Lancaster Liver Up-date 2007

Slides before tea : BP

Case 1
47 year old man

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Case 1 : clinical information

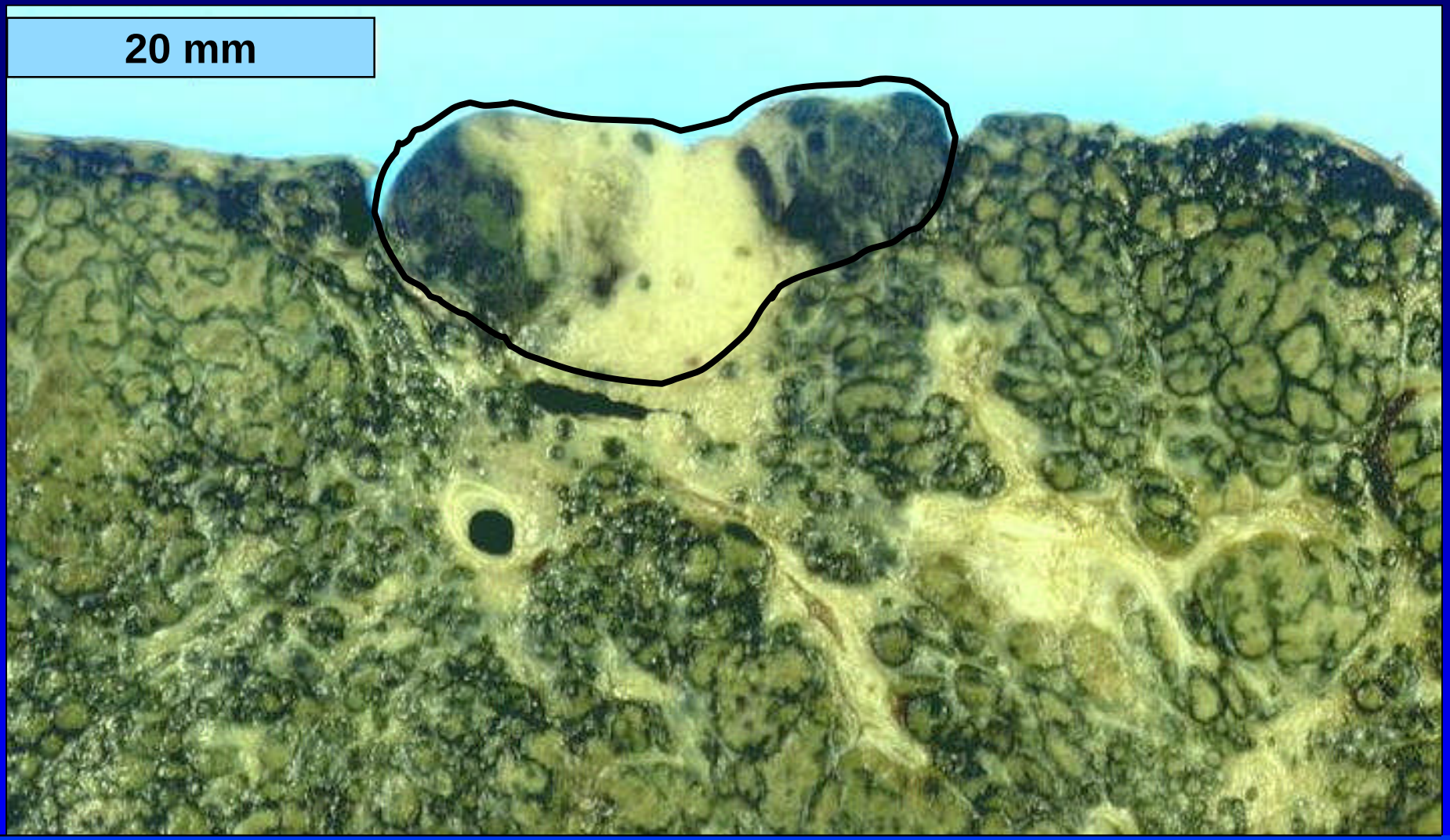
47 year-old man

- Referred at age 33 for sclerotherapy of oesophageal varices
- ERCP : stricture / beading of intrahepatic bile ducts ⇨ sclerosing cholangitis
- No evidence of colitis

Case 1 : clinical information

- In 1989 (age 44) liver function deteriorated
- Hepatic angiogram revealed a 3 cm mass in upper part of right lobe
- Serum α-fetoprotein (AFP) level 1500 ng/ml

- Hepatic arterial chemoembolisation
  ⇨ AFP down to 100
  ⇨ subsequently rose to 700 over 6 months
- Nov 1991 liver transplantation

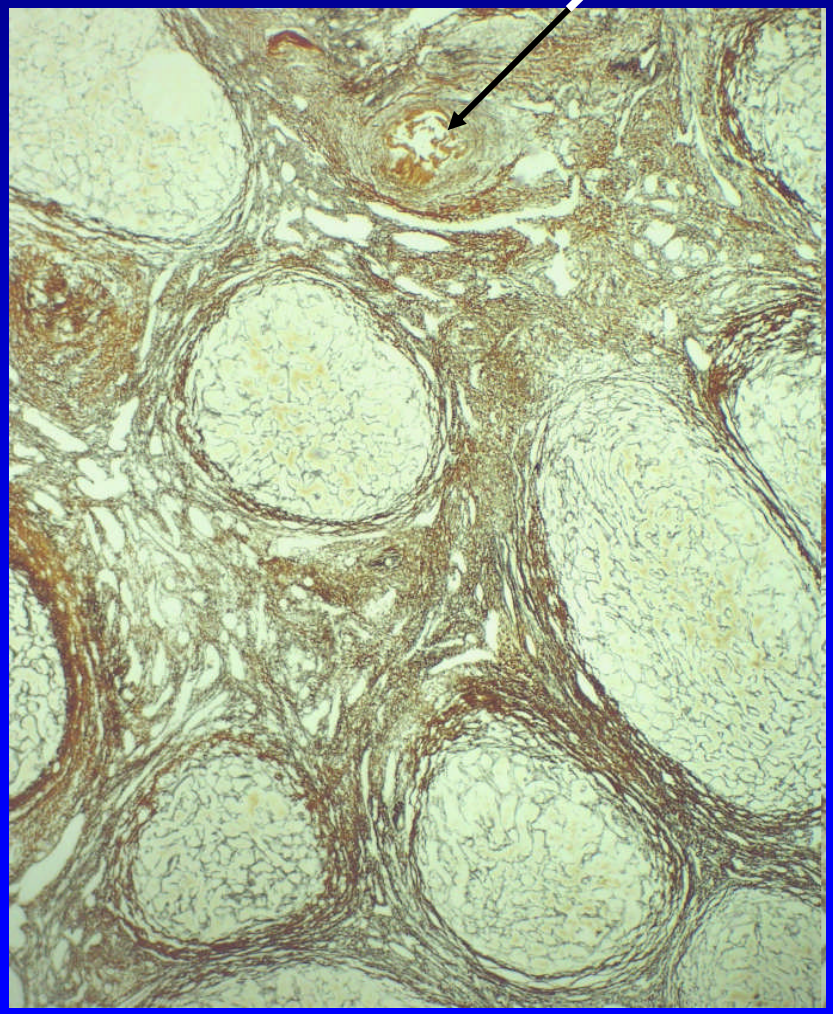


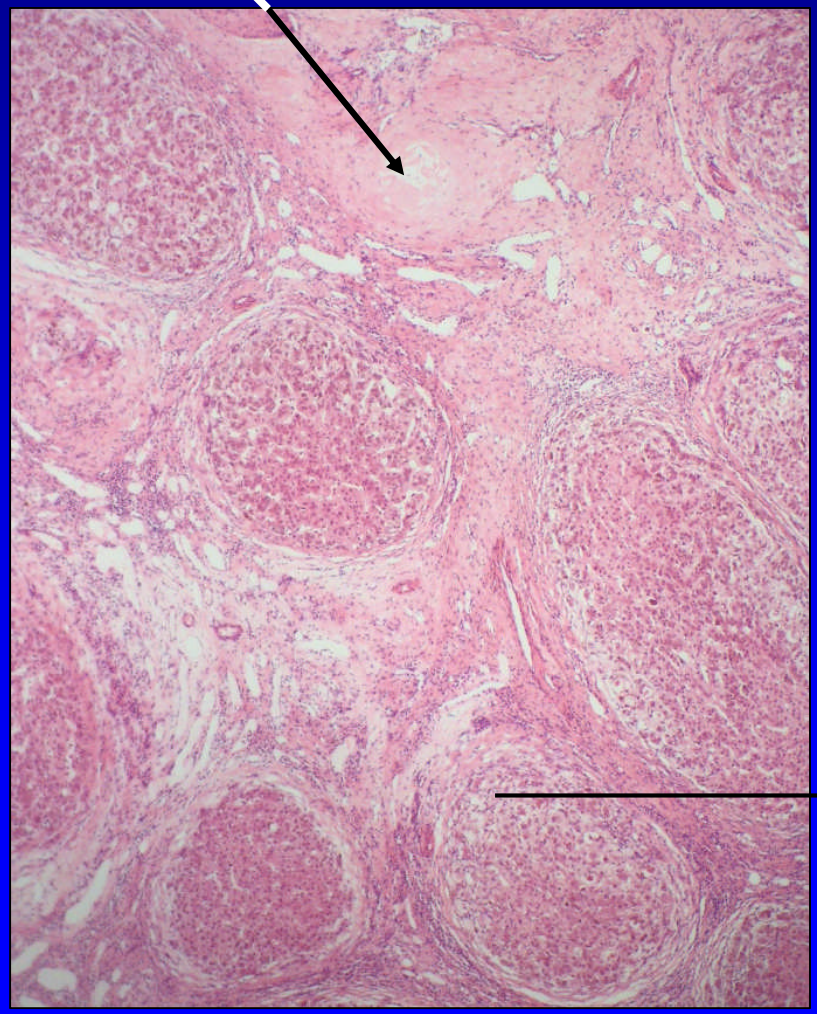
- **Explanted liver 1620g**
- **Micronodular cirrhosis + perinodular cholestasis**

Biliary cirrhosis

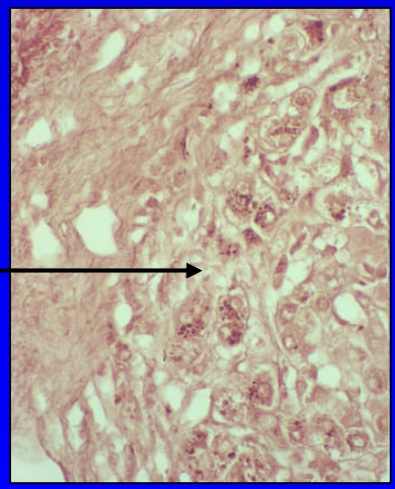
Secondary to sclerosing cholangitis
- small duct disease

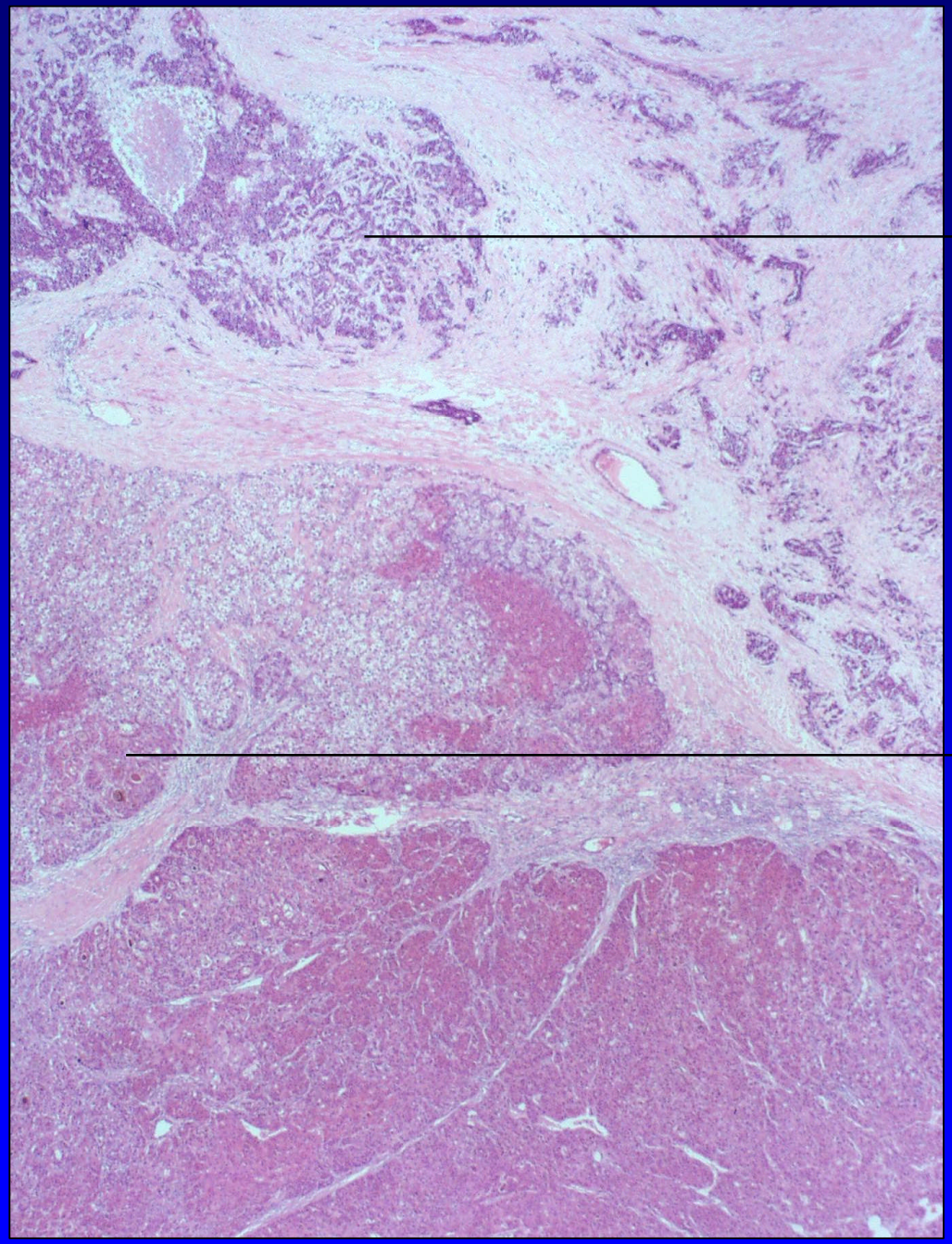
Fibro-obliterative bile duct lesions

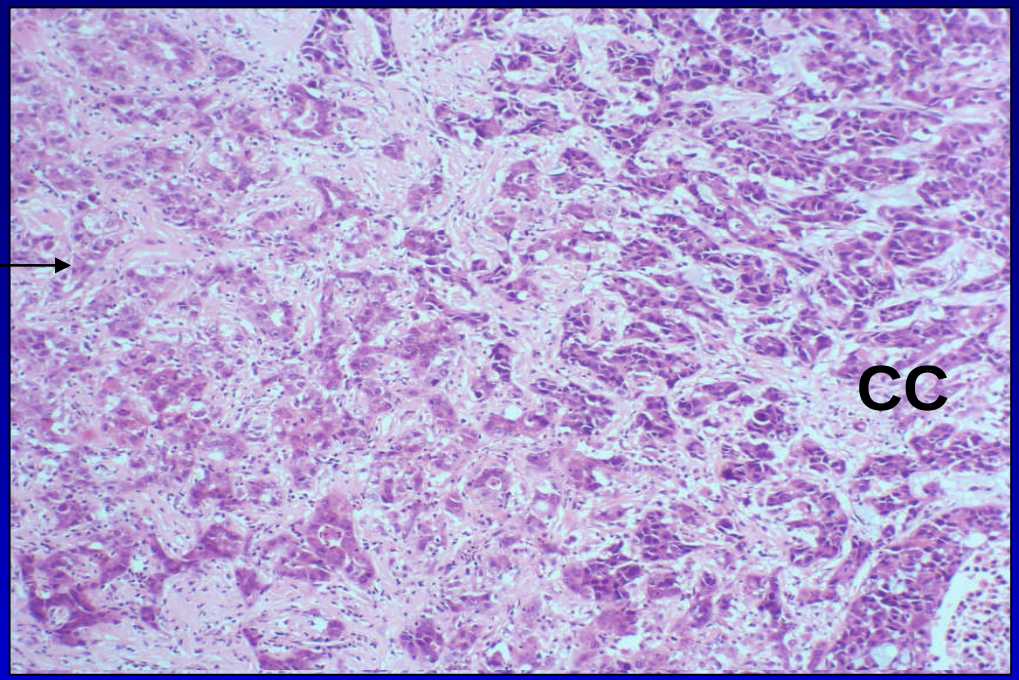




Orcein



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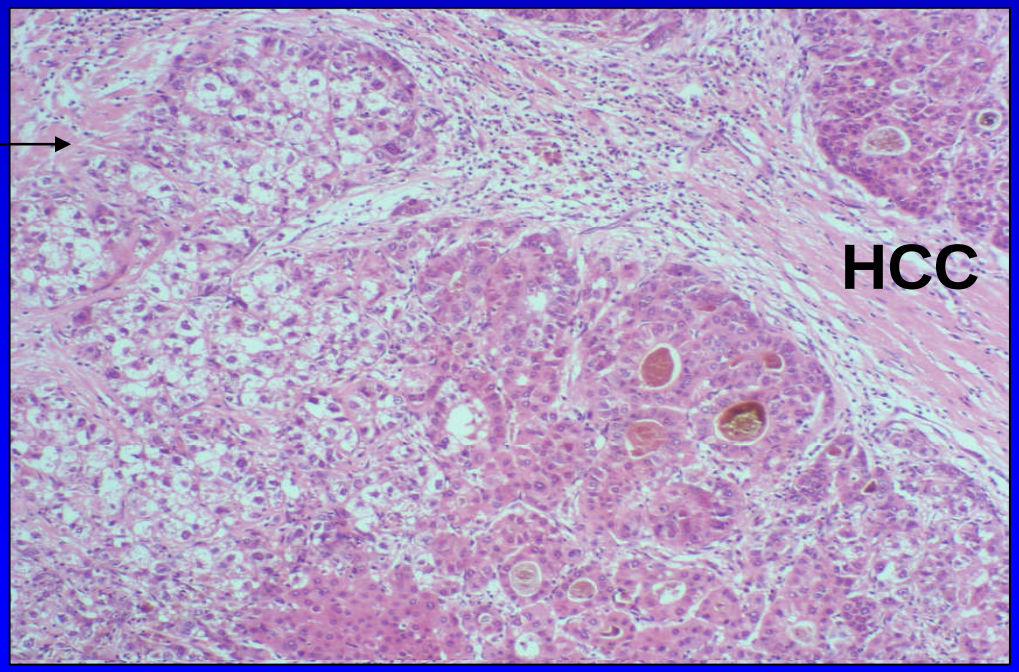
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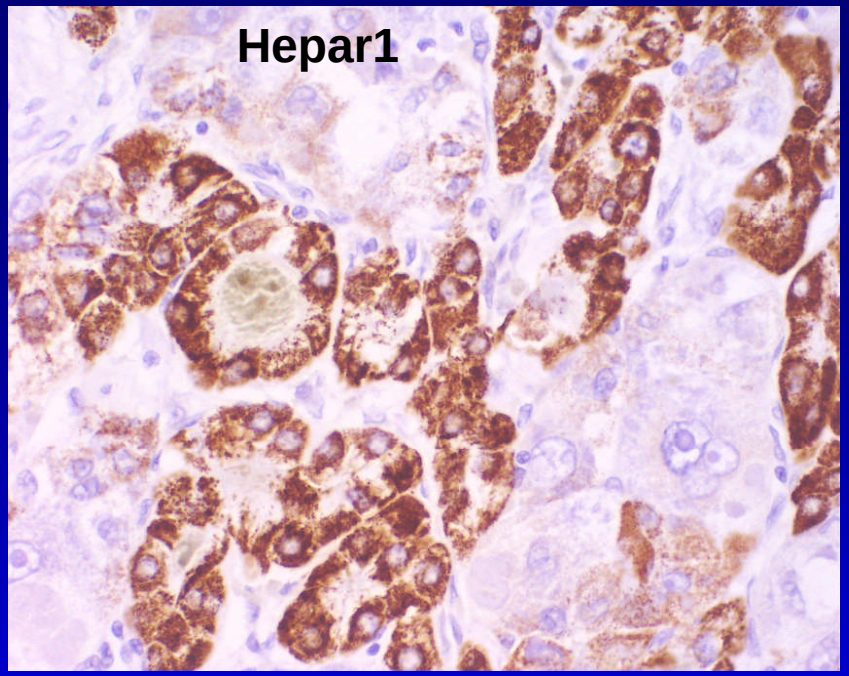

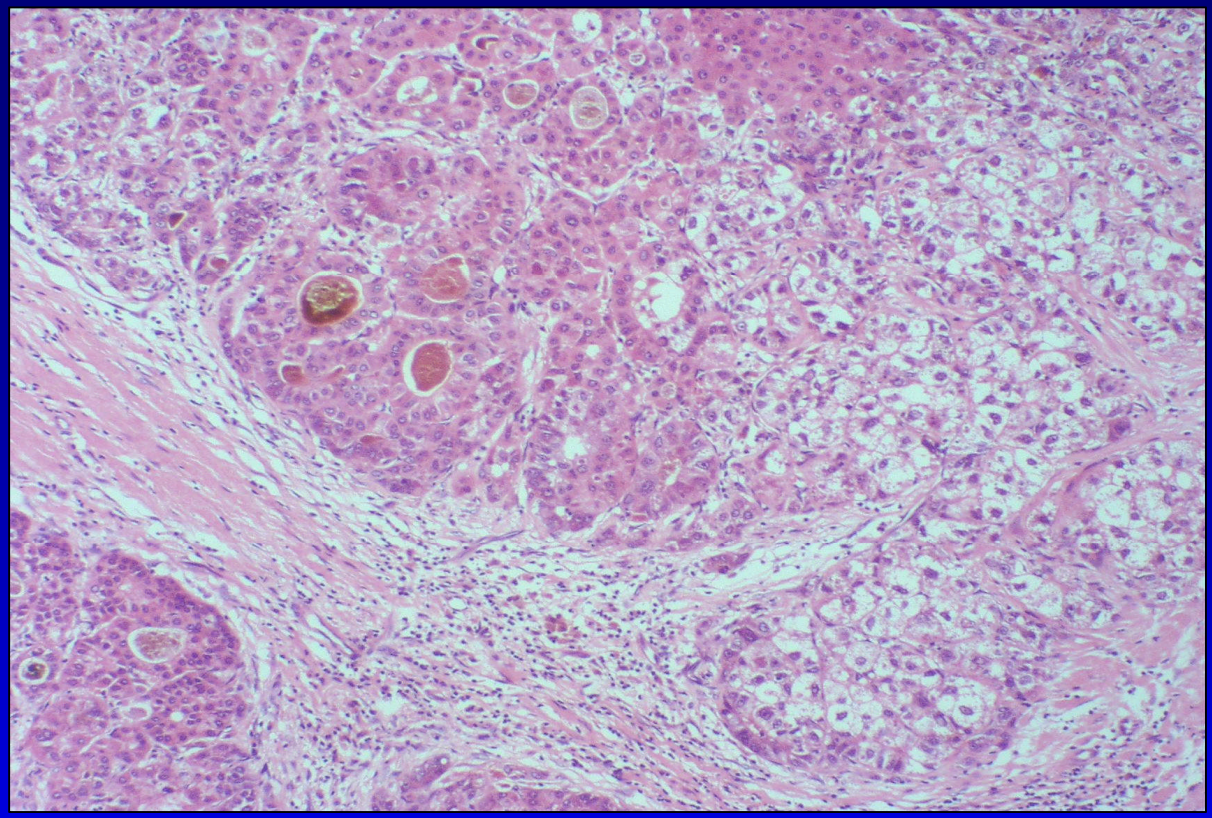

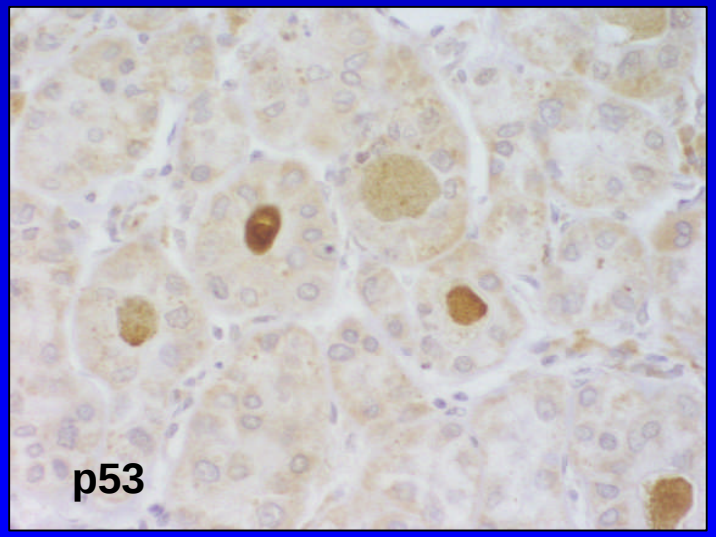

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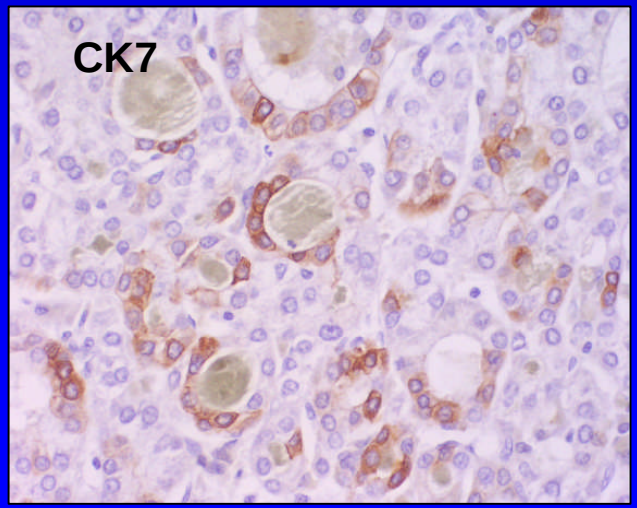

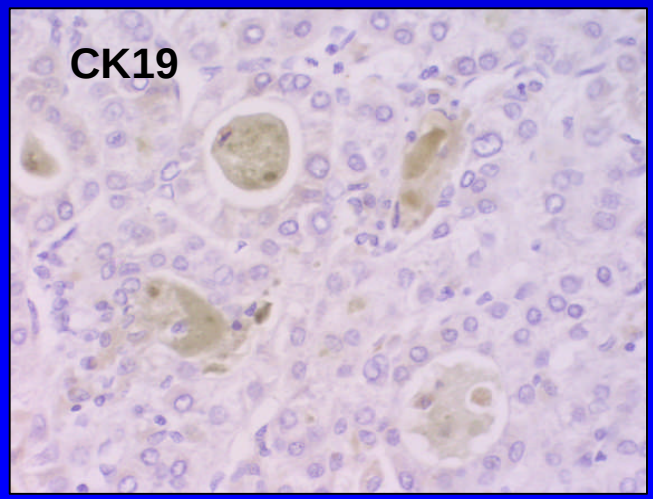

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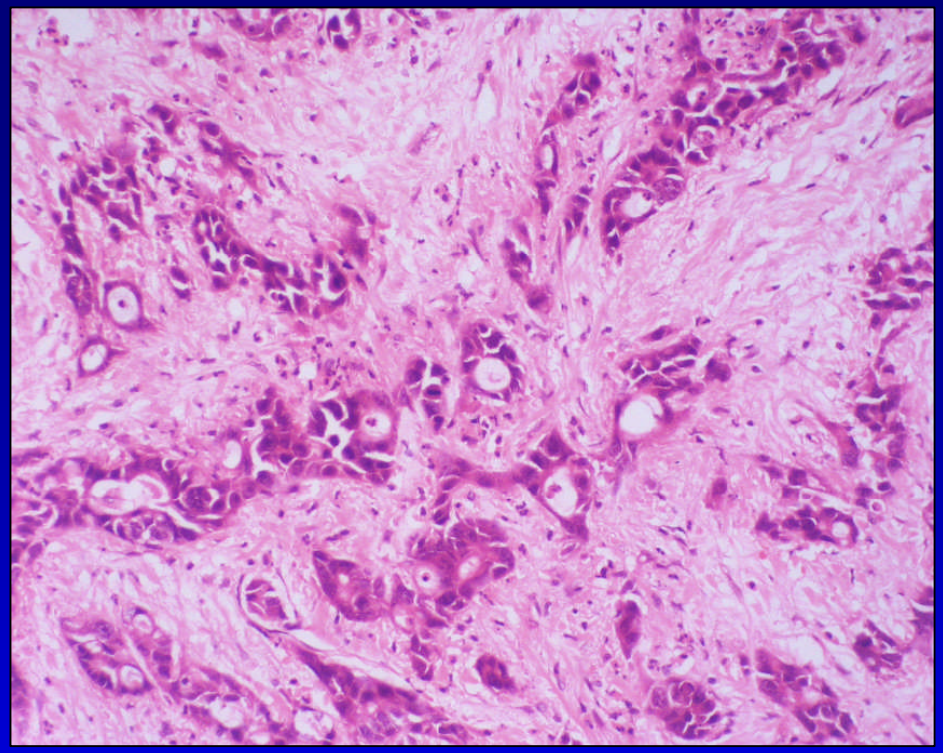

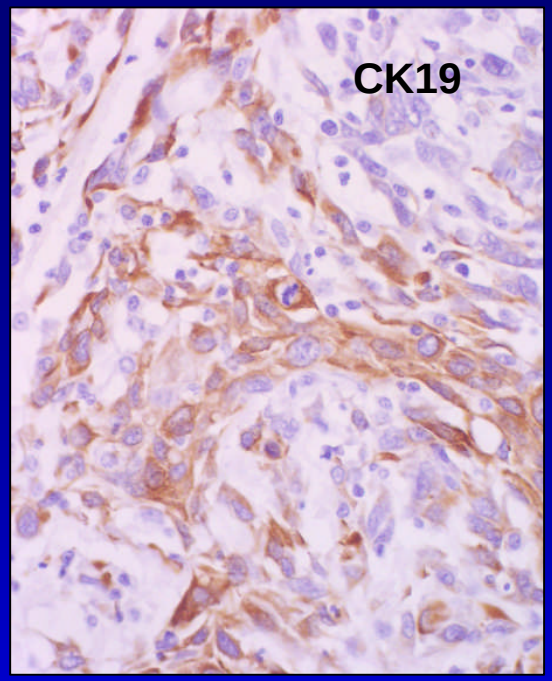

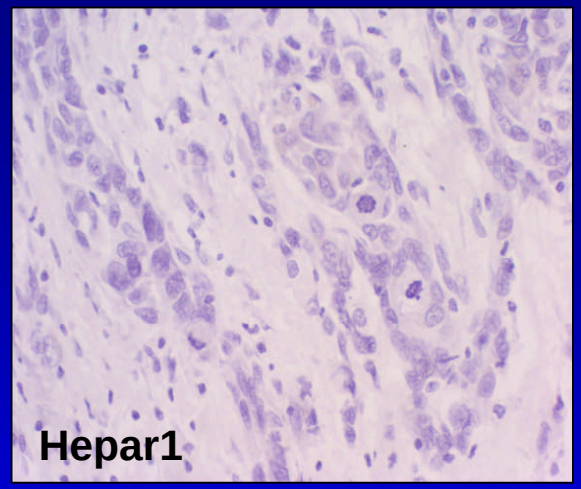

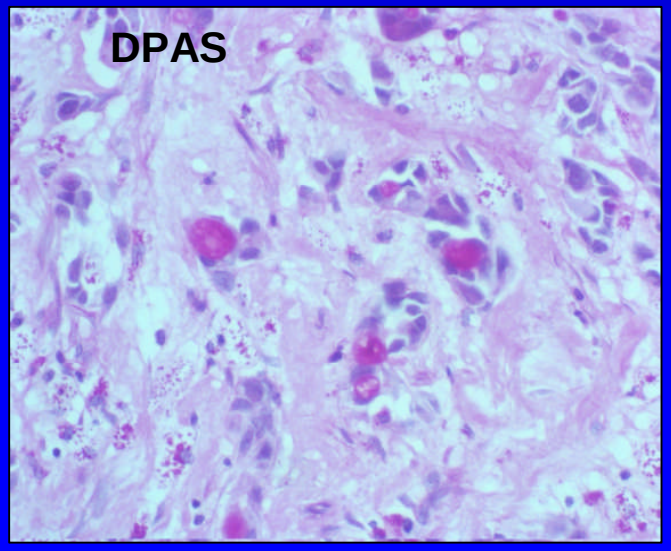

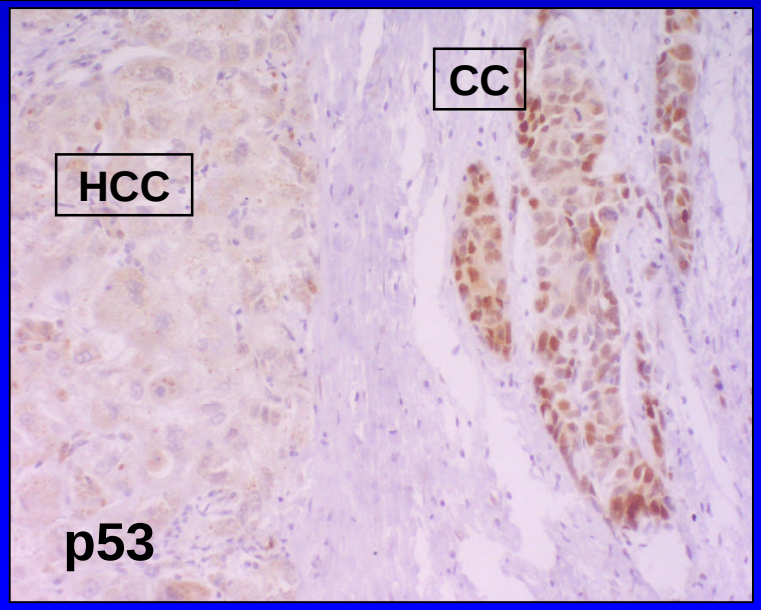

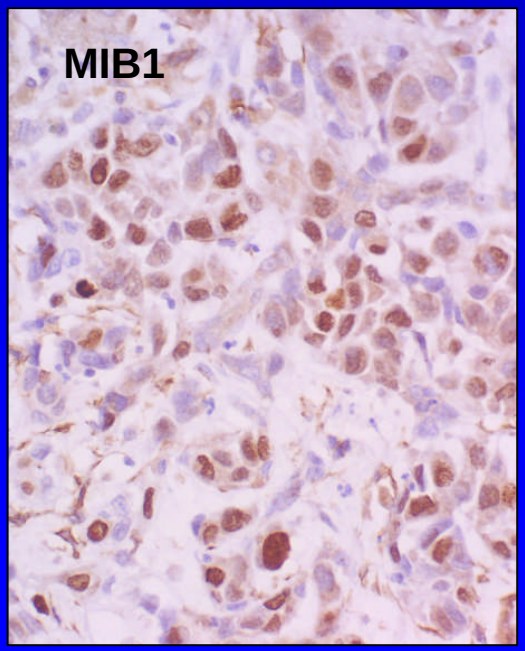

Case 1 : Diagnosis

- Combined hepatocellular carcinoma / cholangiocarcinoma (transitional type) peripheral tumour
- Biliary cirrhosis due to intrahepatic sclerosing cholangitis

Follow up

- Eight months after OLT : ascites due to intraperitoneal dissemination of poorly differentiated carcinoma (CK7 / CK19 +) in keeping with CC
- Died 6 months later from carcinomatosis

Sclerosing cholangitis

⇨ 10% or more increased risk of CC

- Tumour generally affects major bile ducts in a perihilar location
- HCC is occasionally reported
- Present case unusual
  - peripheral location
  - combined HCC and CC

Combined hepatocellular-cholangiocarcinoma

- Primary liver cancer with features of both hepatocellular and biliary epithelial differentiation in variable combination

Goodman et al **N=24**

- **Collision tumours (4)**
- **Transitional tumours (12)**
- **Fibrolamellar tumours (8)**

Haratake et al **N=13**

- **Separate tumour (2)**
- **Collision type (6)**
- **Intermingled type (5)**

Differential diagnosis HCC / CC

	HCC	CC
• EMA, CK7 / 19, AE1	–	++
• CAM 5.2	±	++
• pCEA [CD10]	+ (canaliculi) [+]	± [-]
• Hepar 1	+	–
• AFP	±	–
• Albumin ISH	+	–
• CA19-9	–	+
• p53 (Immuno)	±	++

Combined hepatocellular / cholangiocarcinoma

- Actual prevalence not certain
  (histology alone *vs* immuno – extent of CC features)
- CC component generally more aggressive
- Combined tumours have a worse prognosis
  than pure HCC, but better than CC alone

Liu CL, et al. Arch Surg. 2003;138:86
Koh et al Am J Surg 2005;189:120

- In one series, 28% of HCCs contained cells
  expressing CK7 and/or CK19
- Recurrence rate after OLT higher in CK19+HCC

Dumez A et al. Histopathology 2006;49:138

Pathogenesis / morphogenesis

- **Progenitor cell origin speculated on immunohistochemistry**

Kim H et al, J Hepatol. 2004;40:298
Dumez A, et al. Histopathology 2006;49:138

- **Molecular analysis**

1. Collision tumours : 2 independent neoplastic clones
2. Single clonal tumour
3. Single clonal process with mosaic of closely related subclones

Fujii H, et al. Hum Pathol. 2000;31:1011

⇨ Case 2

Lancaster Liver up-date 2007

Slides before tea

Case 2
9 year old boy

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9 year old boy **(born 1/2/1998)**

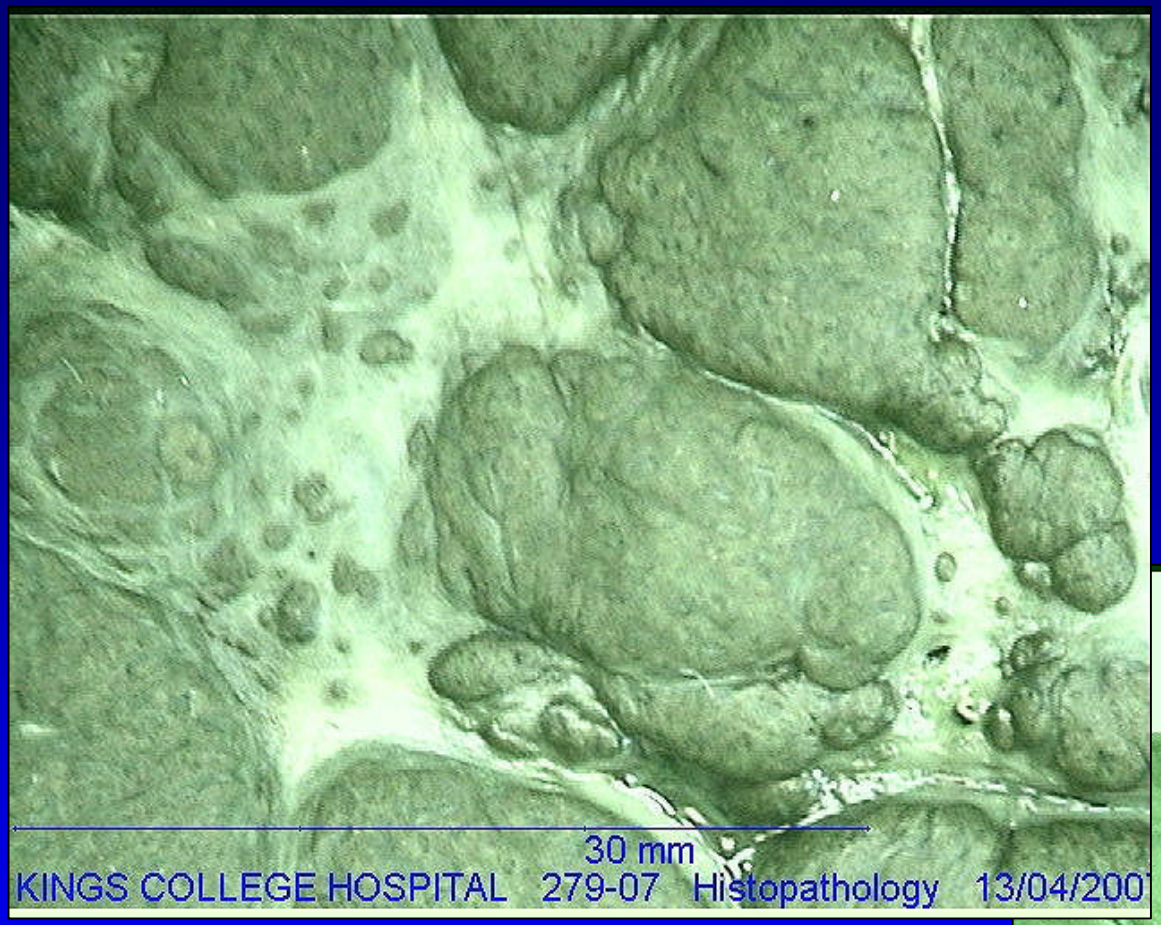
- **At age 3 weeks : diarrhoea + failure to thrive**
- **Several admissions in infancy for respiratory problems**

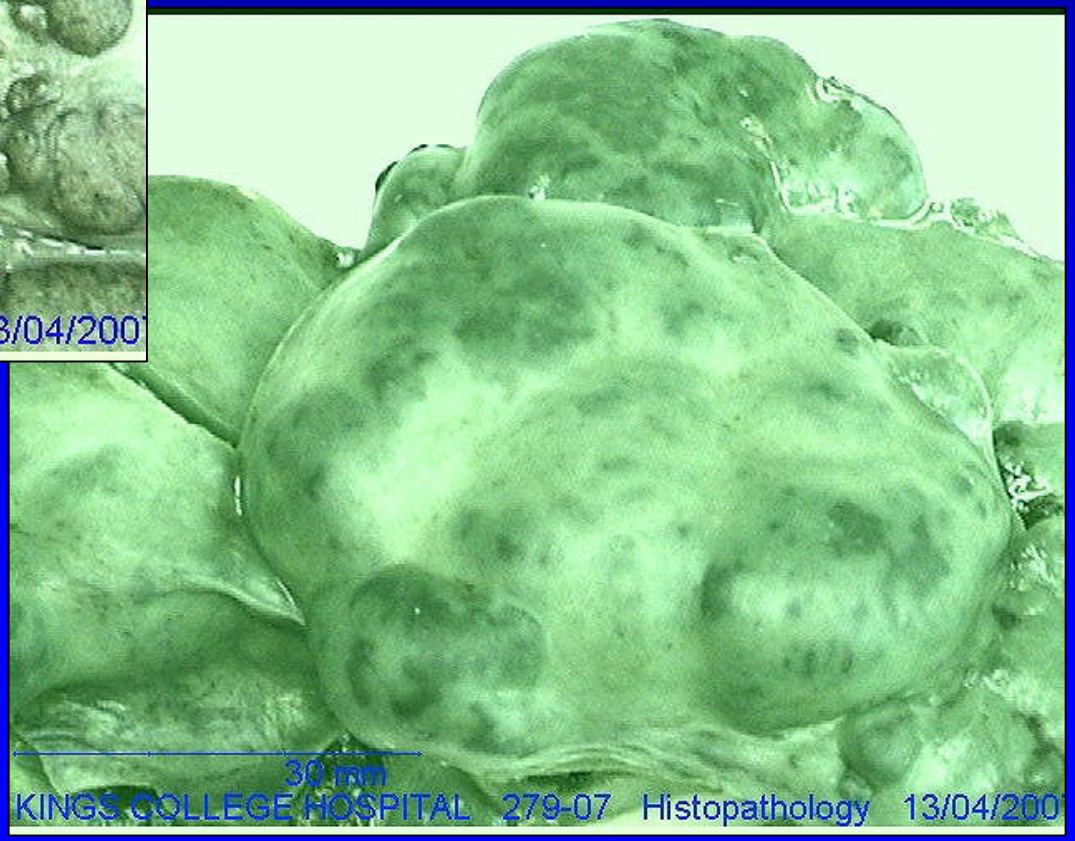
- **Diagnosed with cystic fibrosis when aged 3 (Compound heterozygote for ΔF508 and 1717-1GA)**

- **In 2005 admitted for deteriorating liver function with ascites**
- **LB : marked steatosis + focal biliary fibrosis**
- **Jan 15, 2007 referred for end-stage liver disease**
  - Acute renal failure
  - Vancomycin-resistant *Enterococcus* sepsis
  - Malnutrition - Refractory ascites

⇨ **Liver transplantation on 1 / 2 / 2007**

Case 2

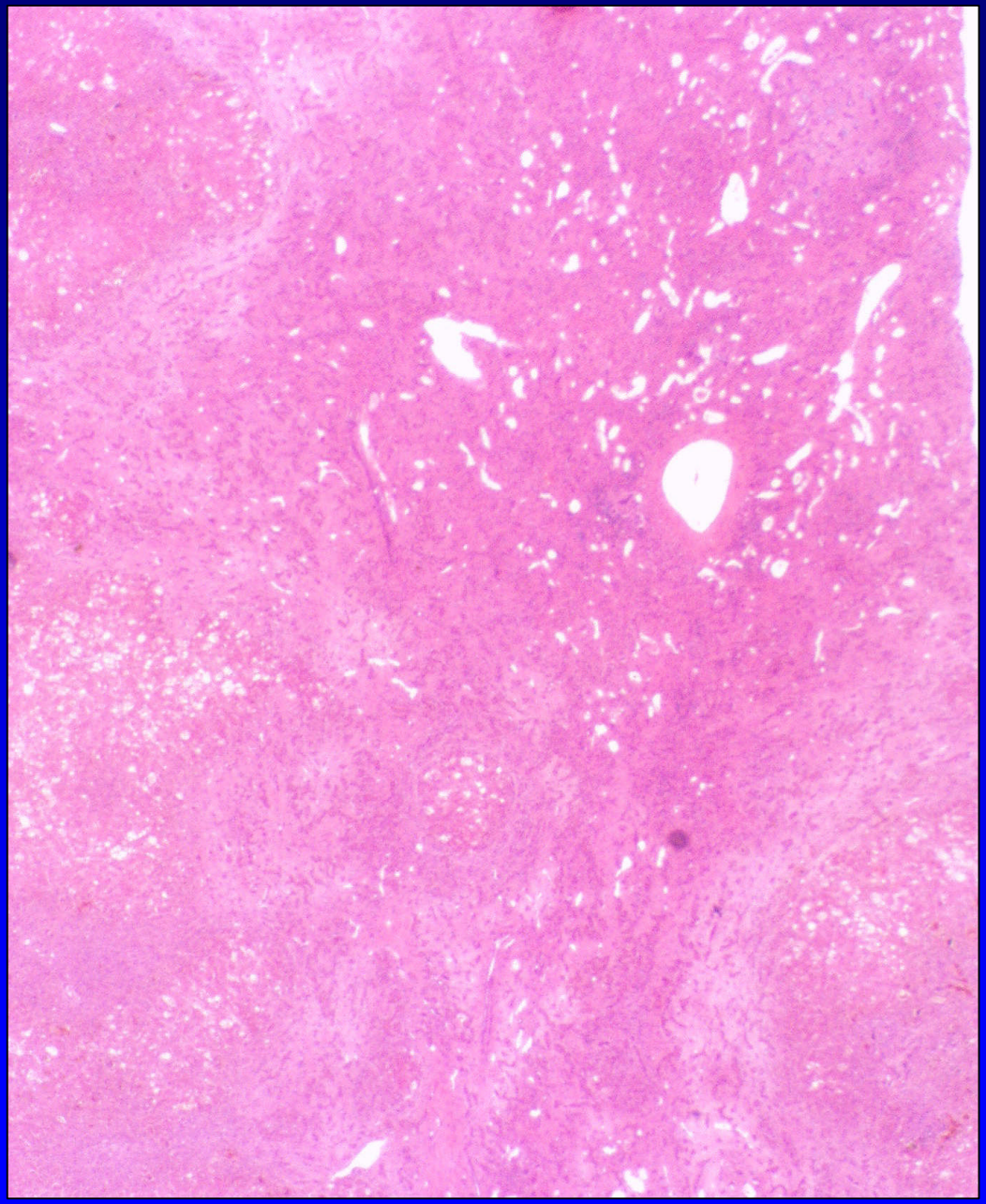


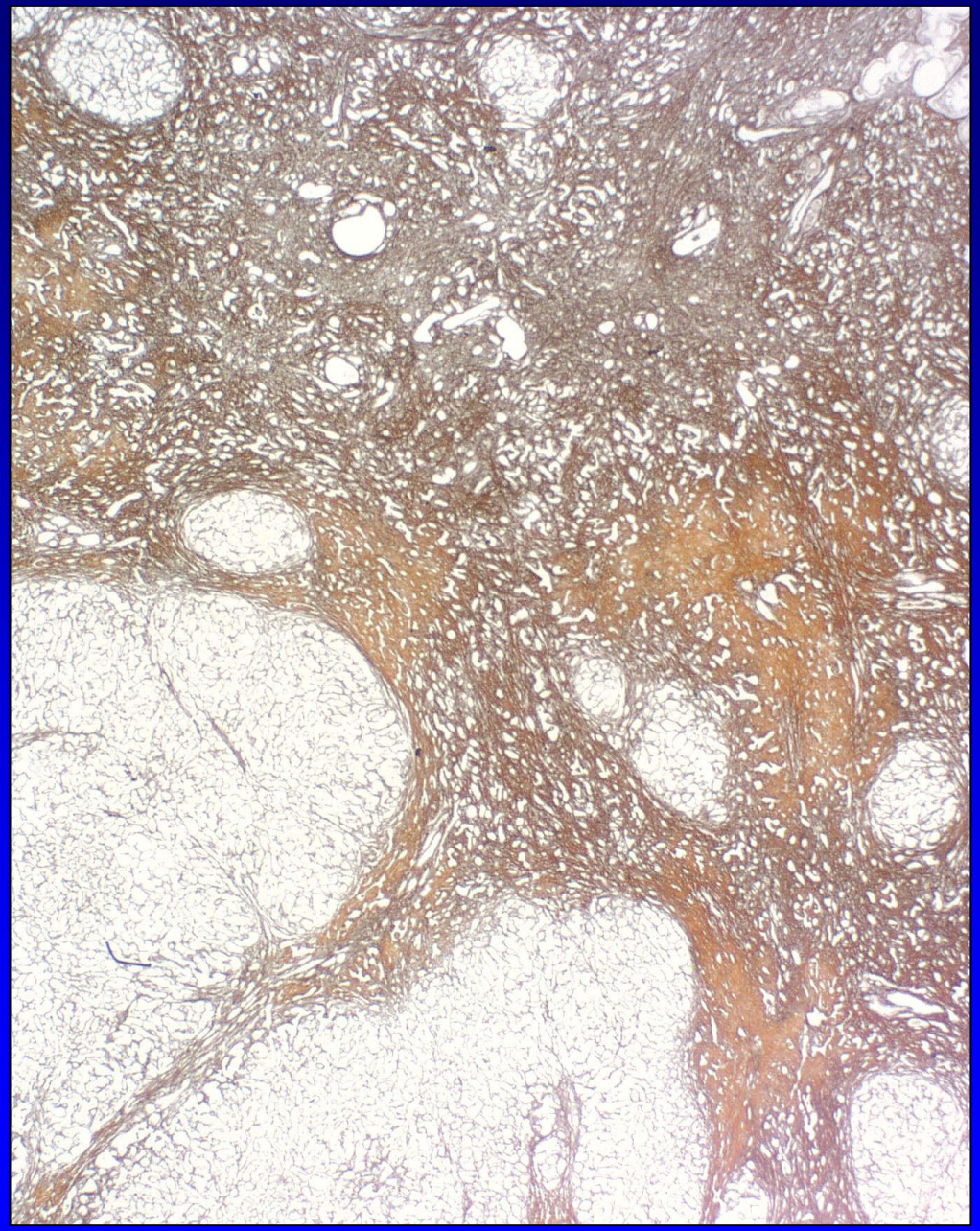


Cirrhotic liver

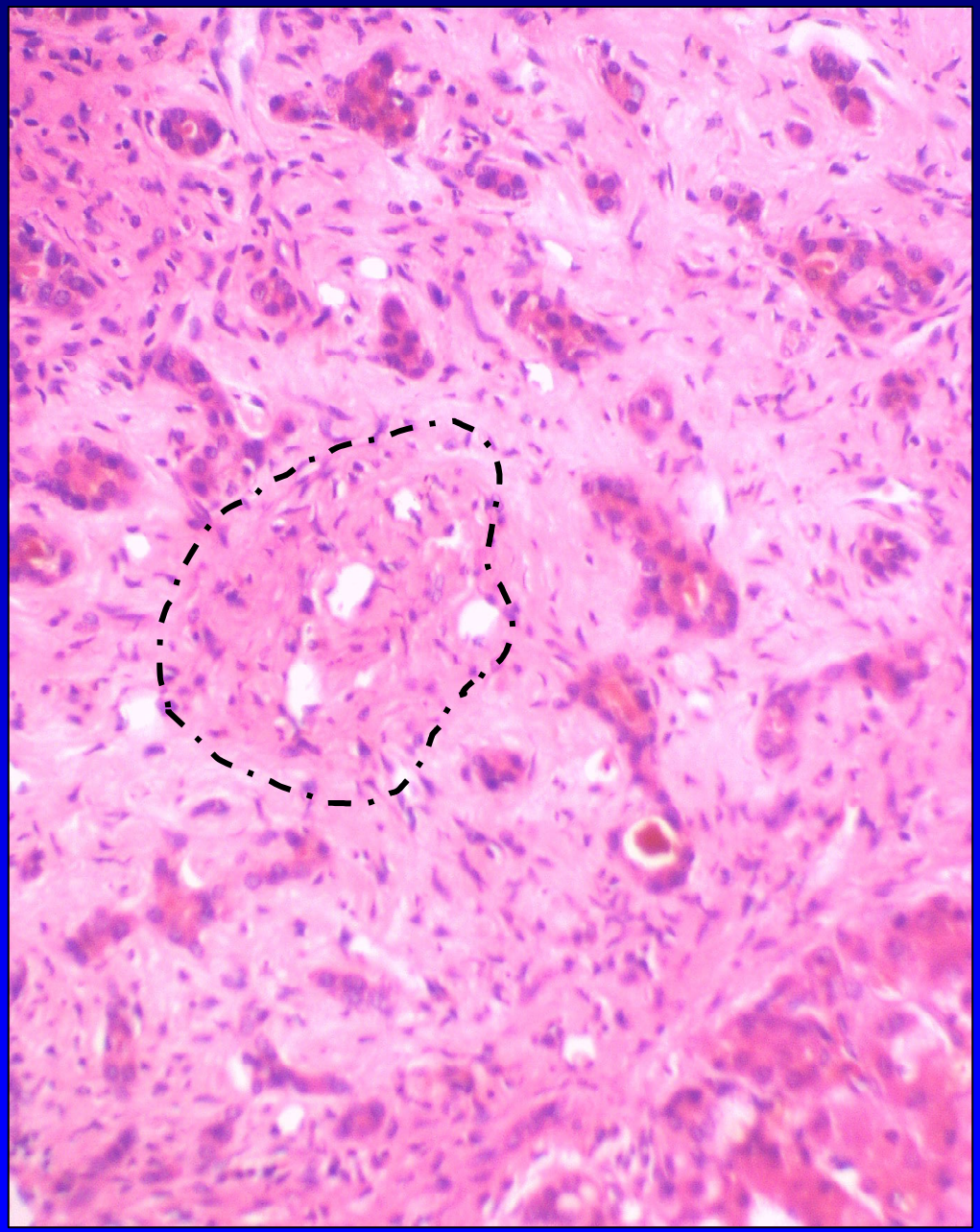
(weight 948 g)

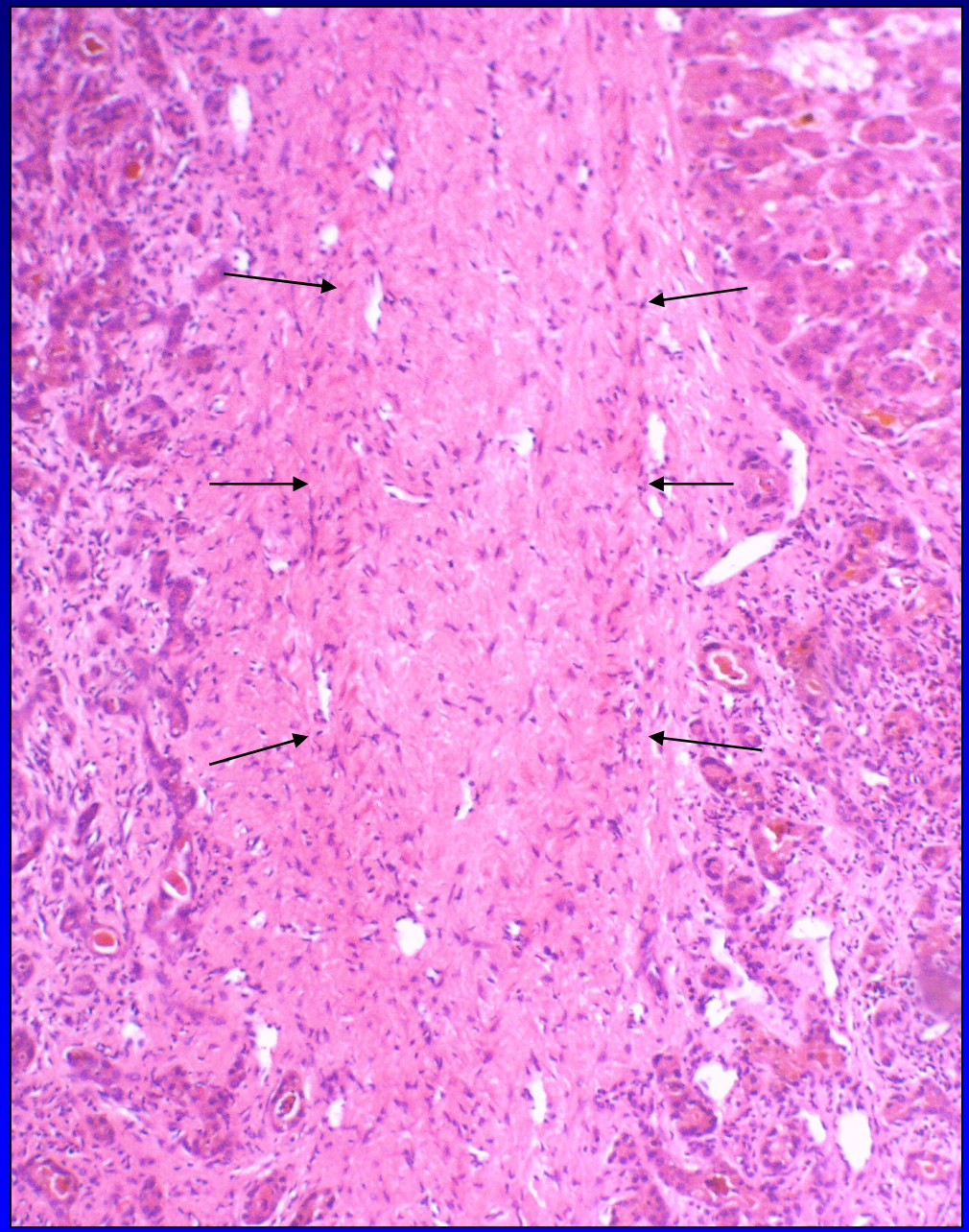
Multiacinar areas of parenchymal extinction



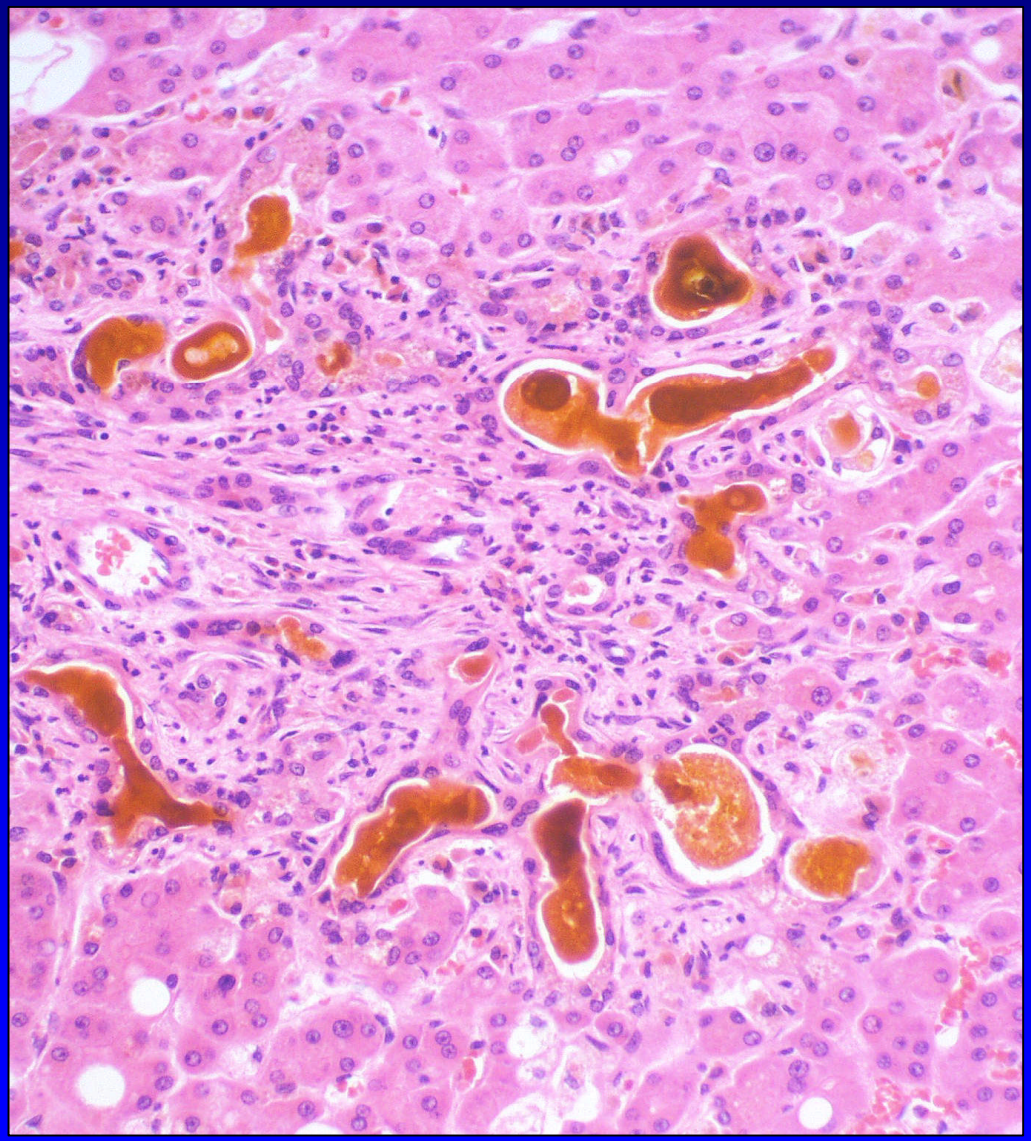


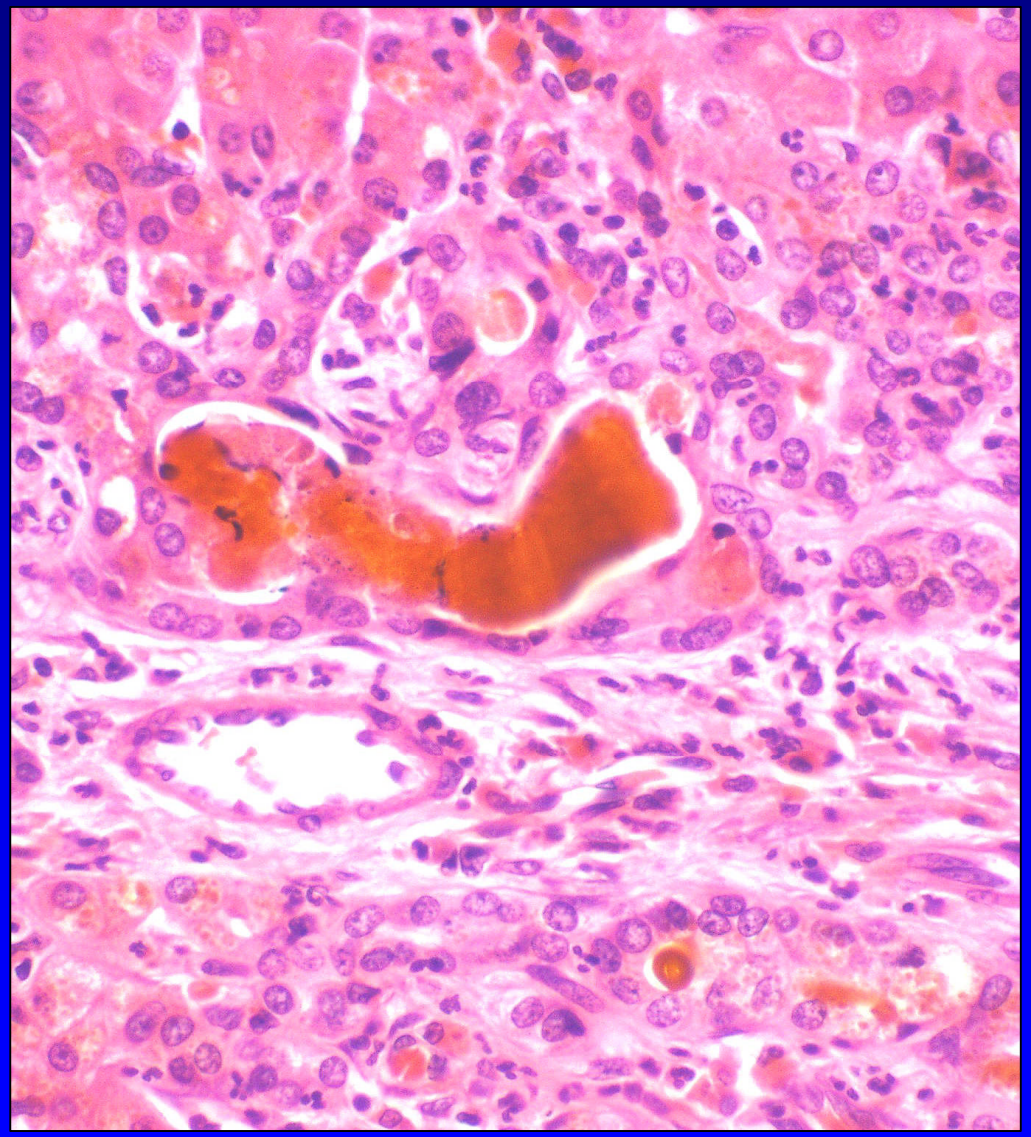
Portal vein thrombi

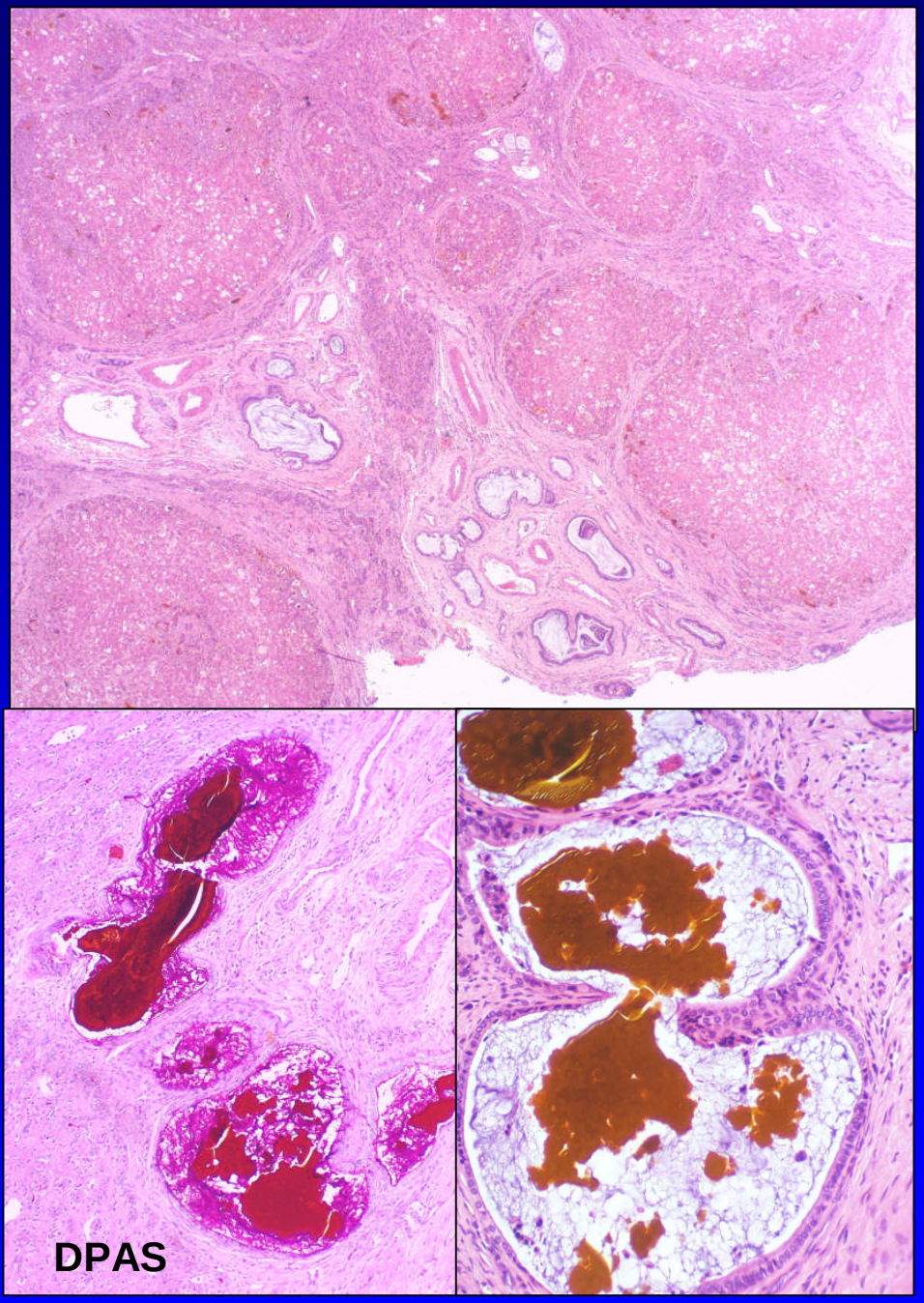


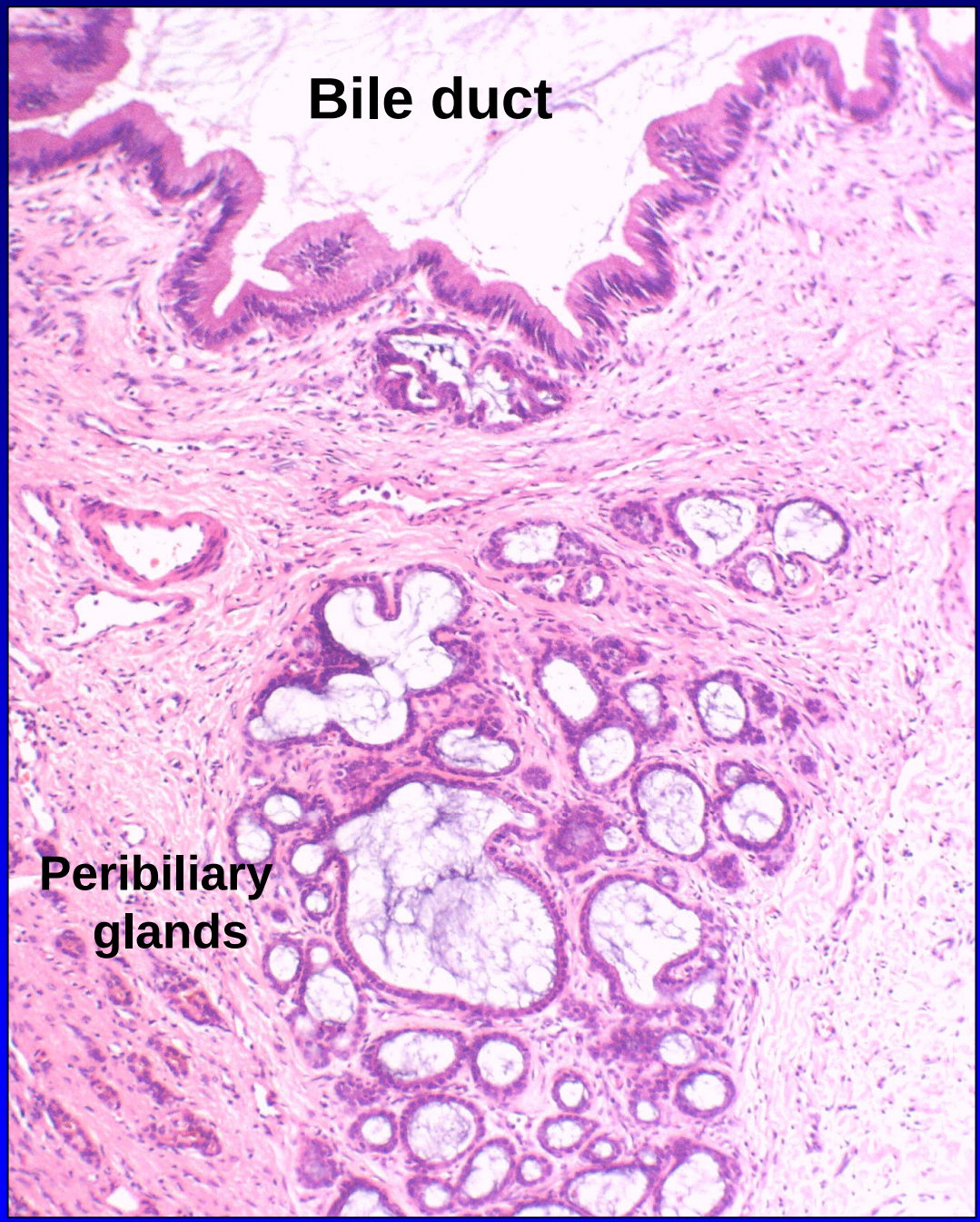


Cholangiolar bile casts






DPAS


Bile duct
Peribiliary glands

Case 2

Morphological diagnosis

Cystic fibrosis - associated cirrhosis

- Particularly prominent ductular bile plugging, destruction and cholangiolitic inflammation
- Mucinous plugging of peribiliary glands and large bile ducts
- Multiacinar parenchymal extinction (? Ischaemic)
- Absence of significant copper deposition suggests that cholestasis may be a relatively late complication (? Role of sepsis, TPN in addition to biliary obstruction)

Cystic fibrosis

- Most common recessive disorder (1:2500 live births)
- Formerly CF of the pancreas (mucoviscidosis)

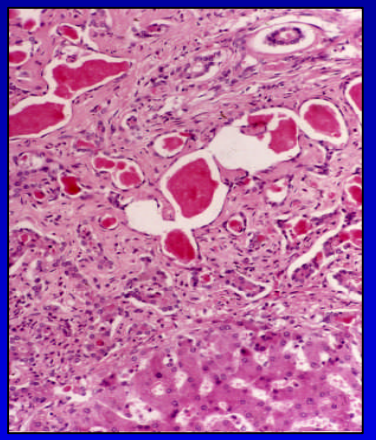
- Gene localized to 7q31.2 codes for CF transmembrane conductance regulator (CFTR)
  ⇨ key role = maintenance of fluid balance across epithelial cells (efflux of chloride ions)

  ⇨ Receptor protein expressed in branching ducts of pancreas, intestinal epithelium, testes, to a lesser degree in respiratory tissue and epithelium of intrahepatic branching ducts

Liver involvement in Cystic Fibrosis

- Significant clinical disease 4 - 6%
- Biochemical liver disease 20 - 50%

- Cause uncertain – probably multofactorial



- Morphology

- Transient neonatal cholestasis (meconium ileus)
- Non-specific neonatal hepatitis
- Steatosis
- Focal biliary fibrosis (eosinophilic plugs in cholangioles)
- Biliary > cryptogenic cirrhosis

King's 2000

⇨ Tea