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REGION

Galdeblæren og galdevejenes patologi

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Patologiafdelingen
Rigshospitalet

Karcinomer i galdeblære og galdeveje

- Ca. 200 nye tilfælde om året i DK
- Uspecifikke symptomer, ofte monosympt. ikterus
- Sen diagnosticering, ofte udbredt sygdom på diagnosetidspunktet

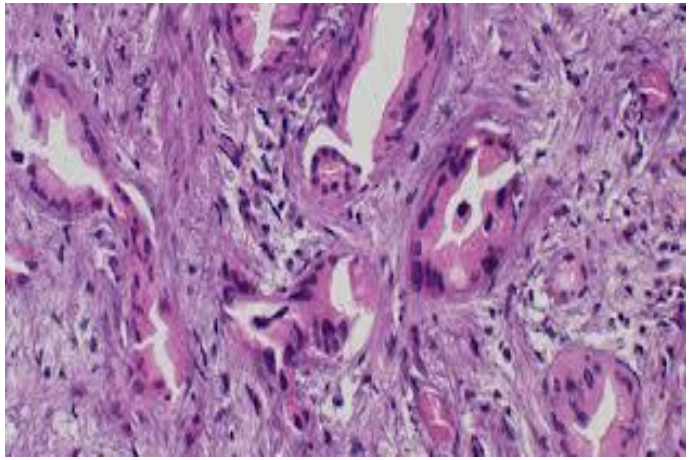
Behandling

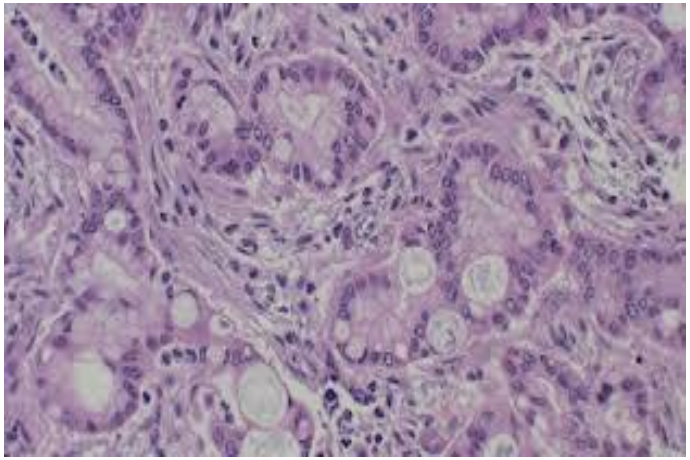
- Kirurgi (mindre end 50% kan op.)
- Adjuverende kemoterapi
- Ca. 30% har effekt af kemobehandling- dog nye muligheder på vej!
- Aflastning med stent eller by-pass

Materiale

- Børstebiopsi, FNA
- Histologisk nålebiopsi
- Resektat
- Frys

- Ofte reaktive forandringer og inflammation

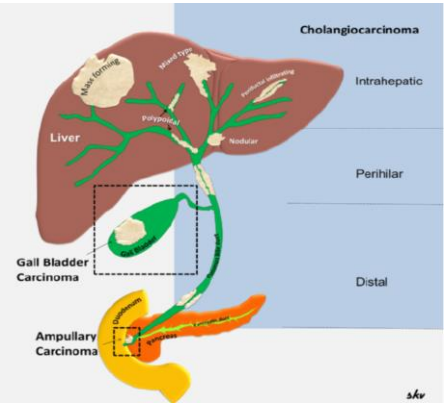




Anatomi

- Cholangiokarcinomer (CCA) udgør en heterogen gruppe af maligne tumorer, som kan udgå fra ethvert sted i galdetræet

- Udfra anatomien inddeles CCA i følgende undertyper:
- - **Intrahepatisk cholangiokarcinom (iCCA)**
- - **Ekstrahepatisk cholangiokarcinom (eCCA)**
  - » Perihilært cholangiokarcinom (pCCA) (til lige over indmundingen af ductus cysticus)
  - » Distalt cholangiokarcinom (dCCA)
- - **Galdeblære cancer (inklusive ductus cysticus)**



Anatomi

- Der er følgende 3 vækstmåder og kombinationer heraf:

- Masseformende (MF) – som udgør de fleste – 60 % og oftest er iCCA.
- Periduktalt infiltrerende (PI)
- Intraduktal vækst (IG)

Intra og ekstrahepatiske galdegange

Benigne og præmaligne

- Galdegangsadenom
- Adenom
- BiiN, low grade
- BiiN, high grade
- IPN-B, low grade
- IPN-B, high grade
- ICPN, low grade
- ICPN, high grade
- MCN, low grade
- MCN, high grade

Maligne

- Cholangiokarcinom
- - Intrahepatisk small duct
- - Intrahepatisk large duct
- Karcinom
- Planocellulært karcinom
- Mucinøst adenokarcinom
- Poorly cohesive karcinom
- IPN-B med associeret karcinom
- ICPN med associeret karcinom
- MCN med associeret karcinom

Biliær intraepitelial neoplasi - BiiN

- Low grade
- High grade

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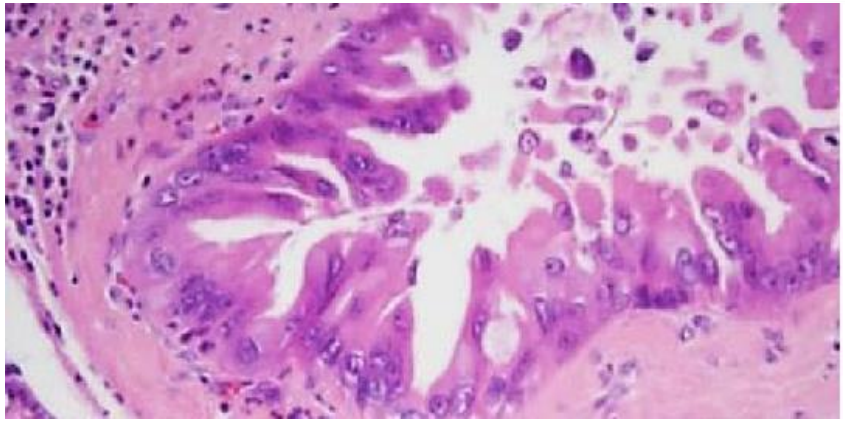

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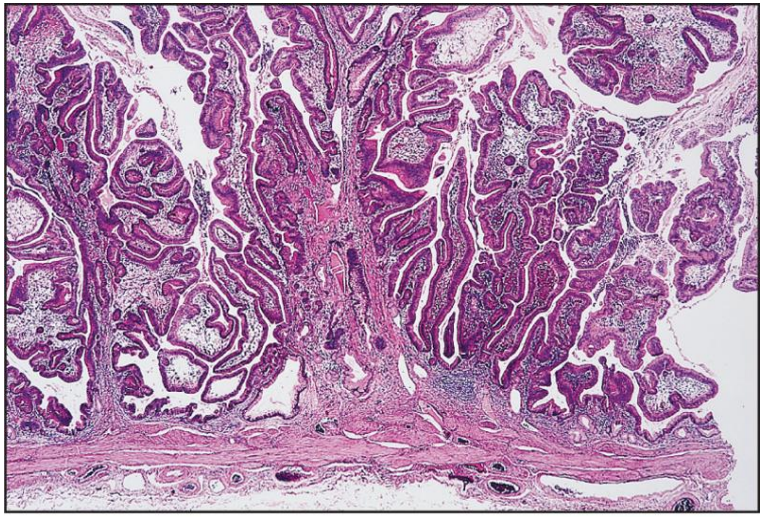
Intraduktal papillær neoplasi – biliær IPN-B

- Biliære, intestinale, gastriske og onkocytære
- F=M, 50-70 års alderen
- Lokaliseret/multifokal
- Invasive foci!



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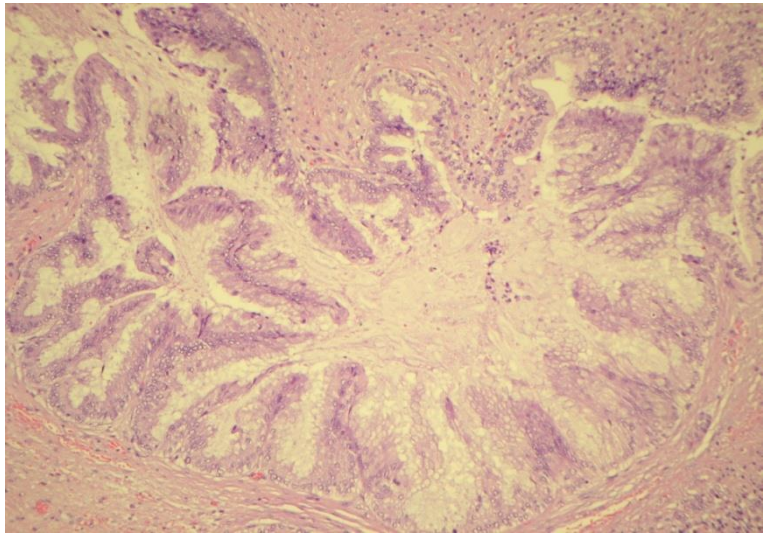

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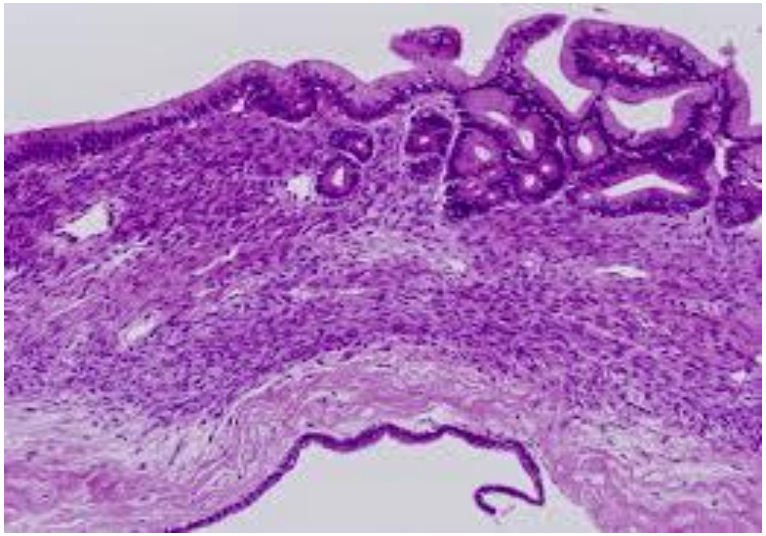
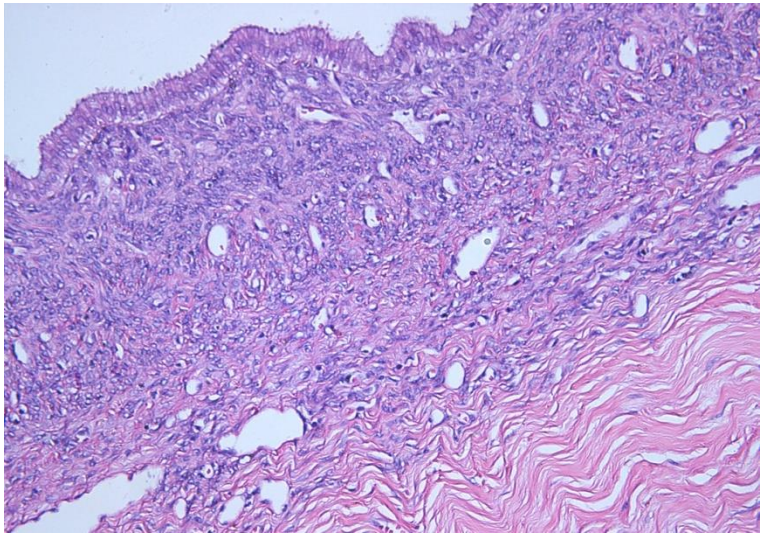
Mucinøse cystiske neoplasier

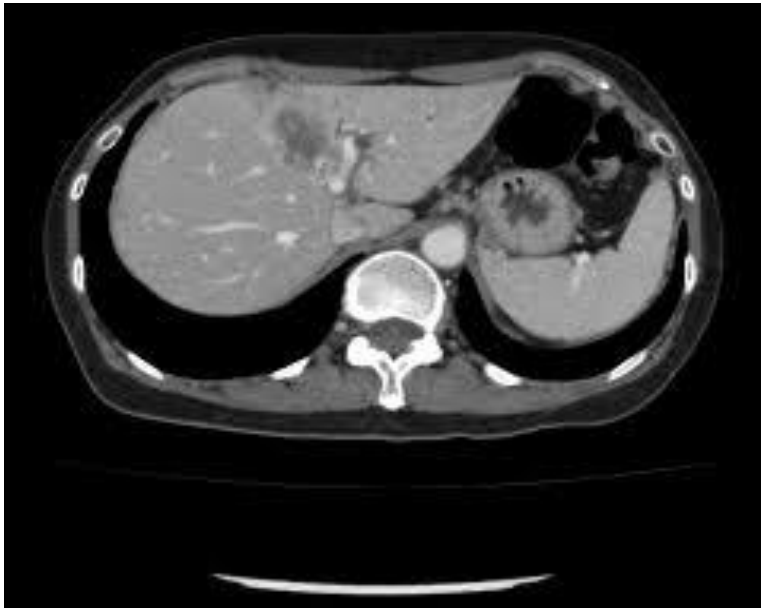
- Yngre kvinder
- Store, multilokulære
- Ovarie-lign. stroma
- Mucinøst epitel
- Dysplasi
- Obs. invasion!





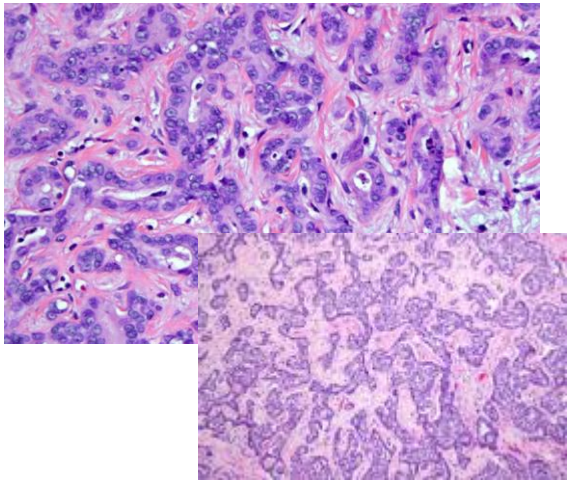
Intrahepatiske CCA

- Kolangiokarcinomer
- Ca. 5-15 % af de primære levercancere
- Øget forekomst
- M>F
- Cirrose (HCV, alkoholisk), HIV, DM, *PSC*, hepatolithiasis, parasitær infestation

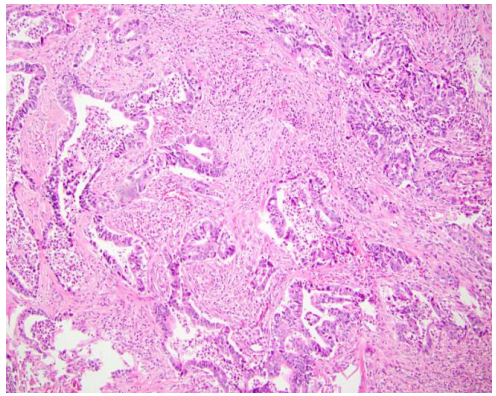


Subtyper af intrahepatisk cholangiocarcinom (iCCA)

	Small duct type iCCA	Large duct type iCCA
Lokalisation	Perifert i leverparenchymet	Proximalt i leveren lige efter pCCA
Makroskopisk vækst	MF (masseformende)	PI (periduktalt infiltrerende) og PI+MF
Risikofaktorer	Ikke biliær cirrose, kronisk viral hepatitis	PSC, hepatolihiasis, leverparasitter
Mucinproduktion	Ikke mucinproducerende kirtler	Mucinproducerende kirtler
Perineural vækst	-/+	++
Udgangspunkt	Små galdegange, galdeductuli, hepatiske progenitorceller	Store intrahepatiske galdegange og peribiliære kirtler
IHC	EMA, CK7, CK19, CD56, CRP	EMA, CK7, CK19, MUC5AC, MUC6, S100P
Mutationer	IDH1/2	KRAS



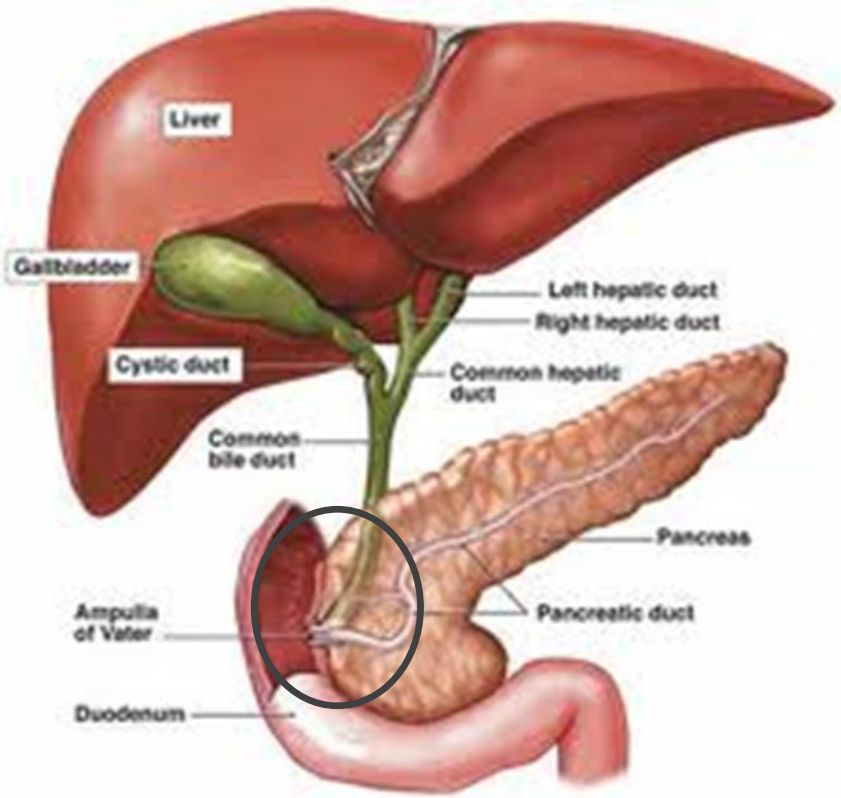
Small duct type



Large duct type

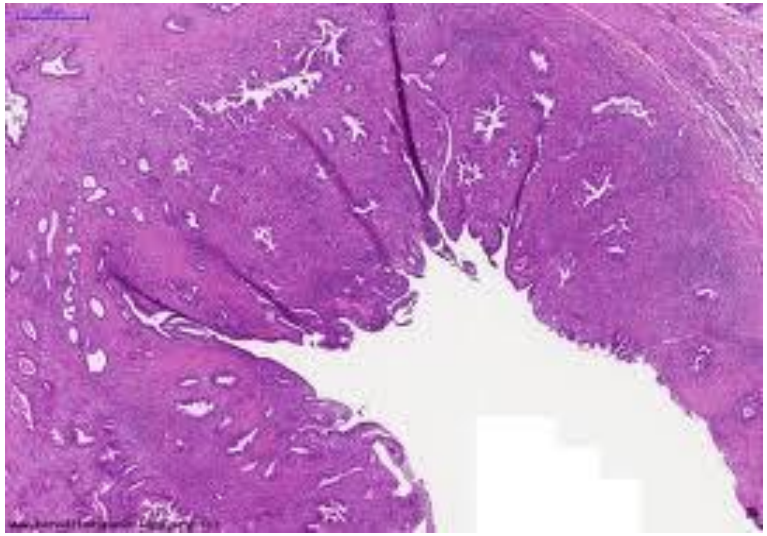
Perihilære CCA

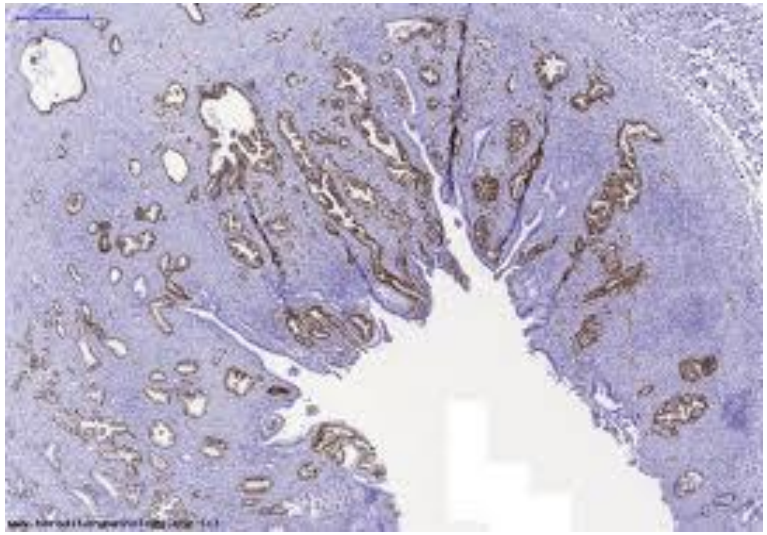
- 60-70 årige
- Ass. med PSC, UC, abnomalier, choledochuscyste, infestationer (asien)
- Tidlige symptomer, ikterus, evt. kolangitis
- Ofte lokaliseret distalt



Distale CCA - choledochus cancer

- Ofte indvækst i pancreas og duodenum
- Kan være svær at skelne fra adenokarcinom i pancreas





Molekylære karakteristika

- Genetiske (ECC) og epigenetiske (ICC) forandringer
- Ofte mange lavfrekvente forandringer, stor heterogenicitet
  - TP53, KRAS, NF1, SMAD4, ARID1A, FGFR2
  - IDH1, BAP1

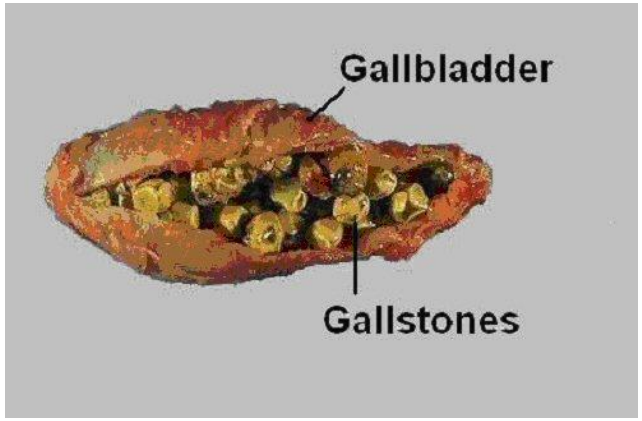
- Op mod 10% har germline forandringer
  - BRCA, MMR
- Betydning for behandling og genetisk rådgivning af familie

TNM 8 for galdeveje

- Intrahepatiske
- Perihilære
- Ekstrahepatiske
- Galdeblæren

Har hver sin TNM-klassifikation !

Lithiasis



- Kolesterolsten
  - 80 %
  - Primært kolesterolkrystaller
- Non-kolesterolsten (= pigmenterede sten)
  - Sorte sten
    - Meget lavt kolesterolindhold
  - Brune sten
    - Bakterielle nedbrydningsprodukter
- Ca.10-20% i DK, F>M
- Øget lipidindhold i blodet
- Østrogentilskud, P-piller
- UC, Mb.Crohn
- Overvægt
- Familiær ophobning

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Akut cholecystitis

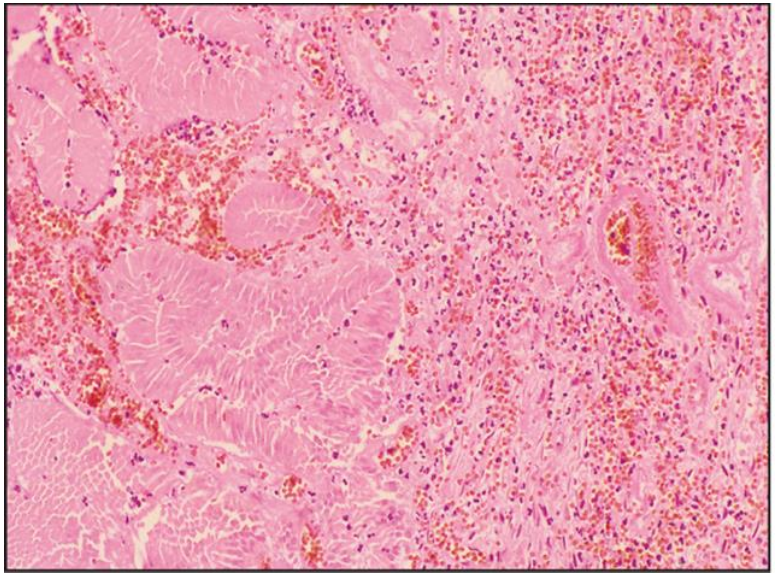
- Kvinder, 50-70 år
- 90 % associeret med galdesten
- Klinik:
  - Smerter øvre hø. kvadrant
  - Feber, leukocytose
  - Mortalitet 4% (!)

Makroskopisk

- Nekrose, pus
- Serosa: mat, fibrinopurulent exudat

Histologi

- Akut inflammation
- Ødem
- Nekrose
- Blødning



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Kronisk cholecystitis

Næsten altid assoc. med galdesten

Mekanisme?

- Serie af subkliniske akutte cholecystitis-tilfælde?
- Traumer mod slimhinden?

Klinik: smerter

Makroskopisk

- Erosion/ulceration
- Tykvægget, fibrøs
- Adhærencer på serosa

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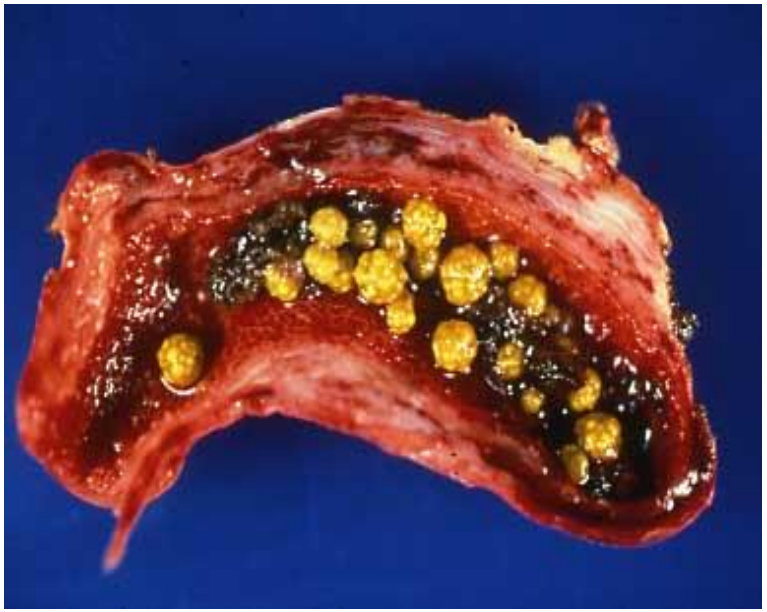

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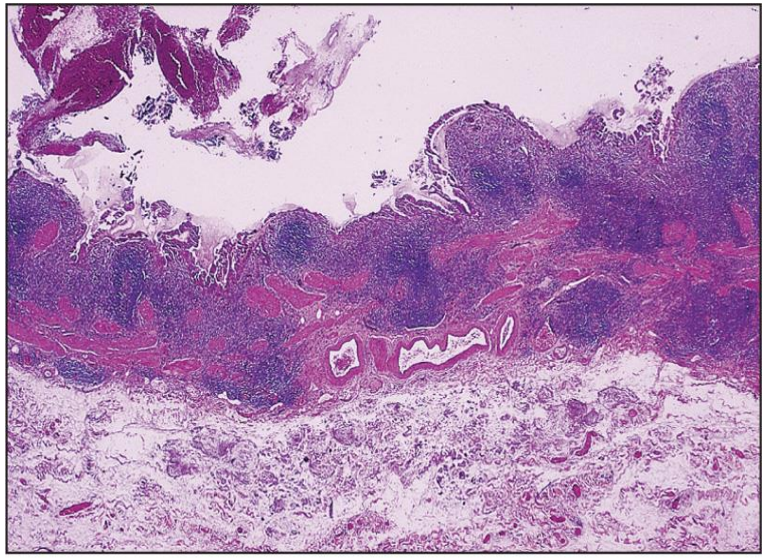
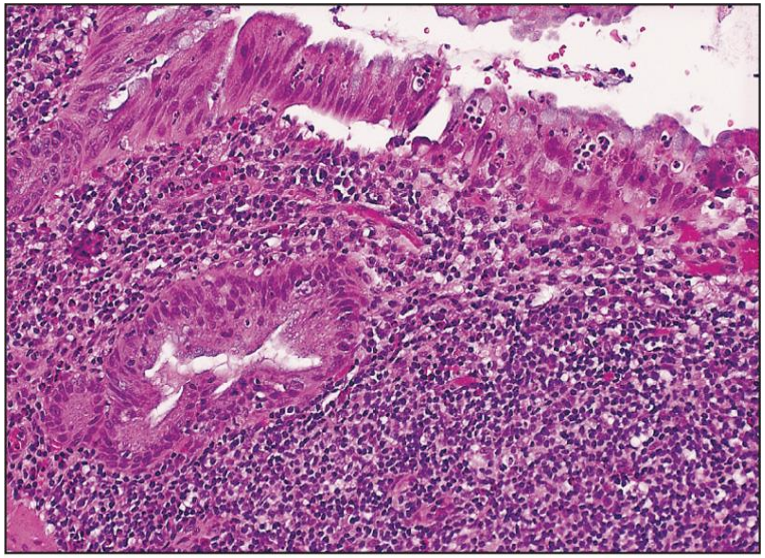
Kronisk cholecystitis

- Mononukleært betændelses-infiltrat
  - m/u udbredning til lamina muscularis el. pericholecystiske bindevæv
- Fibrose
- Metaplasi





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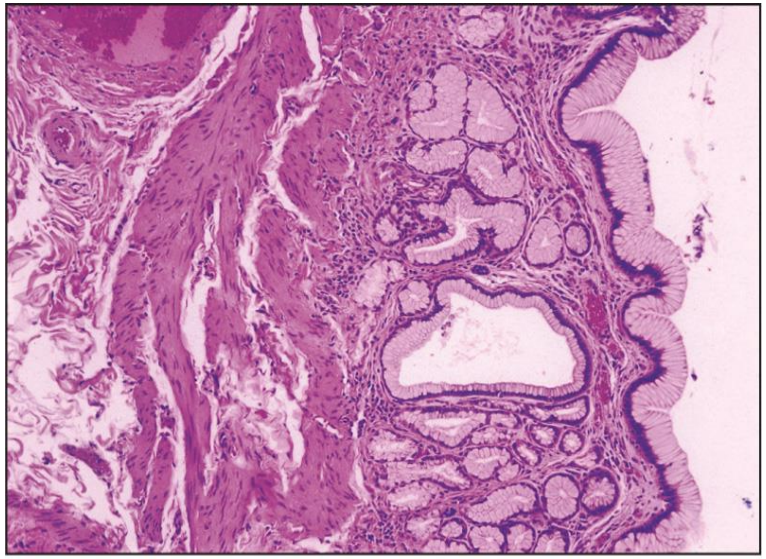

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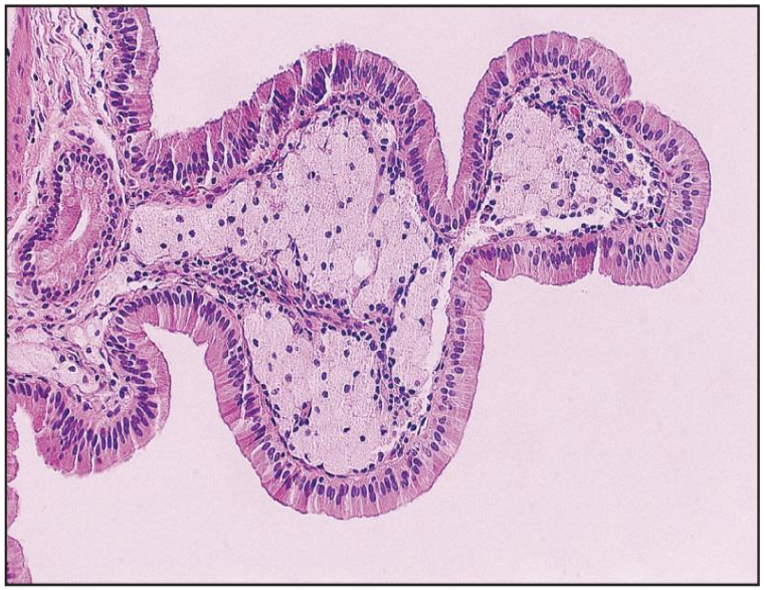
- **Kolesterolose**
  - Aggr. af lipid-holdige makrofager i lamina propria
  - Skyldes overmættet galde
  - Eksakt mekanisme ikke kendt
  - Hos 20 % - ofte samtidig med galdesten

- **Xanthogranulomatøs cholecystitis**
  - Fibrose-inducerende



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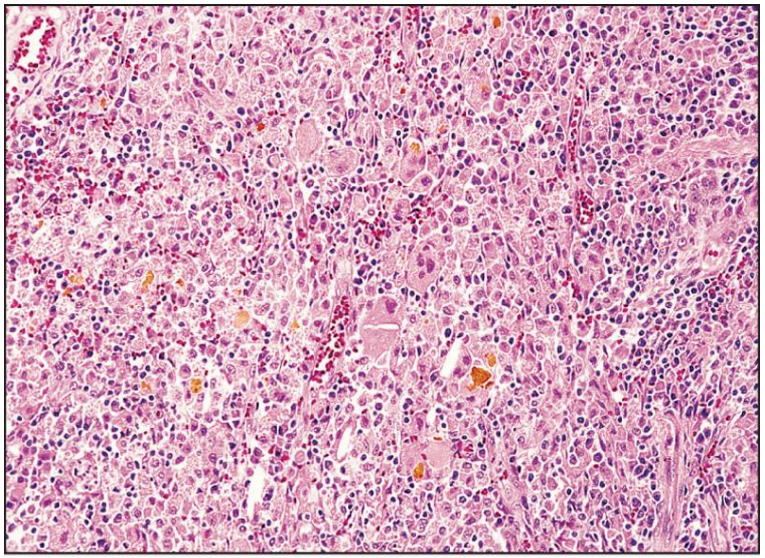

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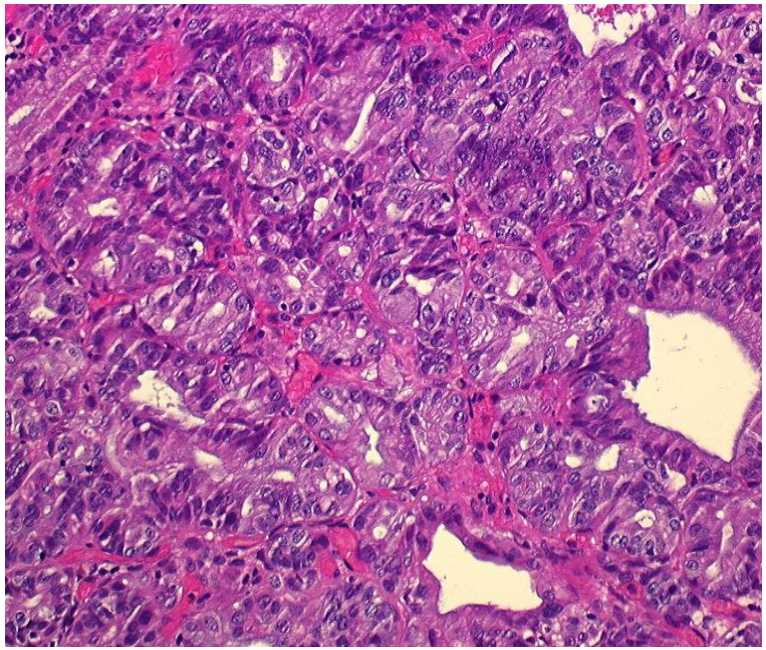
Pyloruskirtel adenom

- Ca. 0,3-0,5% af cholecystektomier
- F>M
- Ass. med lithiasis
- Evt ass. med syndromer, PJ, Gardner



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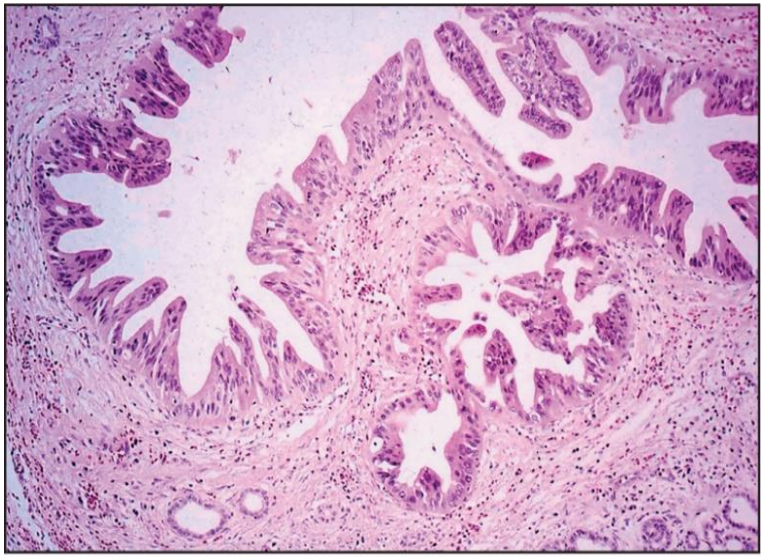
Biliær intraepitelial neoplasi

- Mikropapillære strukturer
- Ass. kronisk cholecystitis
- BilIN 3 i 0,5-3% af cholelithiasis
- Pylorisk/intestinal metaplasi
- Ofte ass. med karcinom



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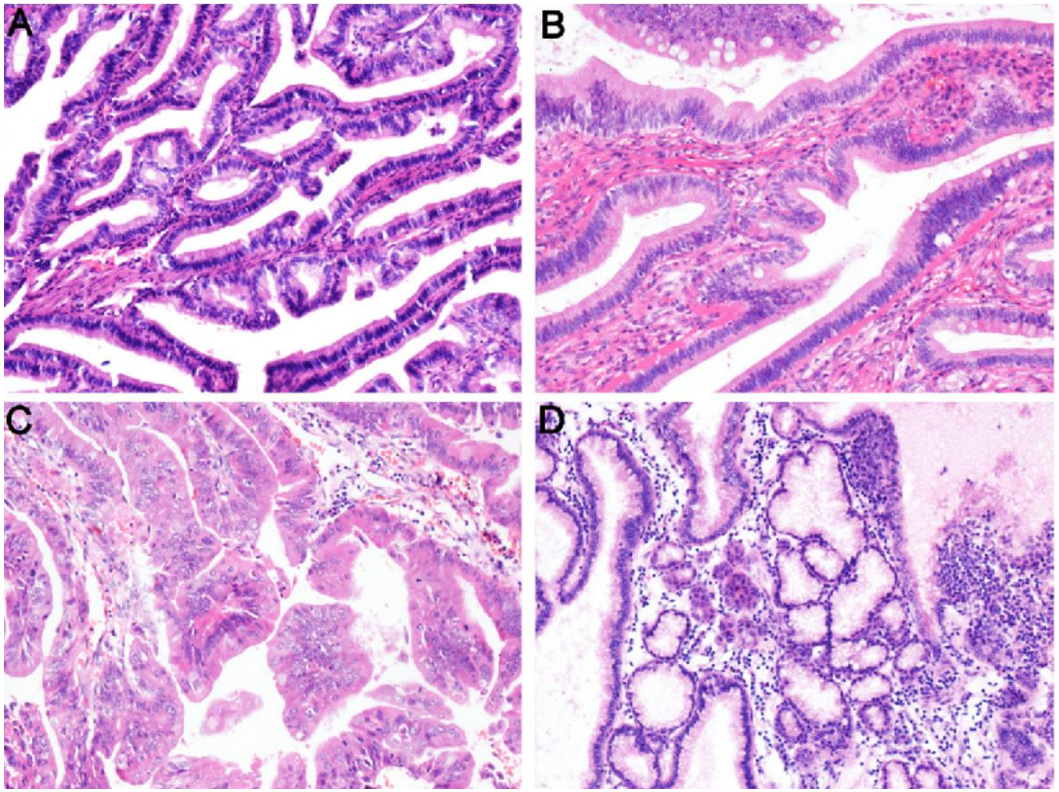
Intracystisk papillær neoplasi - ICPN

- Bililær (A)
- Intestinal (B)
- Oncocytær (C)
- Gastrisk (D)



Gallbladder papillary neoplasms share pathological features with intraductal papillary neoplasms of the bile duct
Xueshauai Wan et al. Oncotarget 2017 May 9;8(19):31532-31539

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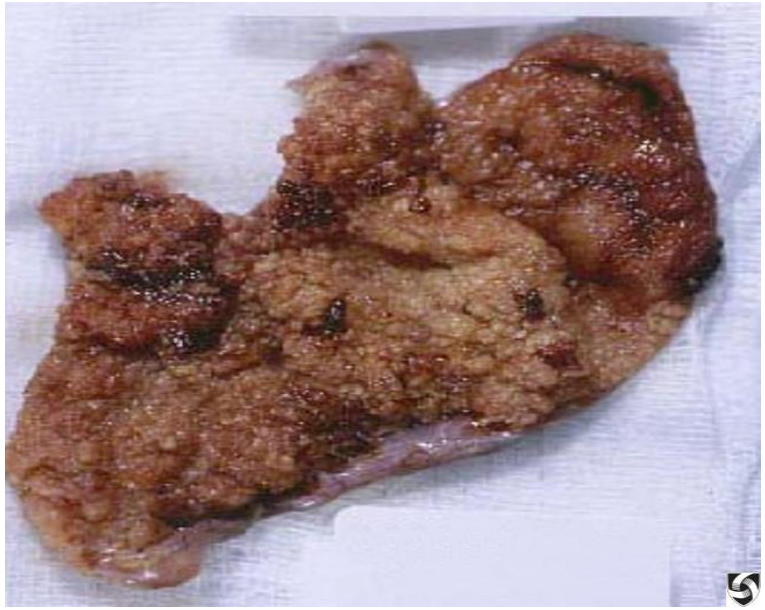
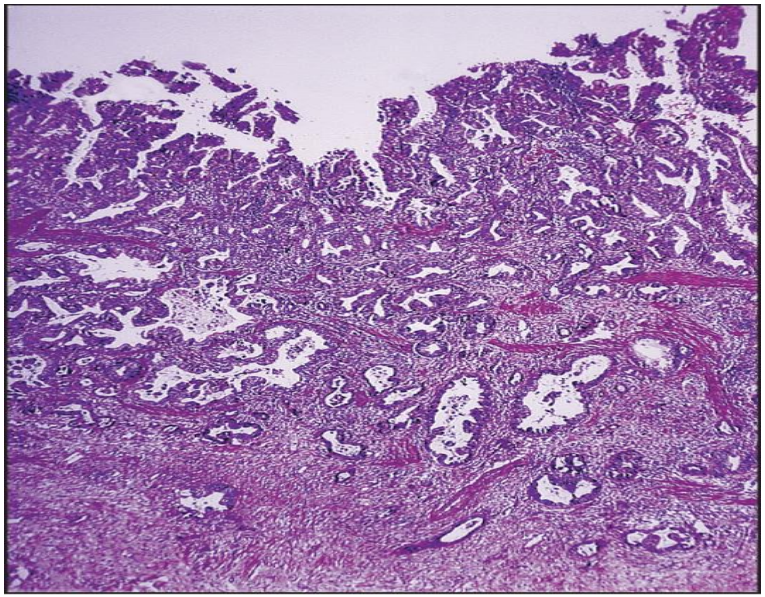
Karcinomer

- 60-70 årige, F>M
- Ass. galdesten, anomalier, FAP, PSC
- Tilfældigt fund, sympt. svt. cholelithiasis
- AC, biliær, intestinal eller foveolær type
- Adenoskvamøse, clearcelle, signetrings celle, mucinøse





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