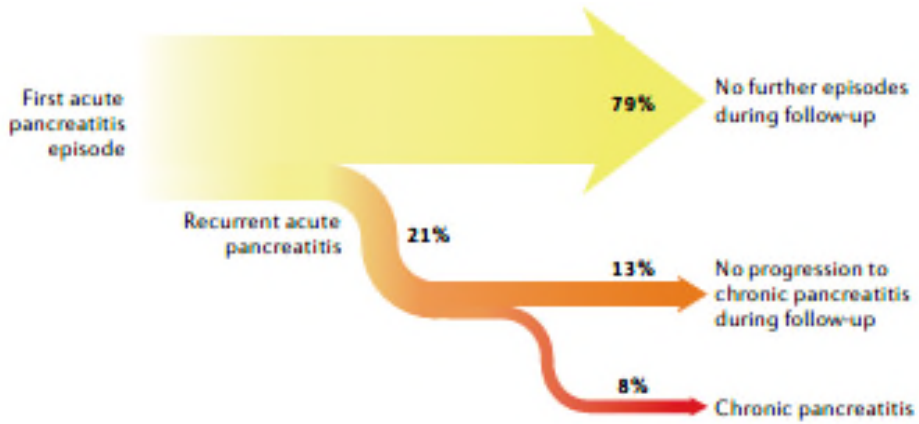
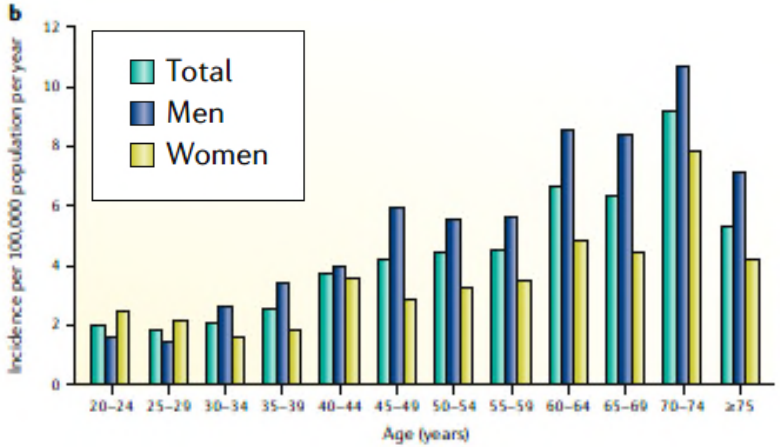
Chronic pancreatitis



- Incidence
  - Early CP 1/100000/yr
  - CP 14/100000/yr
  - M/F = 5
- Symptoms
  - Abdominal pain
  - Weight loss
  - Malabsorption
  - Steatorrhoe



- Complications
  - Masses, pseudocysts (60%) or abcesses
  - Pleural effusions
  - GI bleeding
  - Peptic ulceration
  - Stenosis common bile duct
  - Endocrine insufficiency → diabetes
  - Portal hypertension
  - Pancreatic cancer

Petrov Nat GE Hepatol 2019;16:175

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Chronic pancreatitis: Definition

- CP is a disease of the pancreas in which recurrent inflammatory episodes result in replacement of the pancreatic parenchyma by fibrous connective tissue
- Etiology: genetic, environmental and/or other risk factors causing persistent pathologic responses resulting in parenchymal injury.

  - Progressive exocrine and endocrine insufficiency
  - Pseudocyts
  - Pancreatic duct obstructions
  - Duodenal obstruction
  - Vascular complications
  - Obstruction of the bile ducts
  - Malnutrition
  - Pain syndrome

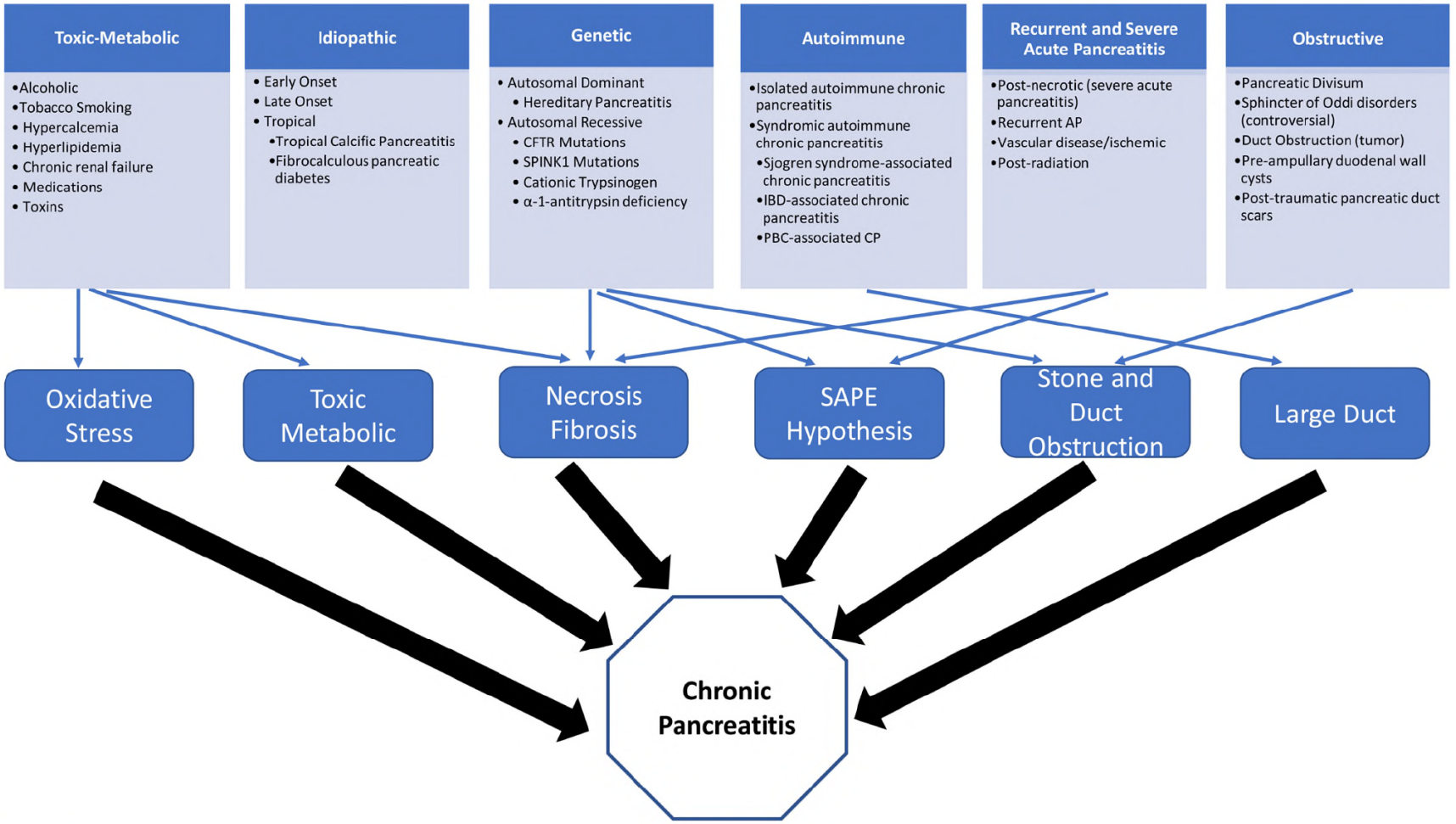
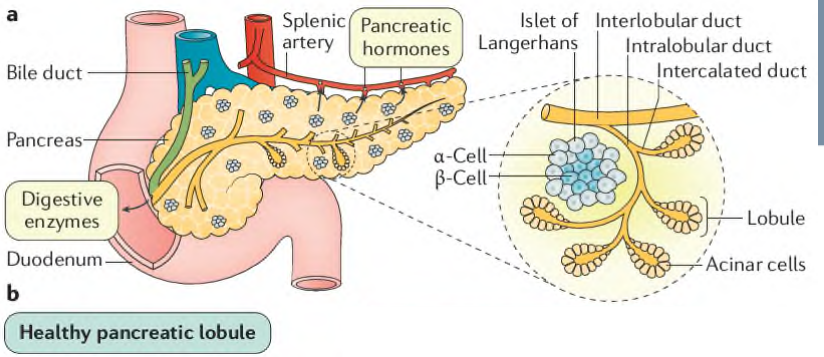
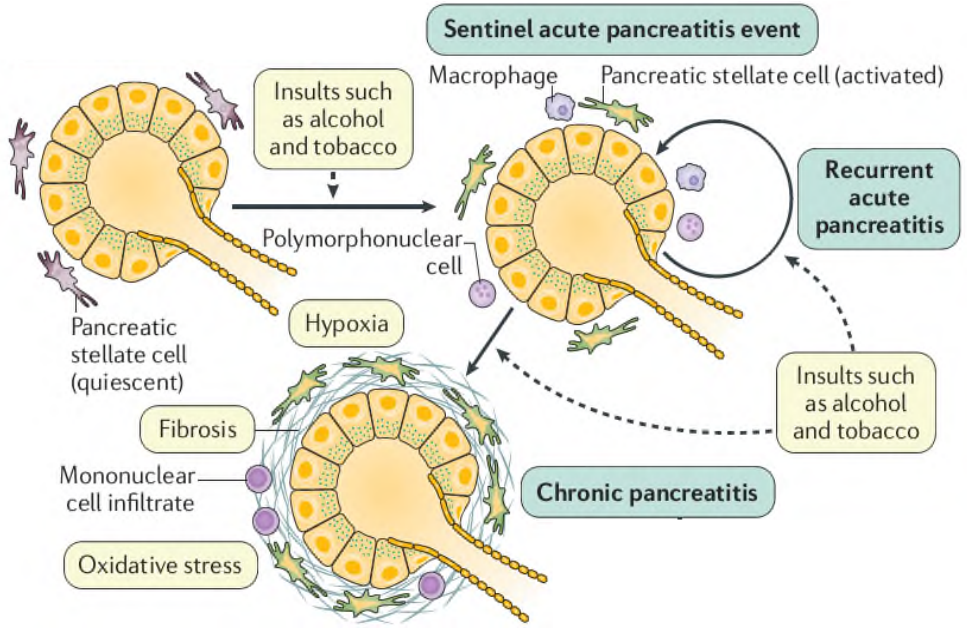
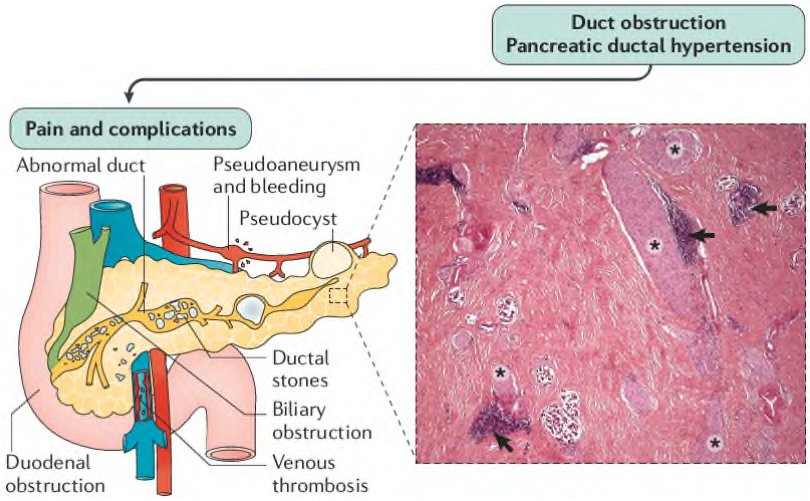


Figure 1. TIGAR-O risk factor classification system. AP, acute pancreatitis; CFTR, cystic fibrosis transmembrane conductance regulator; CP, chronic pancreatitis; IBD, inflammatory bowel disease; PBC, primary biliary cirrhosis; SAPE, sentinel acute pancreatitis event; SPINK1, serine protease inhibitor kazal-type 1; TIGAR-O, Toxic-Metabolic, Idiopathic, Genetic, Autoimmune, Recurrent and Severe Acute Pancreatitis,

https://doi.org/10.12688/f1000research.12852.1



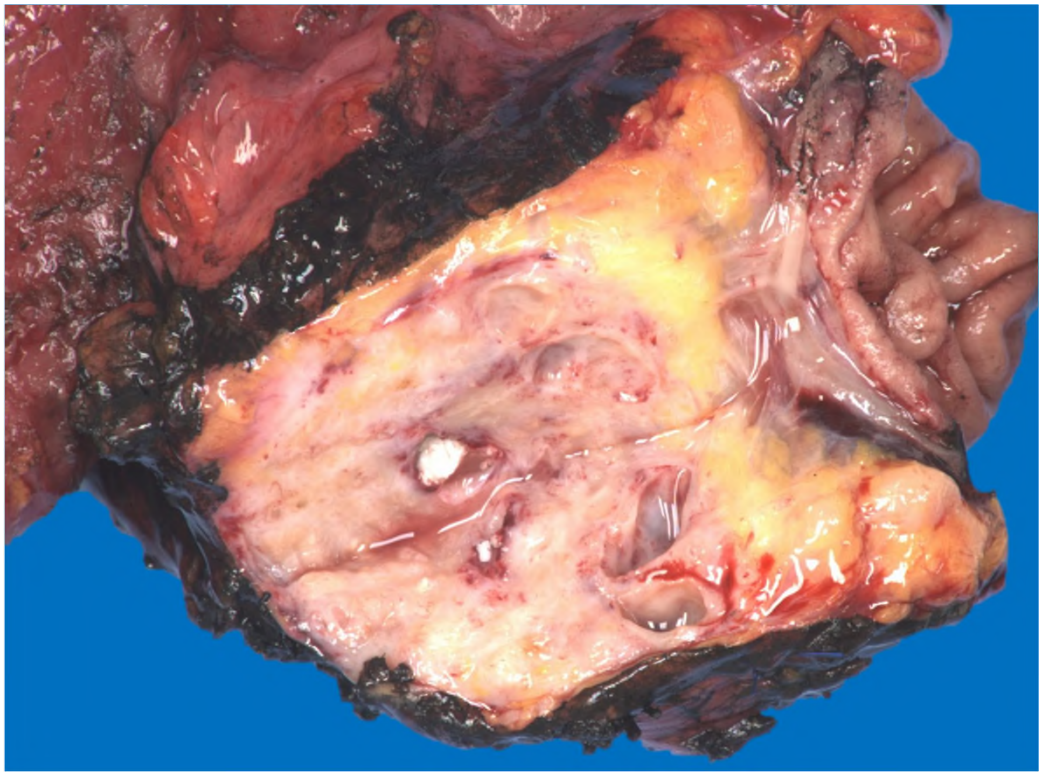




Kleeff et al. Nat Rev Dis Primer 2017;3:17060

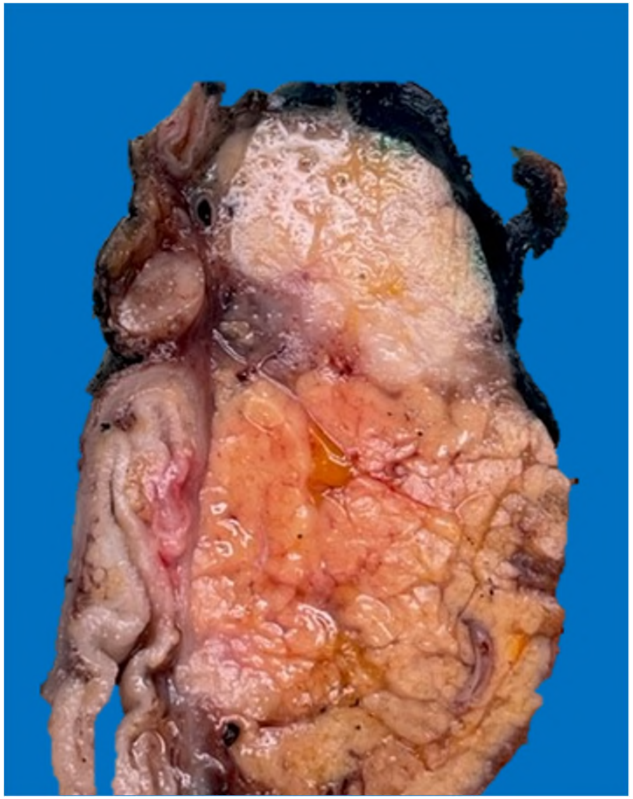
Chronic pancreatitis: Macroscopy

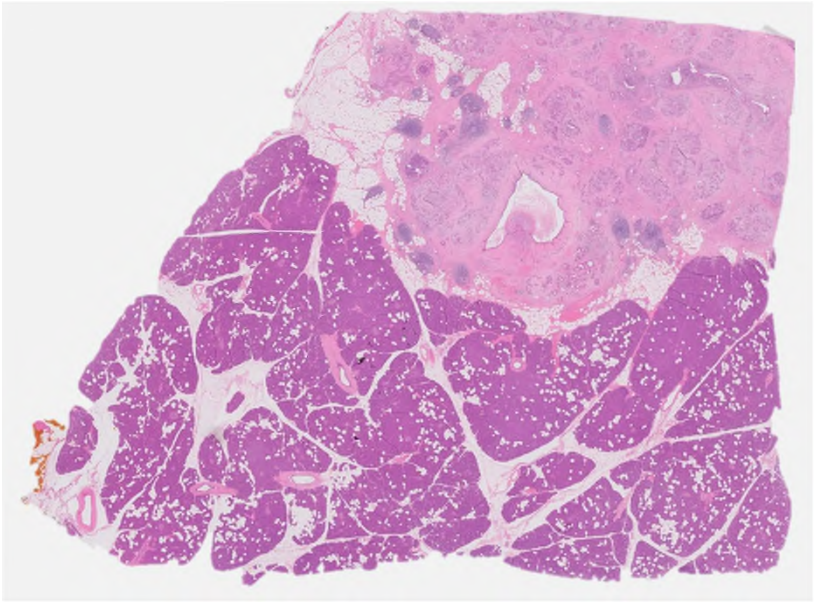
- Enlargement focal, segmental or diffuse
- Induration and/or fibrosis
- Cystic dilatation of pancreatic ducts
- Calcifications
- Atrophy → shrunken and hardened pancreas
- Pseudocyts



Cardinal features

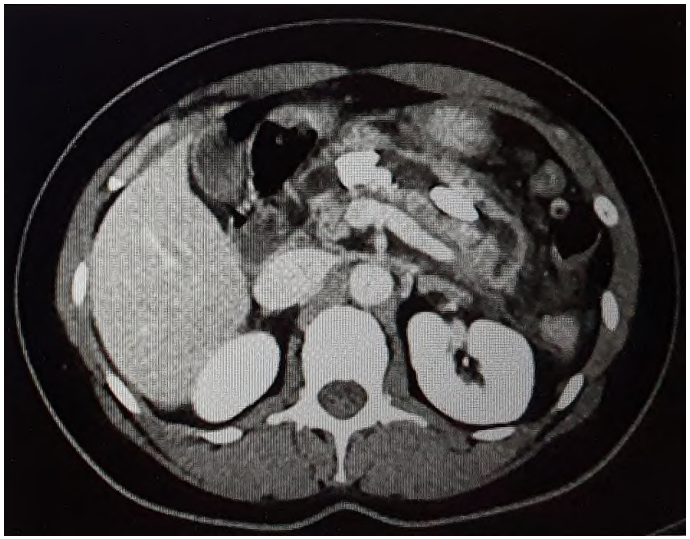
Chronic pancreatitis

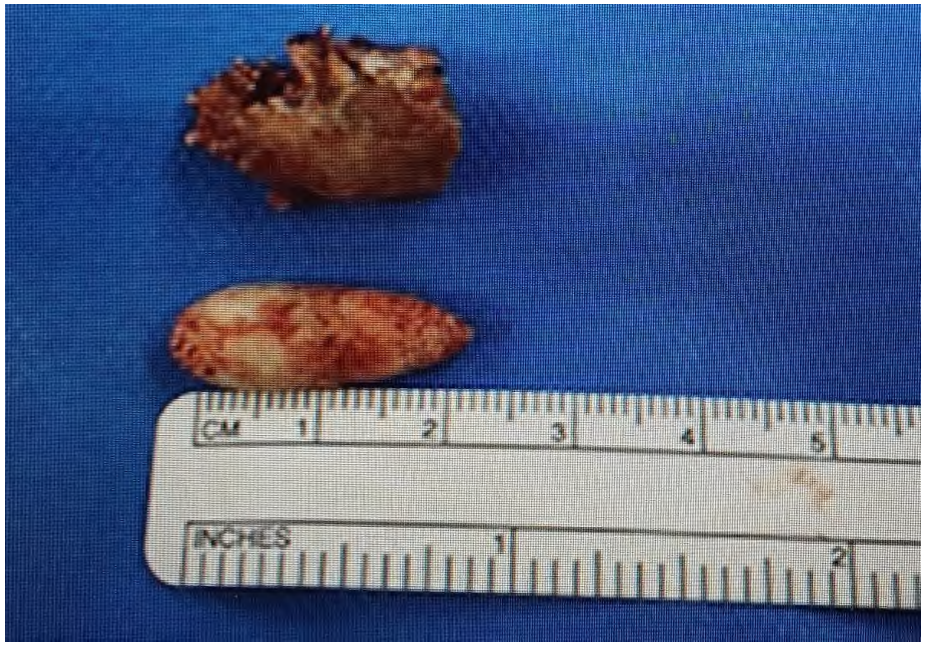




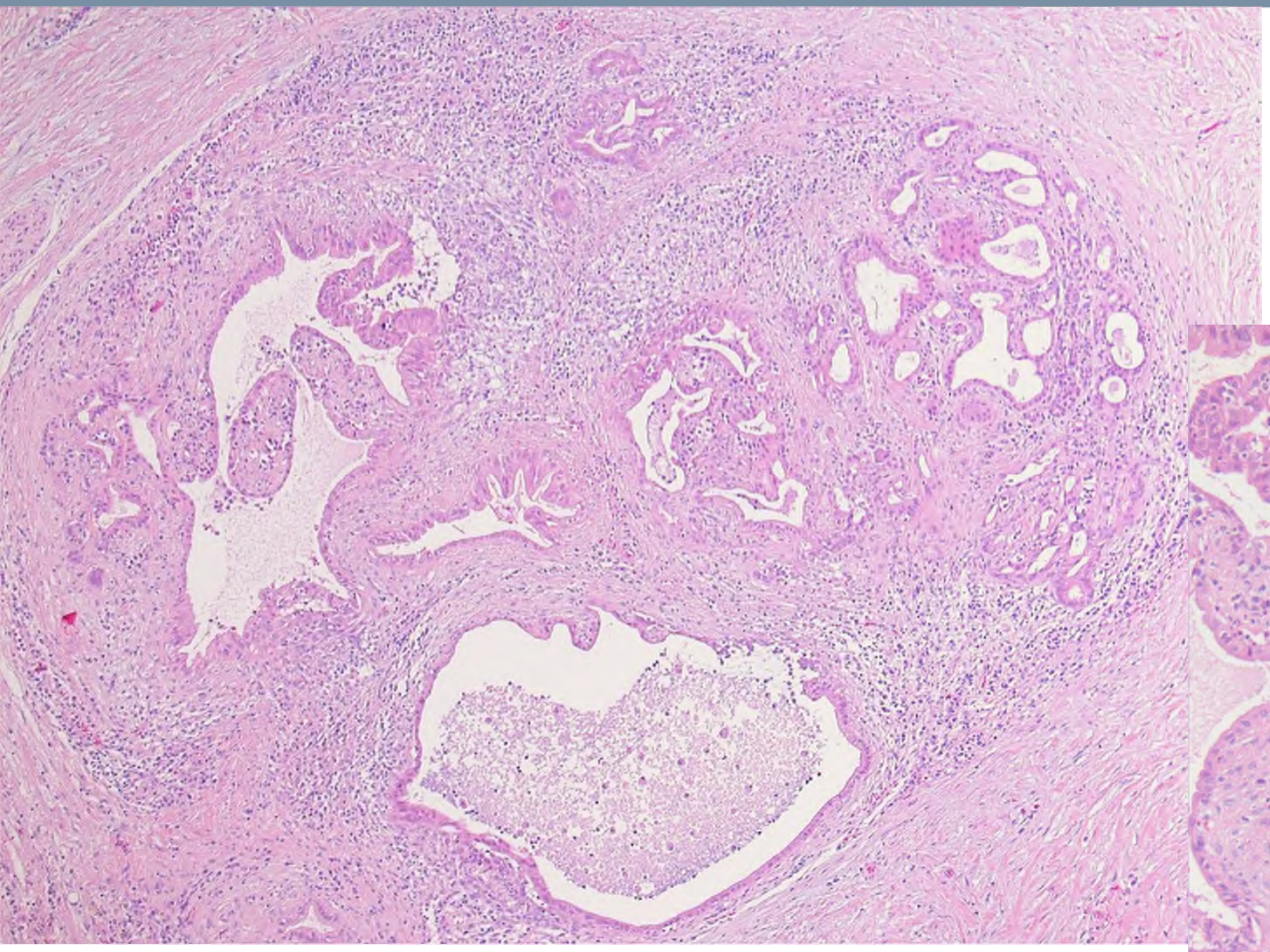
Main differential diagnosis

Pancreatic adenocarcinoma



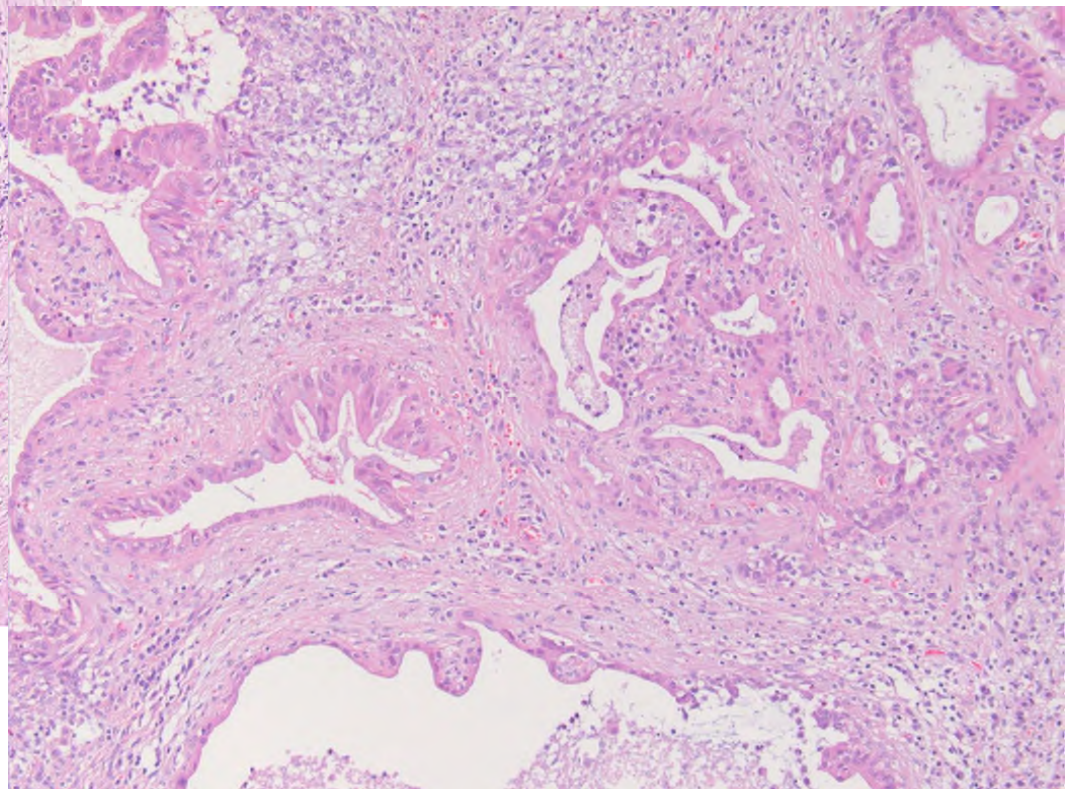

CM
1
2
3
4
5
INCHES
1
2

Chronic pancreatitis: Microscopy

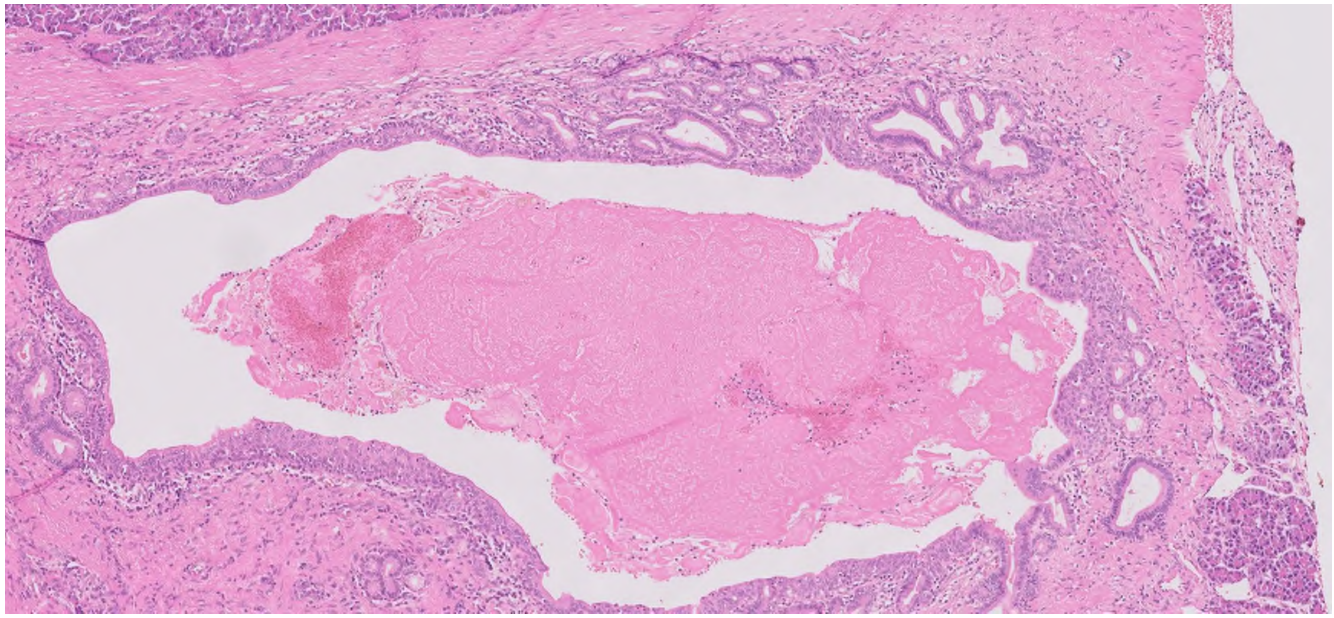


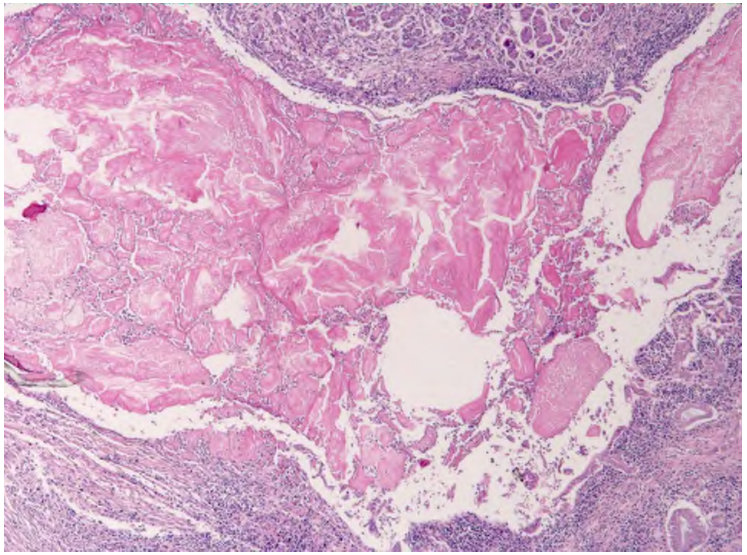
Irregular ducts with duct dilatation

Periductal inflammation

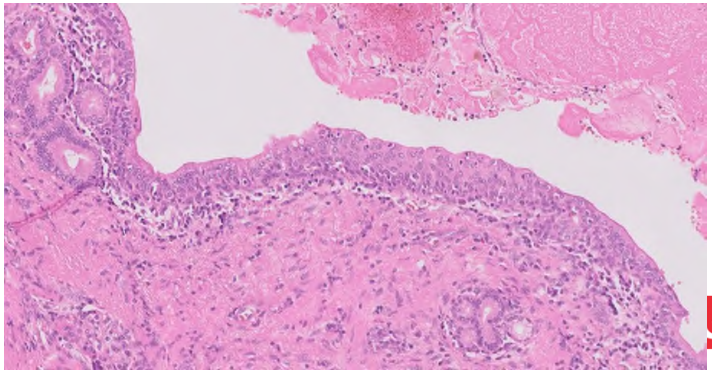


Chronic pancreatitis: Microscopy





Squamous metaplasia



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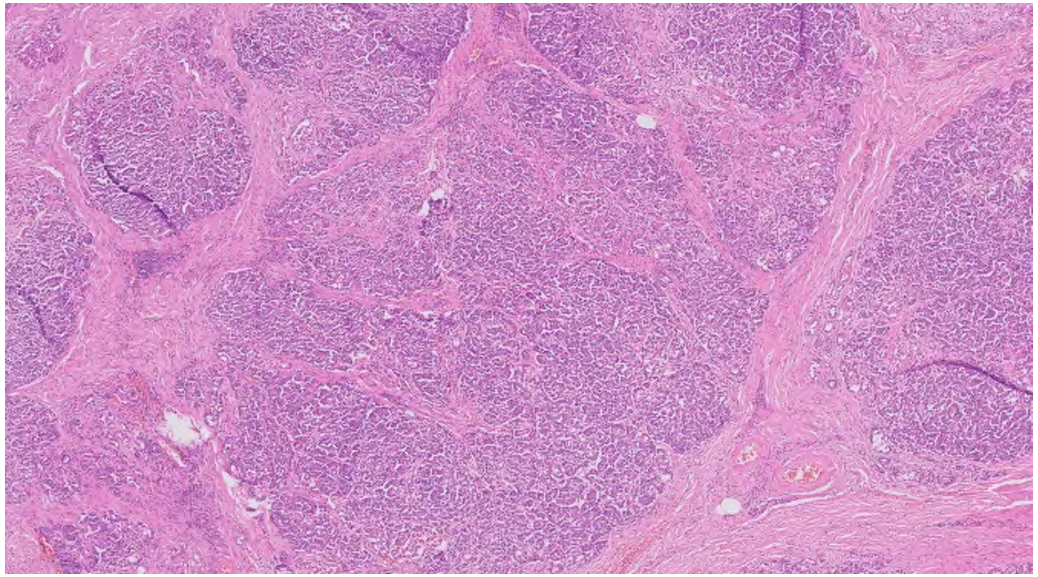
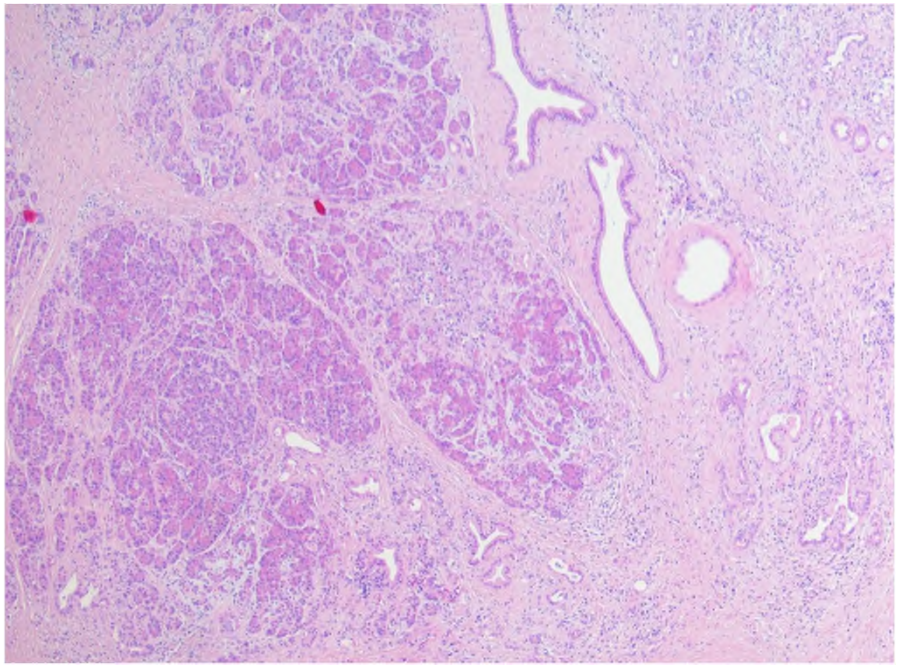
Chronic pancreatitis: Microscopy



Interlobular fibrosis



Interlobular / Intralobular fibrosis

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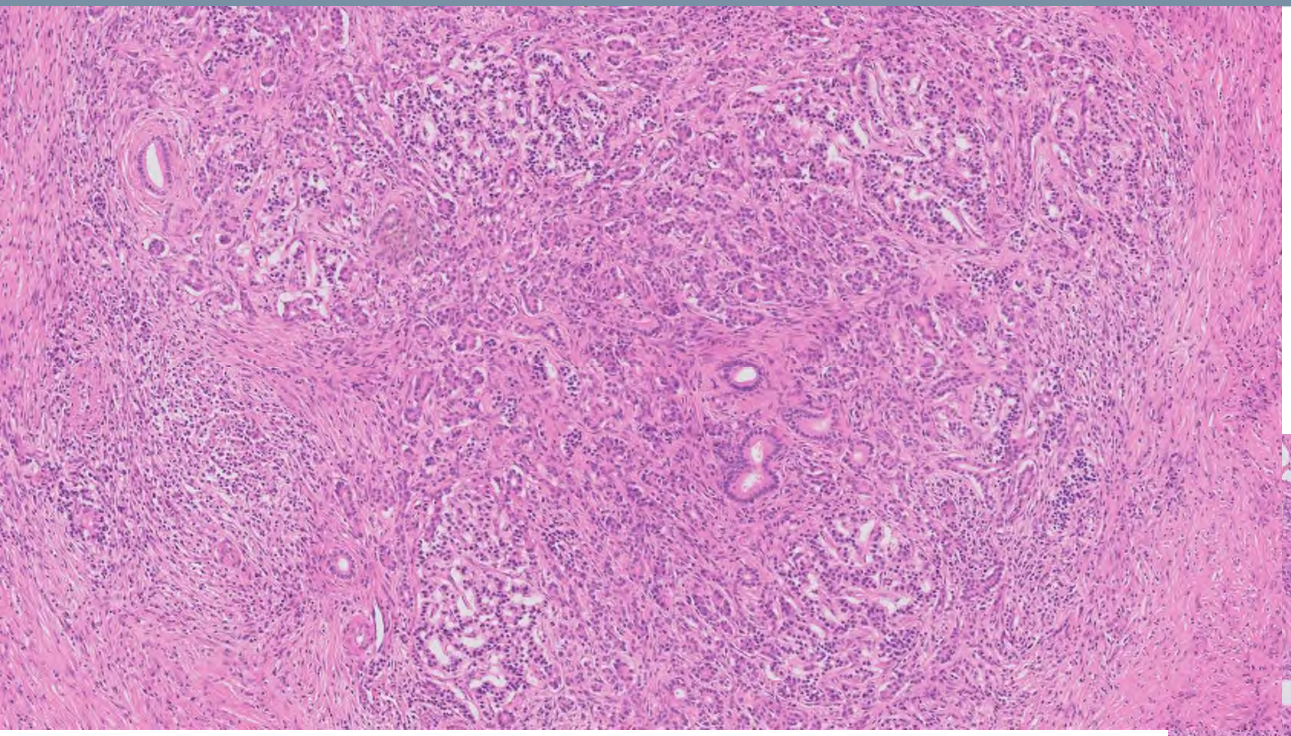
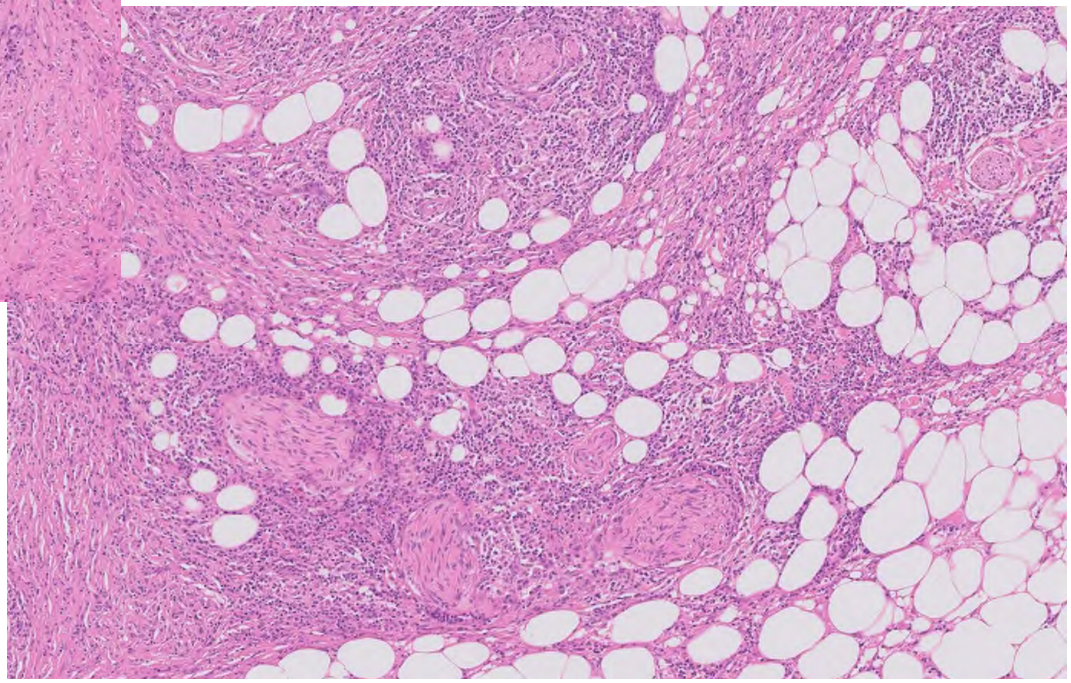
Chronic pancreatitis

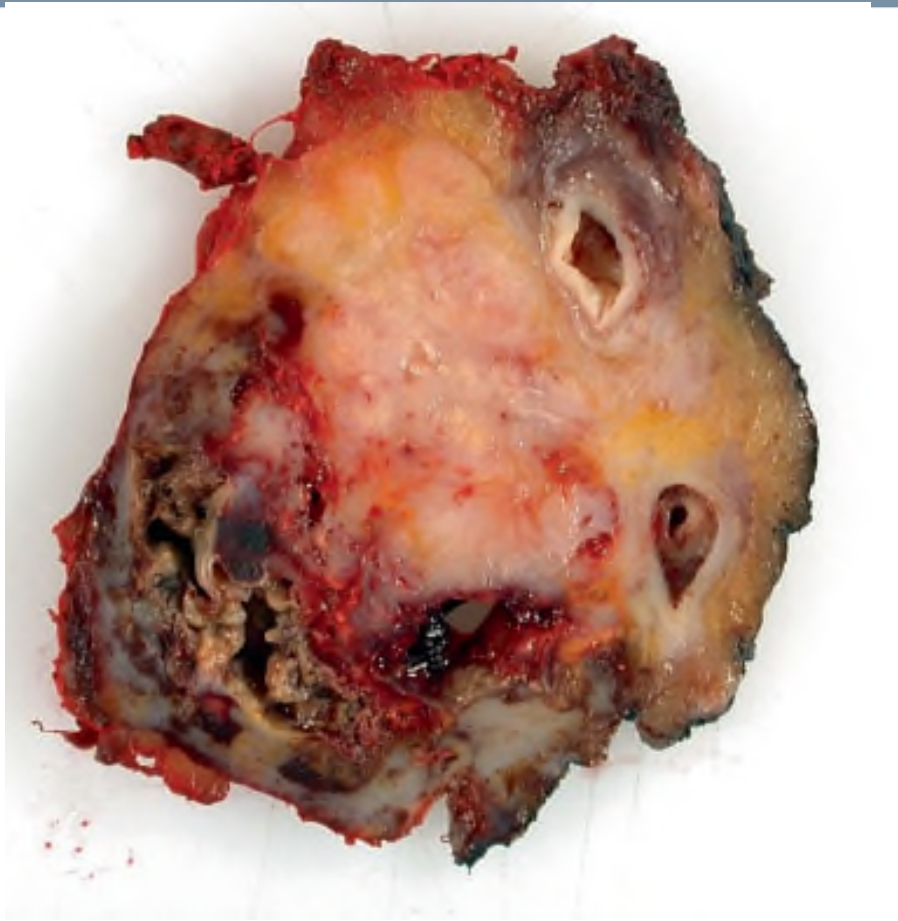


Hyperplasia of endocrine islands

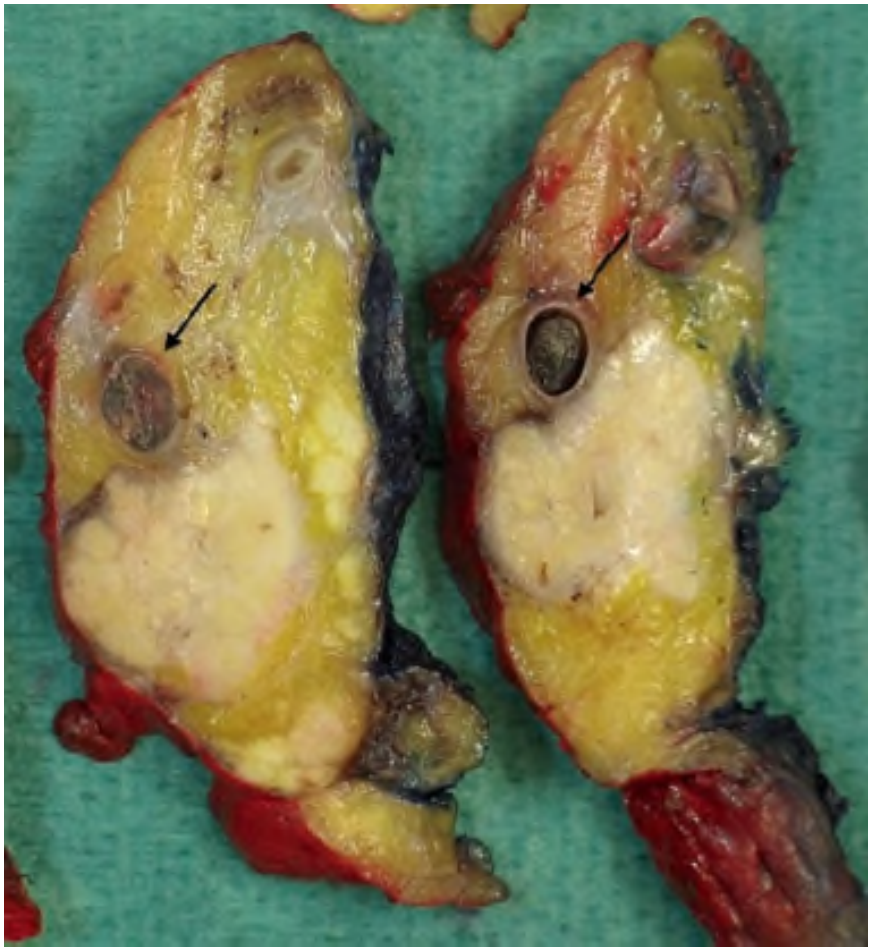


Hyperplasia of nerve fibres

Chronic pancreatitis



Hemorhagia



Thrombosis

Campbell F, Verbeke CS Pathology of the pancreas, 2nd Ed

Chronic pancreatitis

- There is no generally accepted histopathological grading system to determine the severity of chronic pancreatitis

Table 1
Scoring system for the evaluation of the extent of fibrosis in chronic pancreatitis (from Klöppel & Maillet, 1991[10]).

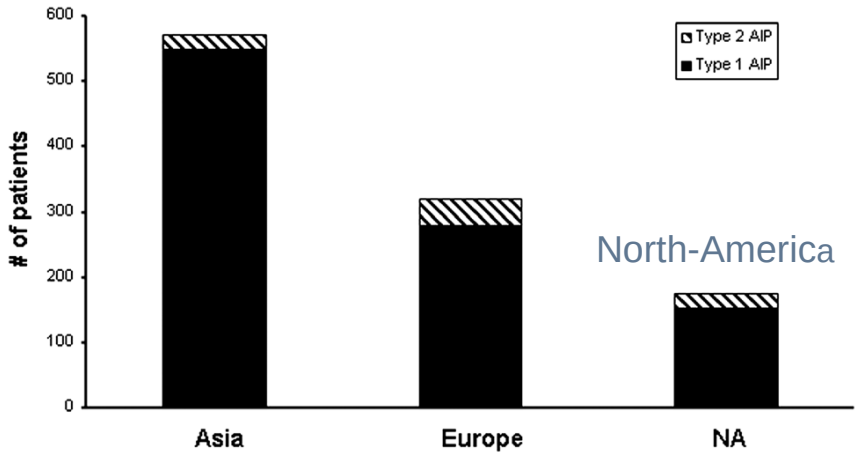
Pattern of fibrosis	Grade of fibrosis		
	Mild	Moderate	Severe
Perilobular fibrosis			
Focal	1	2	3
Diffuse	4	5	6
Intralobular fibrosis[a]			
Focal	1	2	3
Diffuse	4	5	6

[a] Mild intralobular fibrosis: 10–40% fibrous replacement of the acinar cells; moderate intralobular fibrosis: 40–80% fibrous replacement of the acinar cells; severe intralobular fibrosis: 80–100% fibrous replacement of the acinar cells.

Klöppel et al. Pancreas 1991;6:266
Esposito et al. Pancreatology 2020;20:586

Autoimmune pancreatitis

- AIP is a rare, steroid-response fibro-inflammatory condition, presenting as a pancreatic mass and often mimicking pancreatic cancer
- 1995: Yoshida : AIP distinctive entity
- Terminology
  - Lymphoplasmocytic sclerosing pancreatitis
  - Chronic sclerosing pancreatitis
  - Nonalcoholic pancreatitis
  - Inflammatory pseudotumor
- Symptoms: abdominal pain, icterus, weight loss
- Prevalence 4,6/100000, incidence 1,4/100000 Japan



- AIP type 1 =
  - IgG4-related pancreatitis
  - Lymphoplasmocytic sclerosing pancreatitis
  - AIP-lobulocentric
- AIP type 2 =
  - Idiopathic-duct centric pancreatitis
  - AIP with GEL (granulocytic-epithelial lesions)
  - AIP-ductal

Hart PA, Gut 2013;62:1771

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Auto-immune pancreatitis: Clinical

	AIP type 1
Age	Older (Mean age 64 yrs)
Gender	F <10%, M/F 3
Prevalence in Asia	>95%
Prevalence in Europe	<60%
Symptoms: Jaundice Abdominal pain Acute pancreatitis Other symptoms	 75-90% 30% 5-10% New-onset diabetes, weight loss, steatorrhoe
Other organ involvement	50%, multiorgan
IBD	2-6%
Diffuse pancreatic enlargement	30-40%
Serum IgG4 > 2x ULN	60-70%

Shimosegawa T, Pancreas 2011 - Kamisawa T Pancreas 2011 – Sah R, GE 2010 – Klöppel G, GE 2010 – Chari ST, Pancreatology 2010

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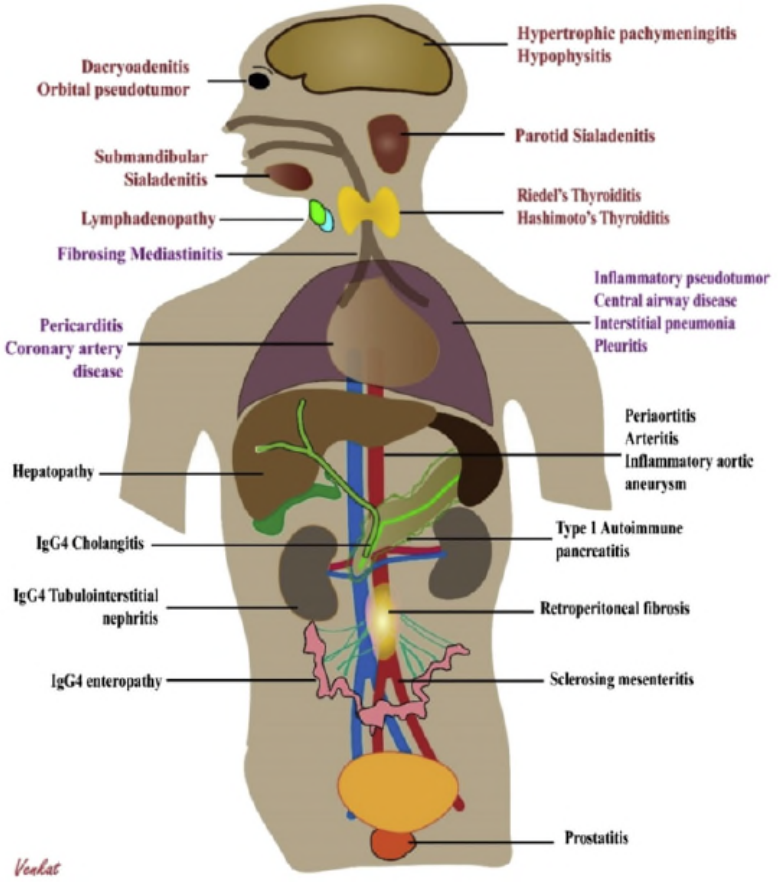
IgG4-related disease



Prevalence of IgG-4 systemic involvement.

IgG-4 Related Systemic Involvement	
Salivary/ lacrimal gland Miculicz's disease	39%
Interstitial pneumonitis	9%
Sclerosing cholangitis	60%
Autoimmune hepatitis	2%
Renal Disease: Interstitial nephritis or Membranous nephropathy	17%
Hypothyroidism	22%
Hilar lymphadenopathy	80%
Type 1 autoimmune pancreatitis	100%
Retroperitoneal fibrosis	13%

Katabathina Radiol Clin North Am 2016
Qureshi Autoimmunity Rev 2021

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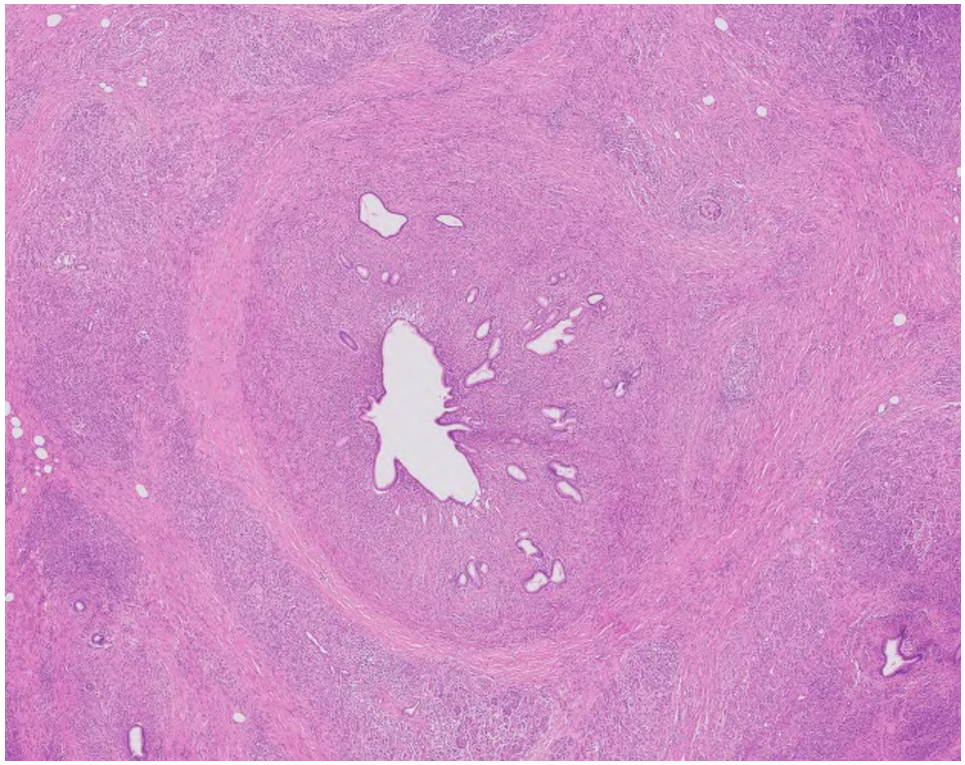
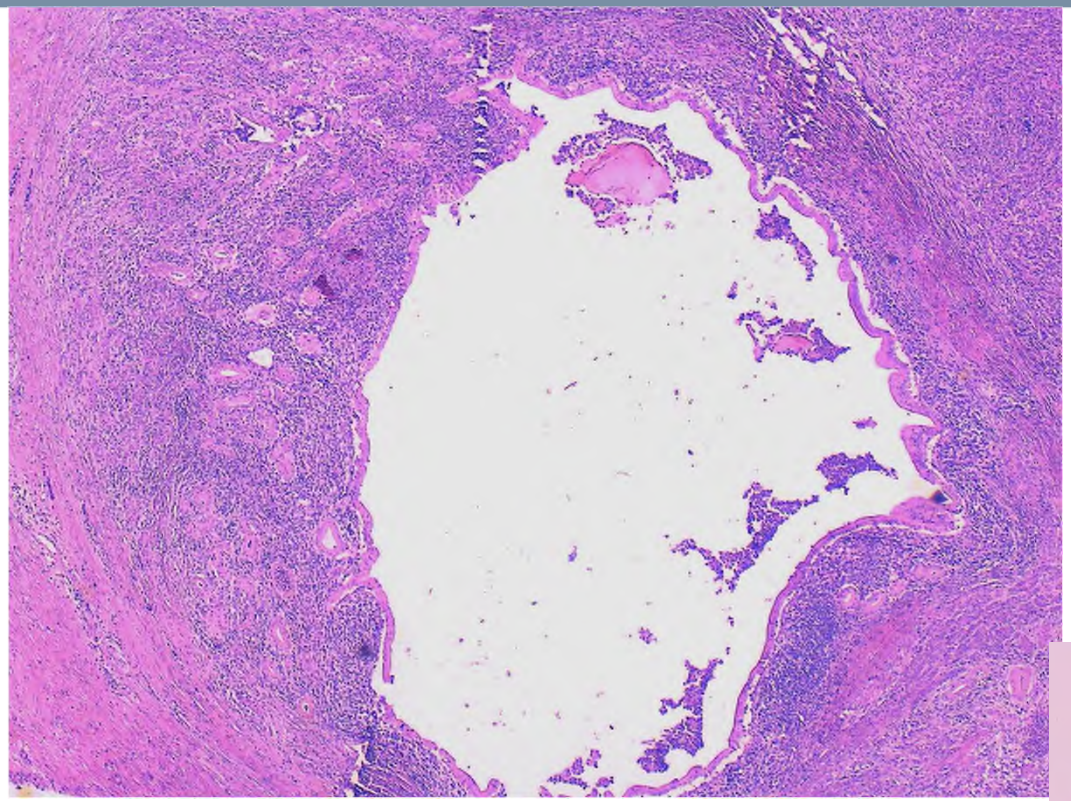
AIP type 1

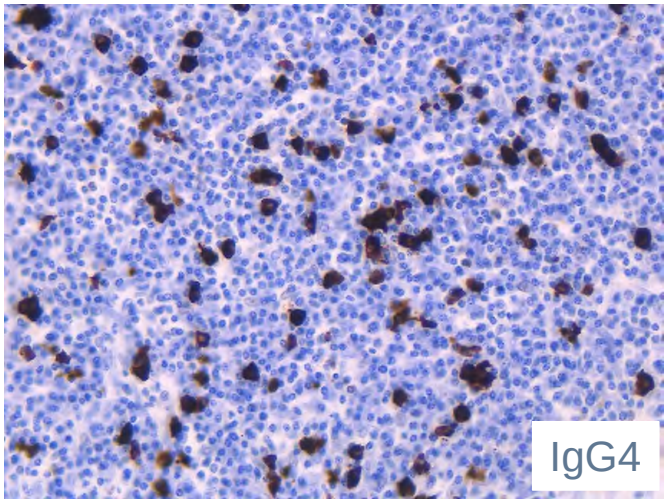
- Localisation:
  - Pancreatic head 76%
  - Body 6%
  - Tail 14%
  - Entire pancreas 3%
- Microscopic findings:
  - Lymphoplasmocytic infiltration
  - Storiform fibrosis
  - Obliterative phlebitis

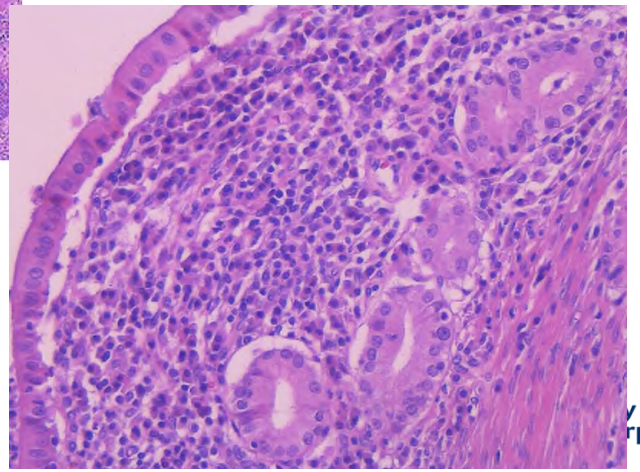


AIP type1

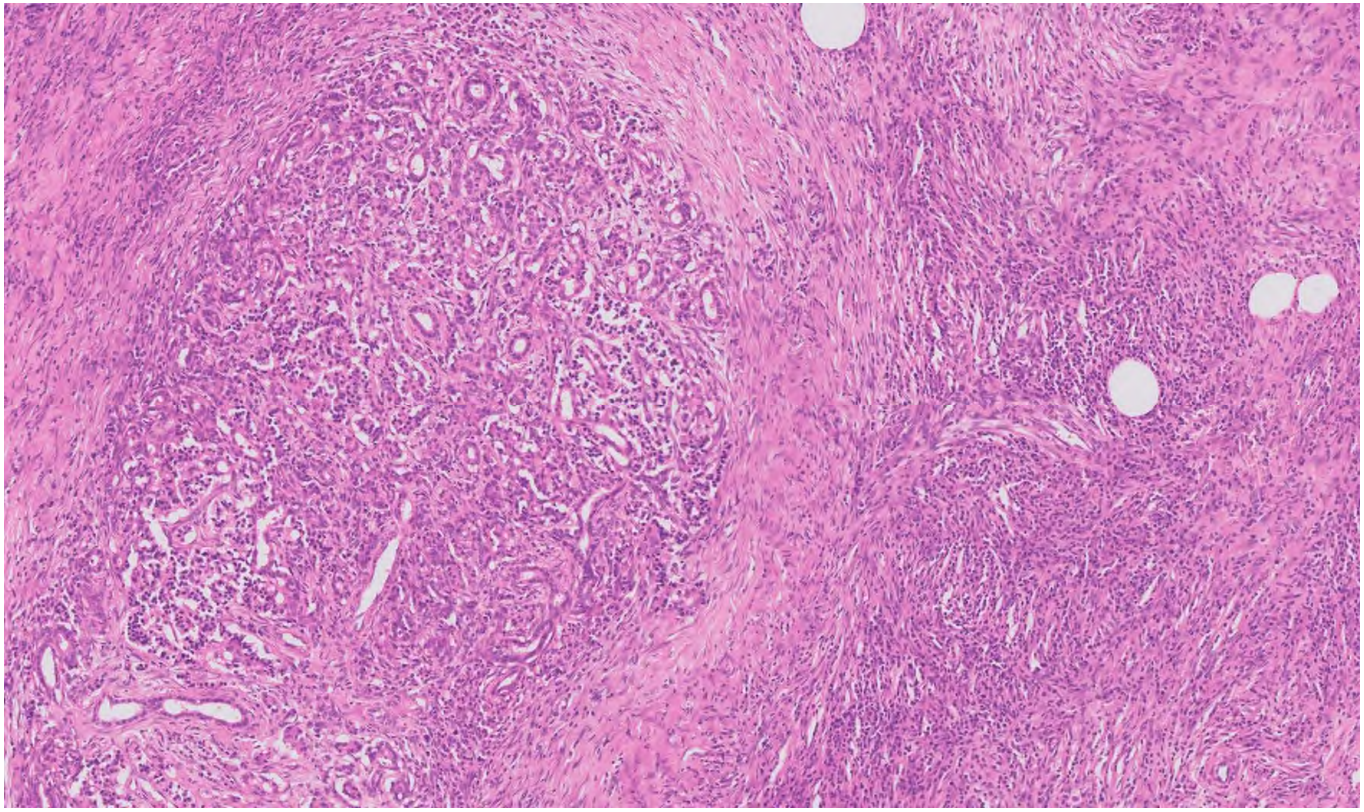


Periductal inflammation



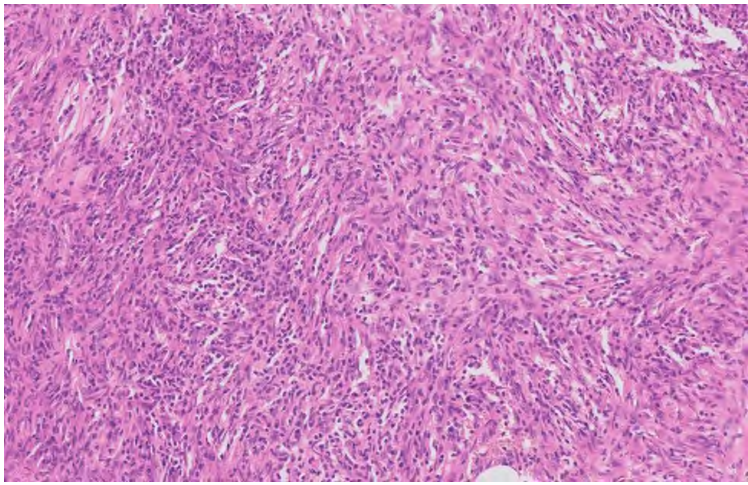


AIP type1



Diffuse lymphoplasmocytic infiltrate

Storiform fibrosis



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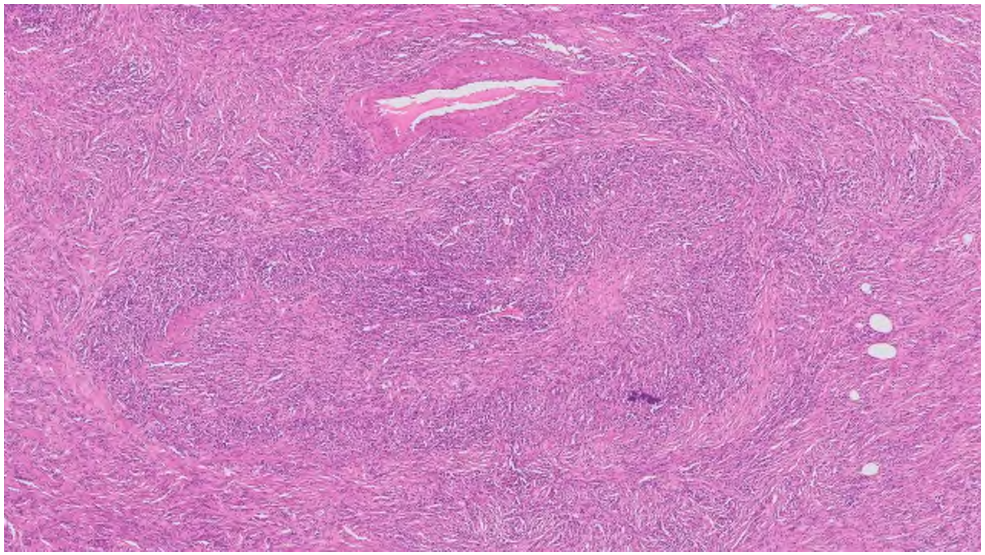
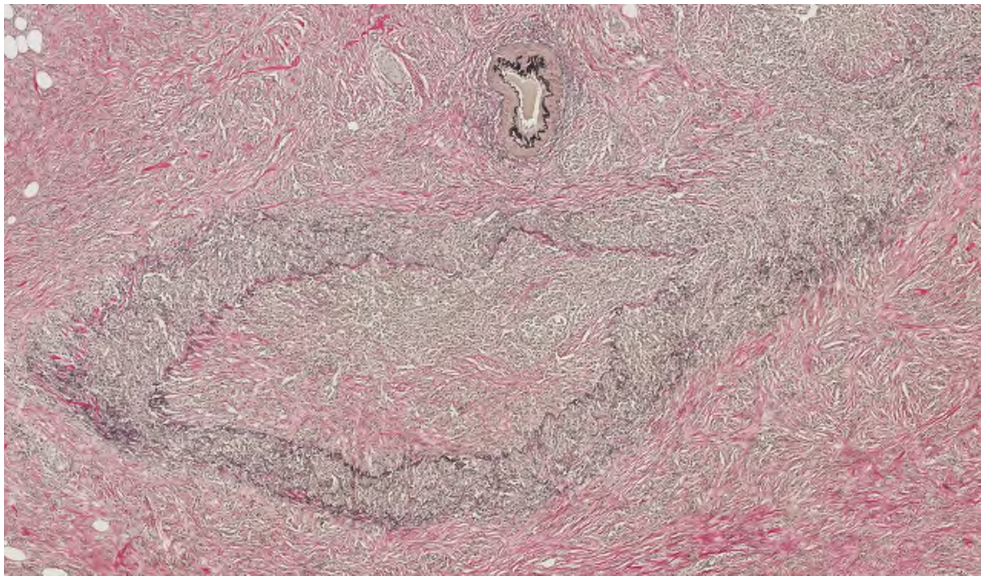
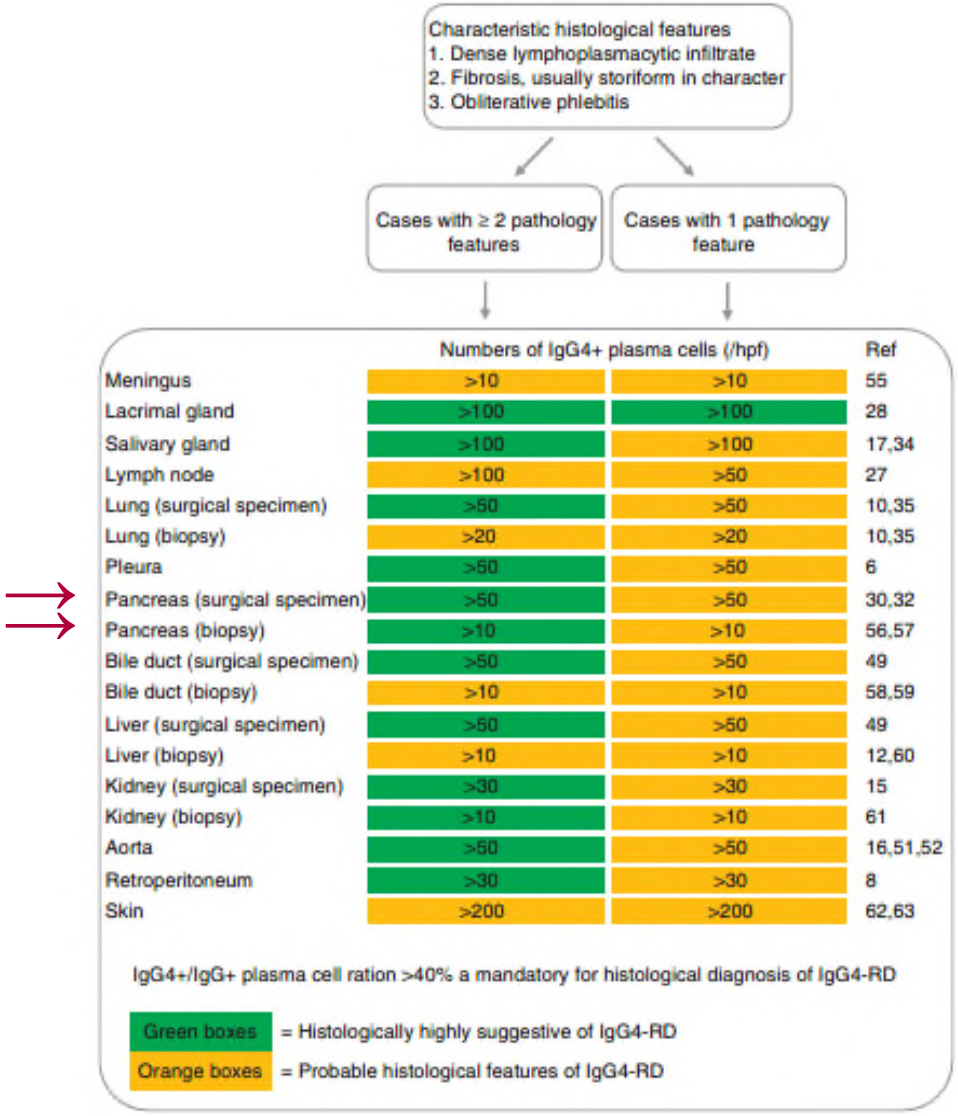




Obliterative phlebitis

AIP type 1



Consensus statement on the pathology of IgG4-related disease

- Primary: dense lymphoplasmocytic infiltrate, storiform fibrosis, obliterative phlebitis
- Secundary: IgG4 count
- Different treshold values ranging from > 10 to > 50 IgG4+ plasmacells/hpf
- >10/hpf for biopsies, > 50/hpf for resection specimens
- Hot spot area
- IgG4+/IgG+ ratio > 40% recommended cut off value

Deshpande V Modern Pathol 2012;25:1181

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AIP 1

Grades of Severity of Autoimmune Pancreatitis	
Grade 1	Scattered periductal lymphoplasmacytic infiltrates; mild duct obliteration; almost no interlobular and acinar involvement
Grade 2	Multiple periductal lymphoplasmacytic infiltrates; mild periductal fibrosis and duct obliteration; mild interlobular and acinar involvement; focal inflammatory storiform fibrosis; occasional, mild venulitis
Grade 3	Diffuse periductal lymphoplasmacytic infiltrates; marked periductal fibrosis and duct obstruction; moderate interlobular and acinar involvement; moderate focal inflammatory storiform fibrosis; frequent venulitis; scattered lymphoid follicles
Grade 4	Diffuse periductal lymphoplasmacytic infiltrates; severe periductal fibrosis and duct obstruction/disappearance; severe interlobular and acinar involvement; severe inflammatory storiform fibrosis and diffuse sclerosis; frequent venulitis and occasional arteritis; scattered and occasionally prominent lymphoid follicles

- Inflammation
- Fibrosis
- Vascular changes

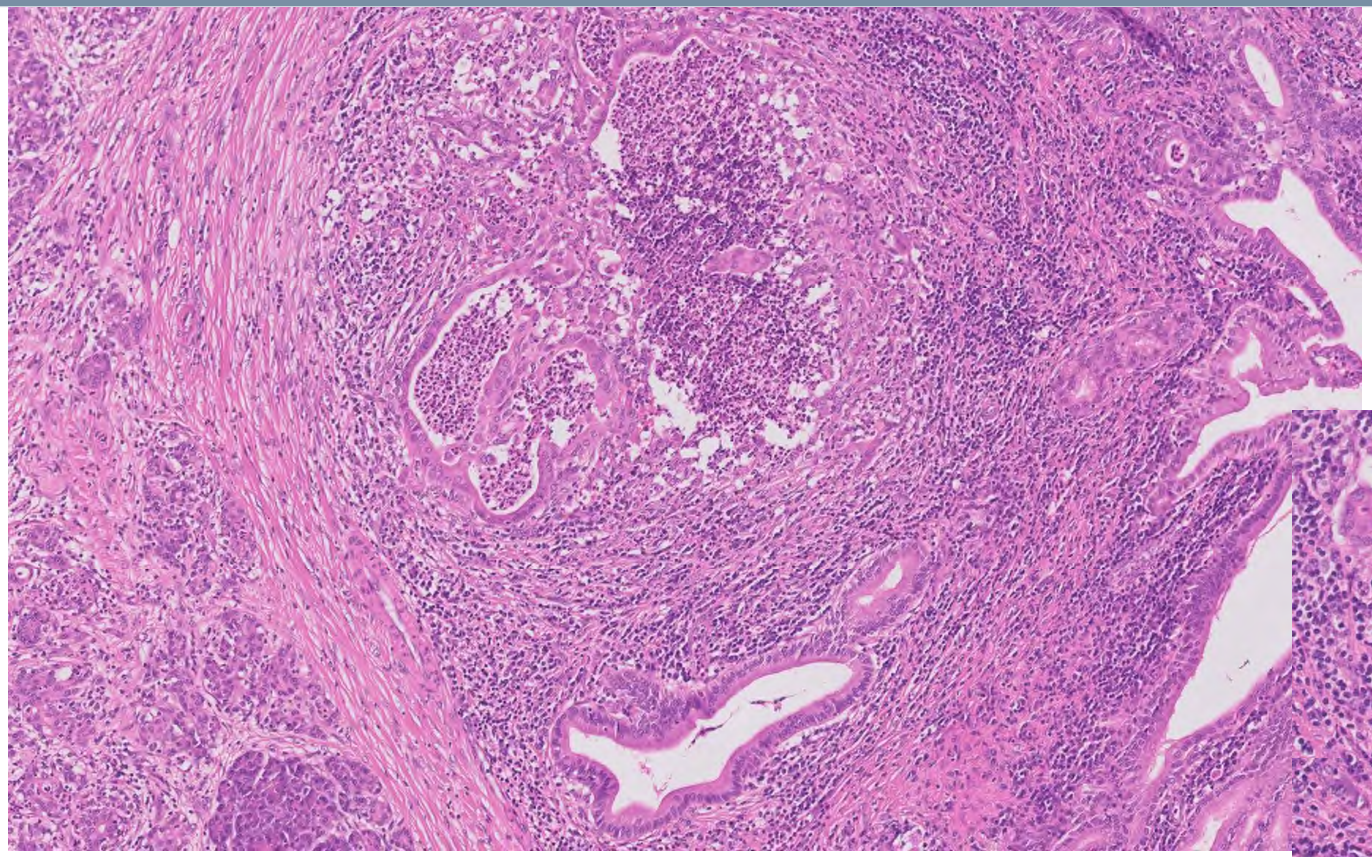
Zamboni et al., Archiv Pathol Lab Med 2009

Auto-immune pancreatitis: Clinical

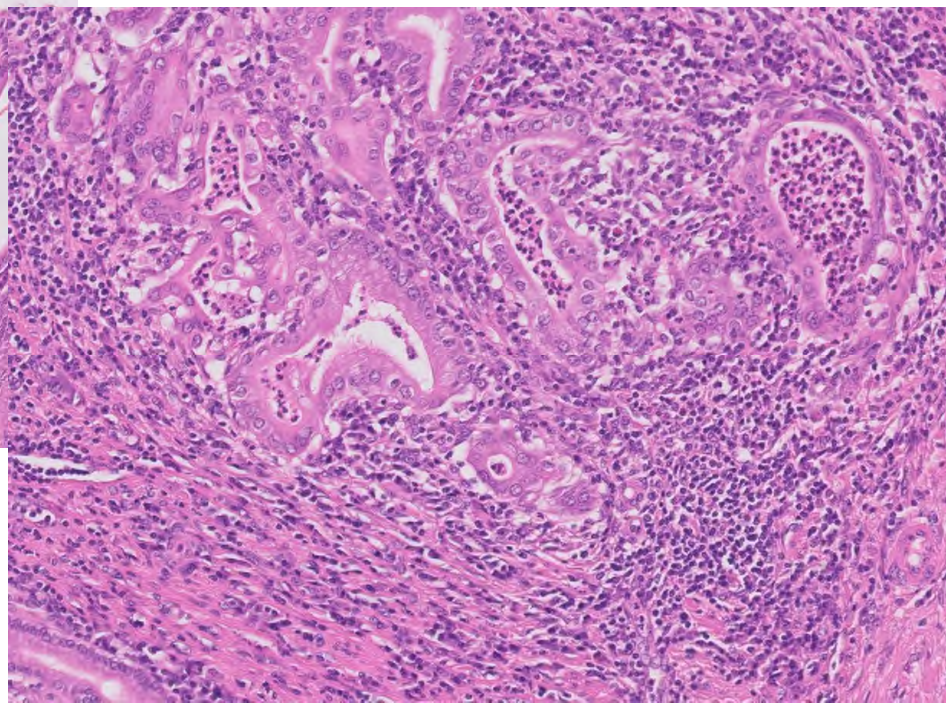
	AIP type 1	AIP type 2
Age	Older (Mean age 64 yrs)	Younger (mean age 40 yrs)
Gender	F <10%, M/F 3	F > 30 %, M/F ≤ 1
Prevalence in Asia	>95%	5%
Prevalence in Europe	<60%	> 30%
Symptoms: Jaundice Abdominal pain Acute pancreatitis Other symptoms	 75-90% 30% 5-10% New-onset diabetes, weight loss, steatorrhoe	 50-70% 60% 30% New-onset diabetes, weight loss, steatorrhoe
Other organ involvement	50%, multiorgan	40%, ulcerative colitis
IBD	2-6%	16%
Diffuse pancreatic enlargement	30-40%	15-25%
Serum IgG4 > 2x ULN	60-70%	15-25%

Shimosegawa T, Pancreas 2011 - Kamisawa T Pancreas 2011 – Sah R, GE 2010 – KlöppelG, GE 2010 – Chari ST, Pancreatology 2010

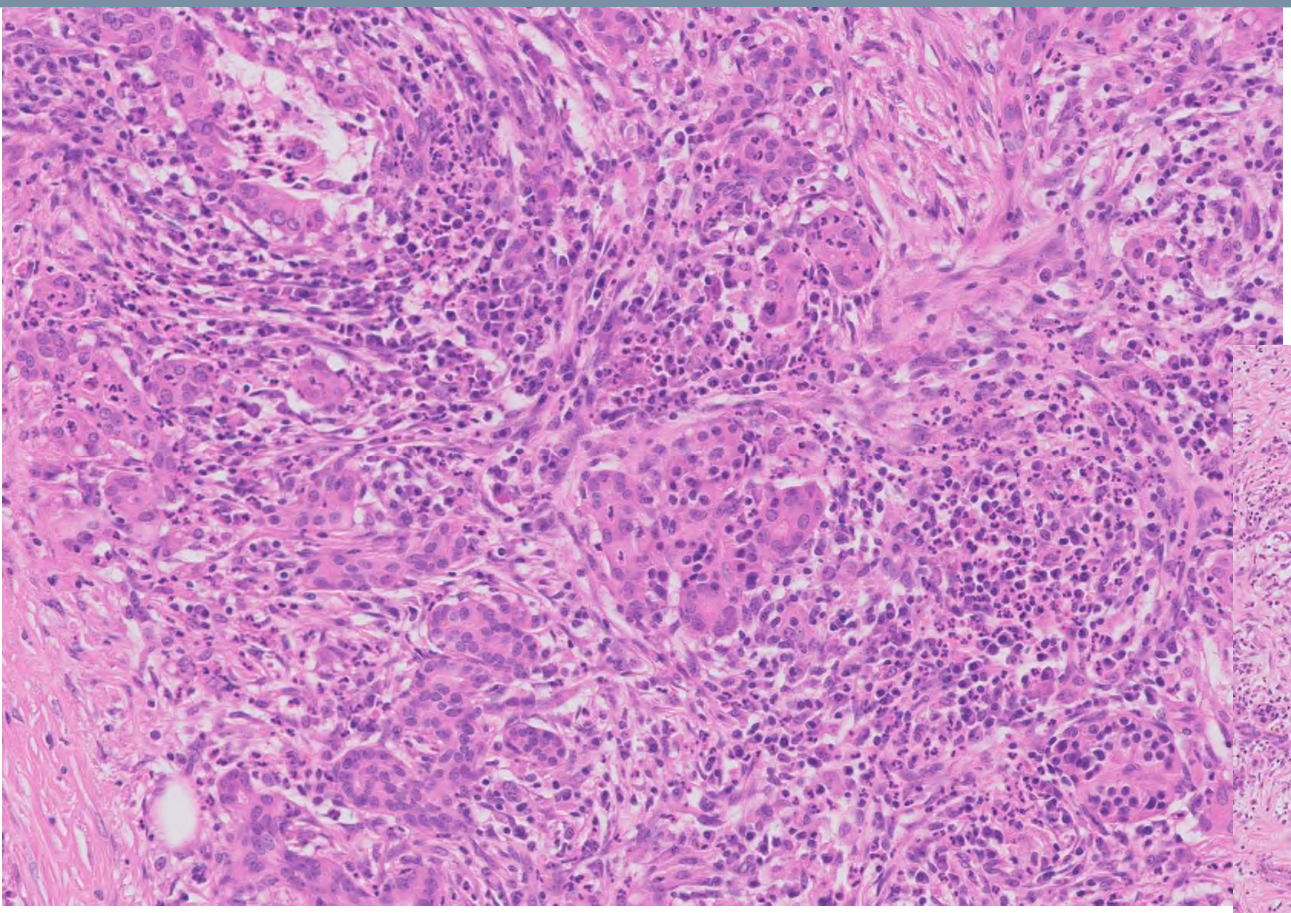
AIP type 2

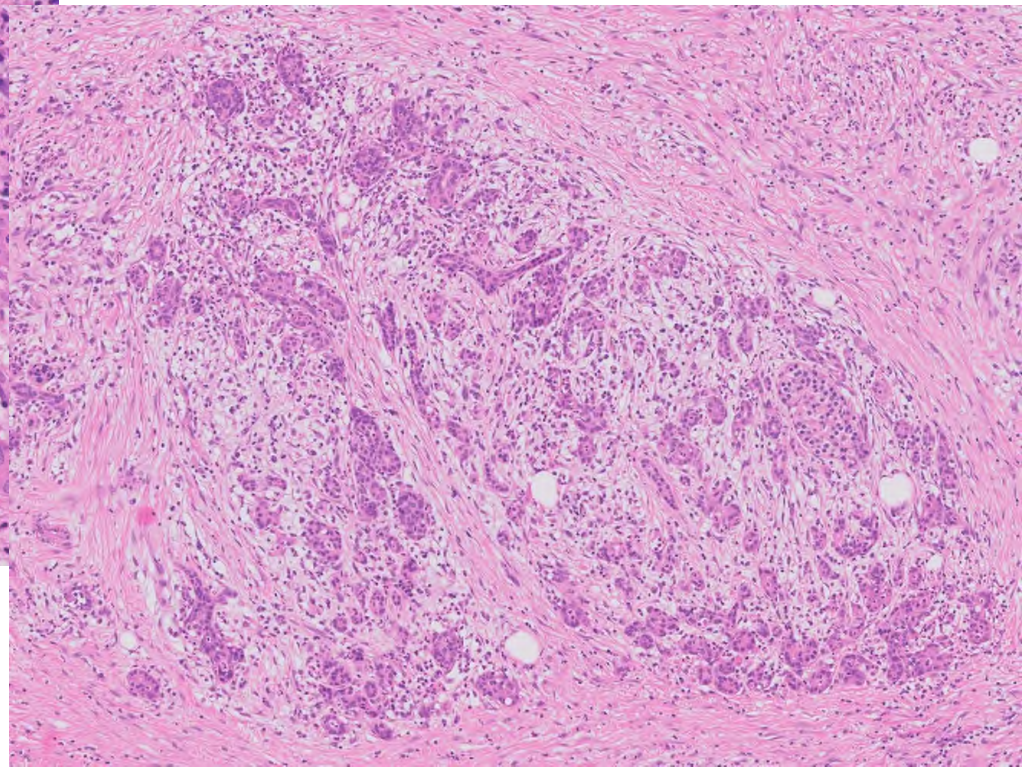


Granulocytic epithelial lesion



AIP type 2

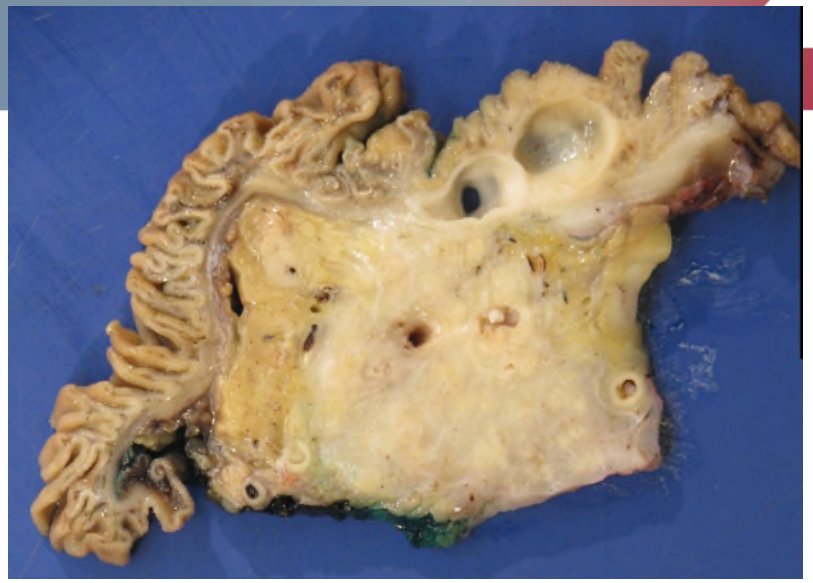


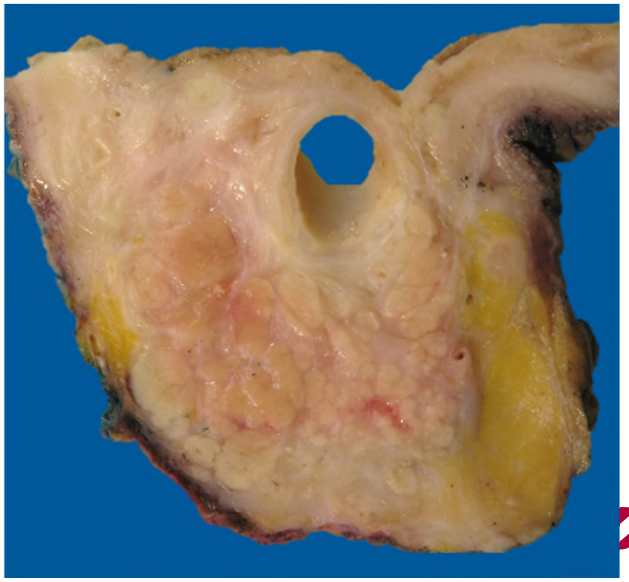


Scanty or absent IgG4 plasmacells

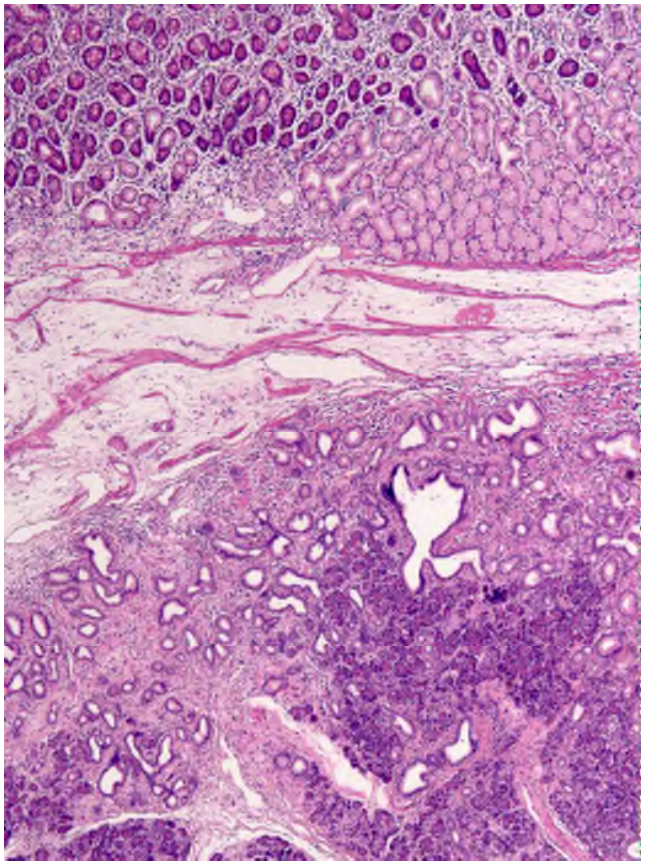
Groove pancreatitis

- Paraduodenal pancreatitis
- Described by Becker in 1973
- rare segmental chronic pancreatitis affecting the groove between the head of the pancreas, the duodenum and the common bile duct.
- Cystic dystrophy of heterotopic pancreas
- results in fibrosis of paraduodenal region in vicinity of minor ampulla
- Alcohol is precipitating factor, commonly in young to middle-aged adults

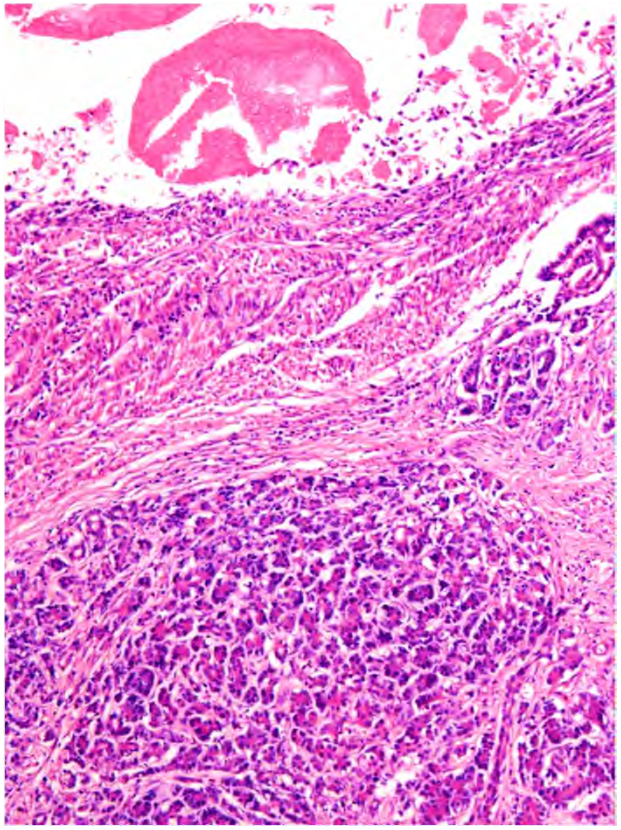




Groove pancreatitis



Heterotopic pancreasparenchym



Pseudocyst/Cyst

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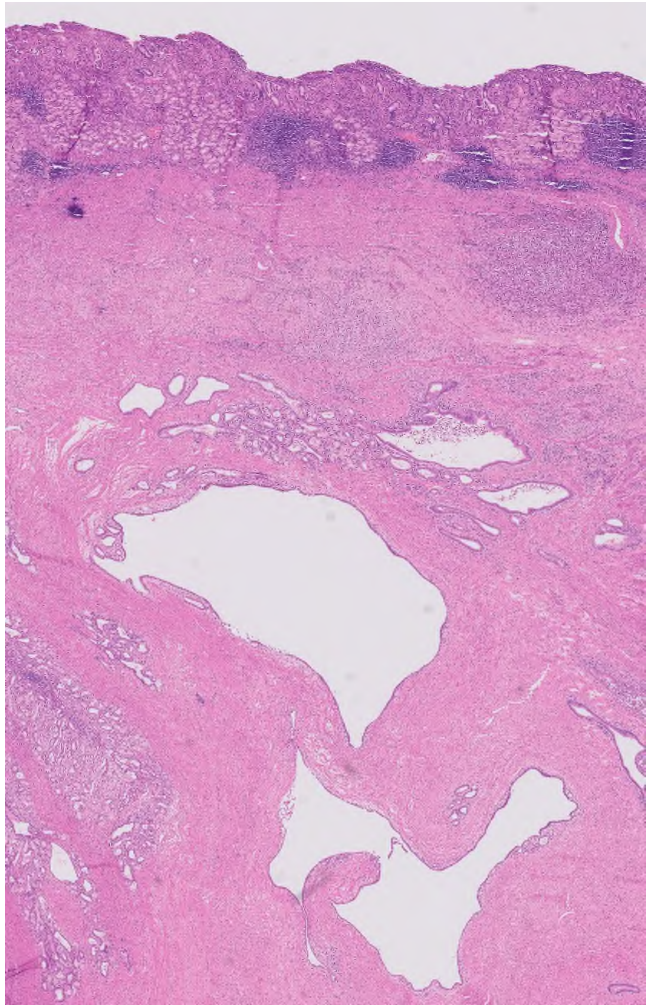
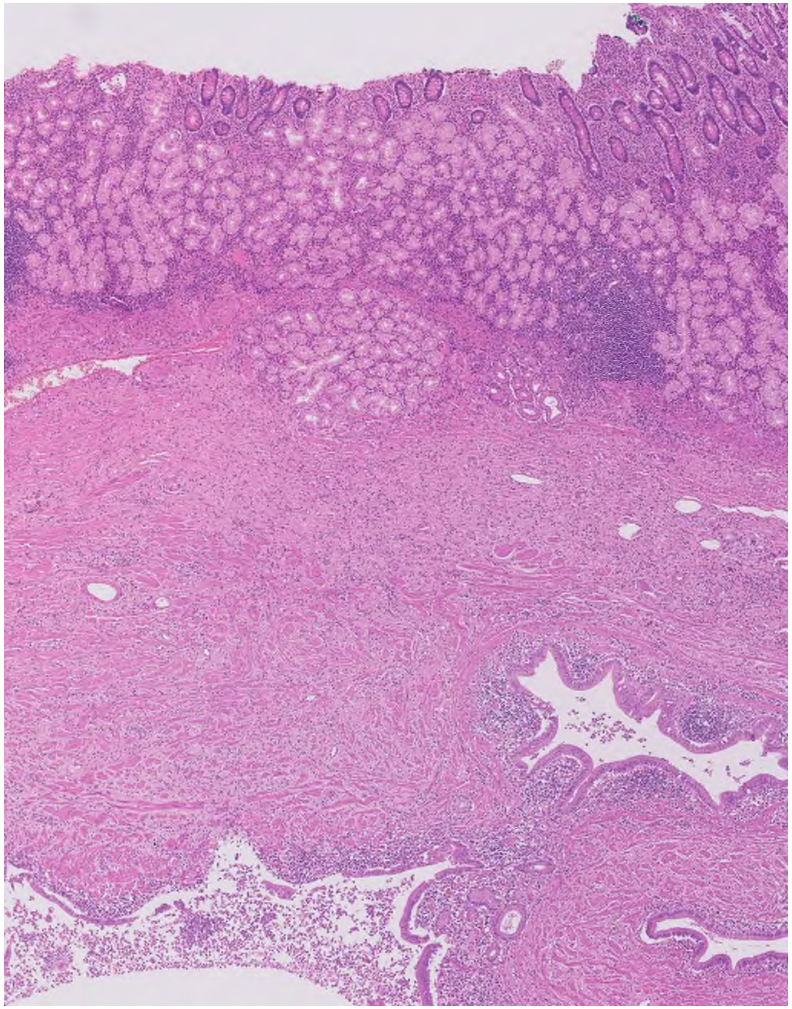
Groove pancreatitis





- Hyperplasia Brunner’s gland
- Ductectasia
- Fibrosis, inflammation

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Conclusion

- Pancreatitis is an inflammatory disorder of the pancreas
- Morphological classification
  - Acute pancreatitis: interstitial / necrotic pancreatitis
  - Chronic pancreatitis: inflammation, fibrosis, atrophy
- Etiology:
  - Frequent causes: bile stones, alcohol
  - Rare: auto-immune pancreatitis (type I/II), Groove pancreatitis ….
- Morphology ~~------~~> Etiology
- No generaly accepted grading of the severity of pancreatitis
- Peritumoral pancreatitis