LIVER PATHOLOGY

ALCOHOLIC LIVER DISEASE

- spans 3 major morphologic and clinical entities :
    - fatty liver
    - alcoholic hepatitis
    - cirrhosis

Alcoholic hepatitis

- acute necrotizing lesion along with collagen deposition, superimposed, usually, on an existing fatty liver
- characterized by
  1. necrosis of hepatocytes
  2. Mallory bodies
  3. neutrophilic inflammatory response
  4. perivenular fibrosis

15% of alcoholics progress to alcoholic cirrhosis

CHRONIC VIRAL HEPATITIS

Two morphologic types :

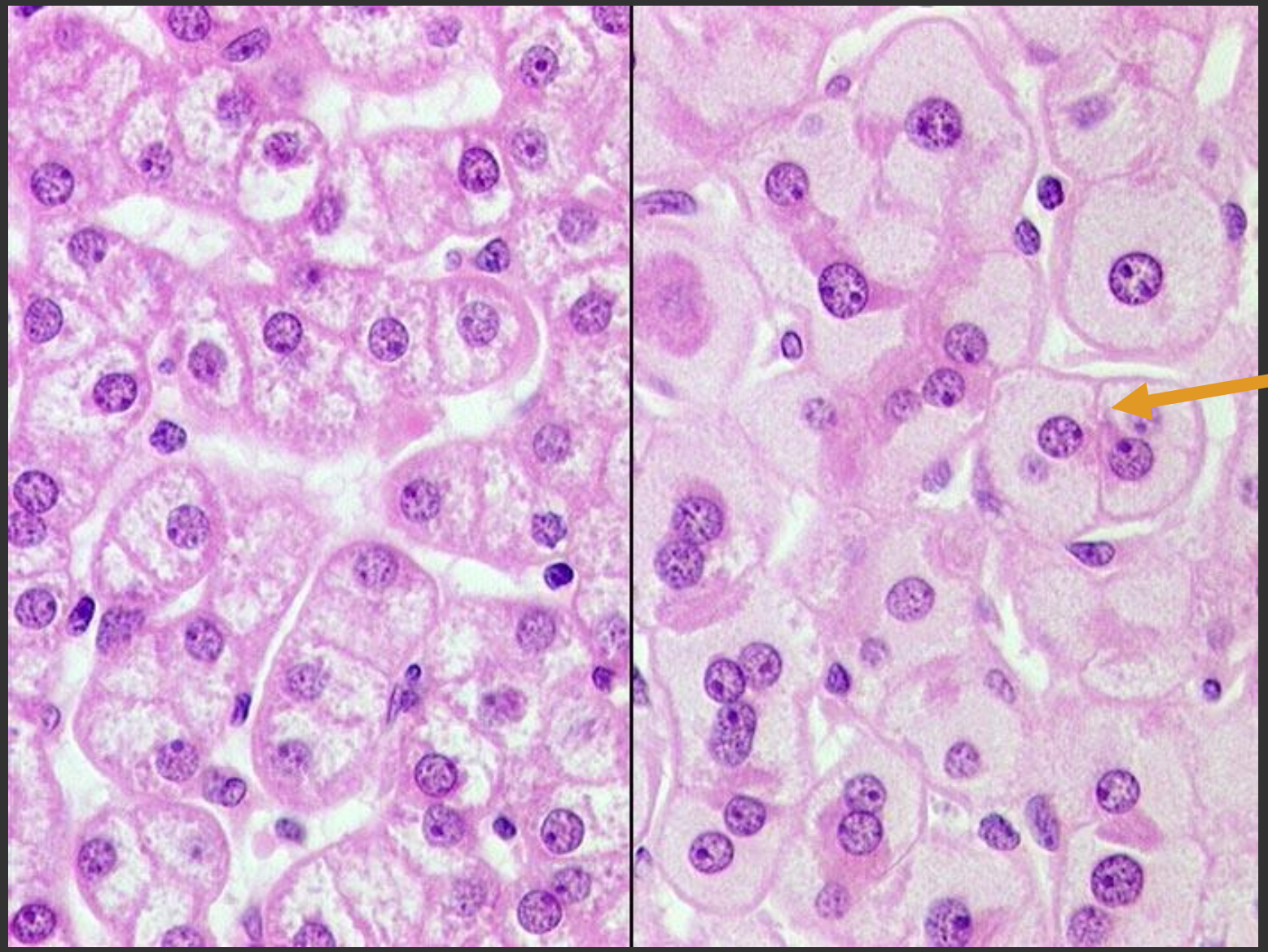
- chronic persistent hepatitis
  - lymphocytic infiltration limited to portal tracts
- chronic active hepatitis
  - piecemeal necrosis / bridging necrosis

Chronic persistent hepatitis

- mild form
- lymphocytic infiltration limited to portal tracts

In case of HBV infection :

- "ground glass hepatocytes" (large granular eosinophilic cytoplasm, which contains abundant HBsAg)
- minimal liver cell necrosis
- minimal lobular inflammation

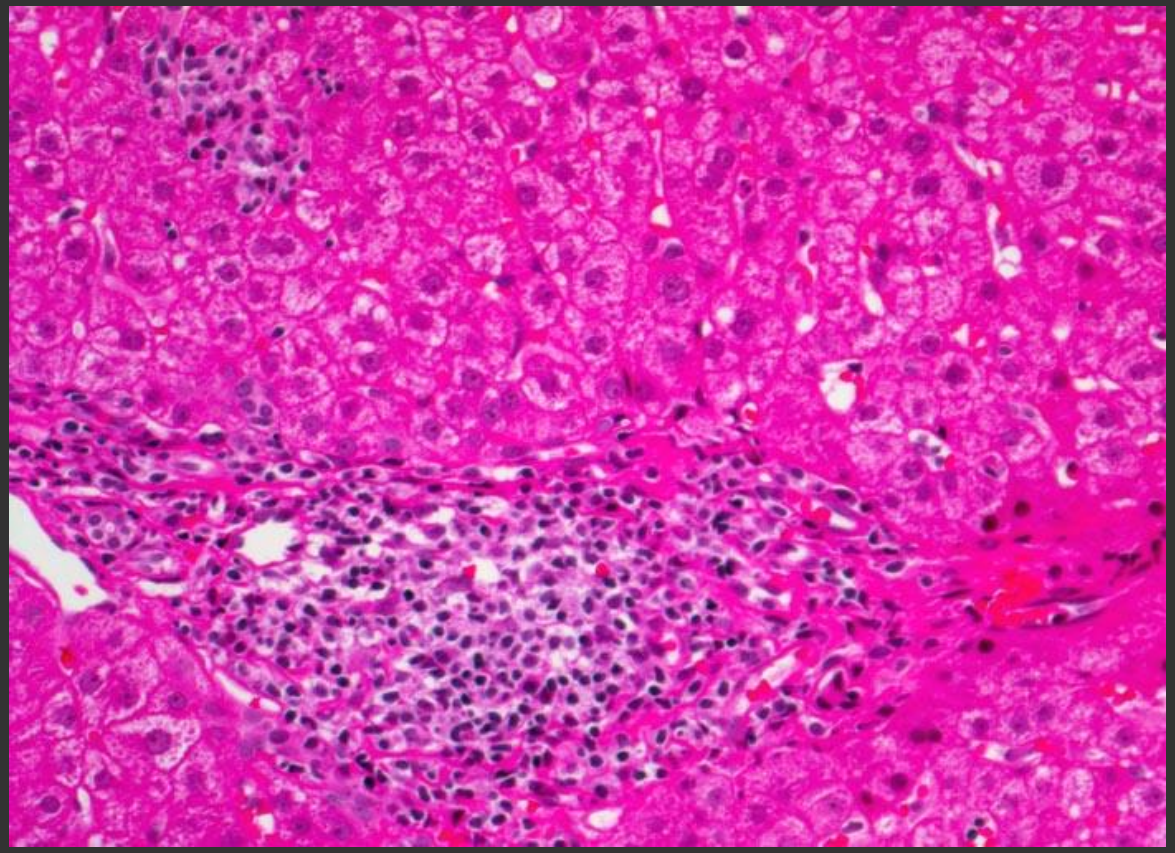


ground glass hepatocytes

Chronic active hepatitis

- necrotizing inflammatory disease
- may progress to cirrhosis
- “piecemeal necrosis/periportal necrosis”
  - ➢ inflammatory cells penetrating the limiting plate
- “bridging necrosis”
  - ➢ confluent hepatic necrosis
  - ➢ rapid progression to cirrhosis

End-stage : dense collagenous septa, destroying the lobular architecture and dividing the liver into hepatocellular regenerative nodules



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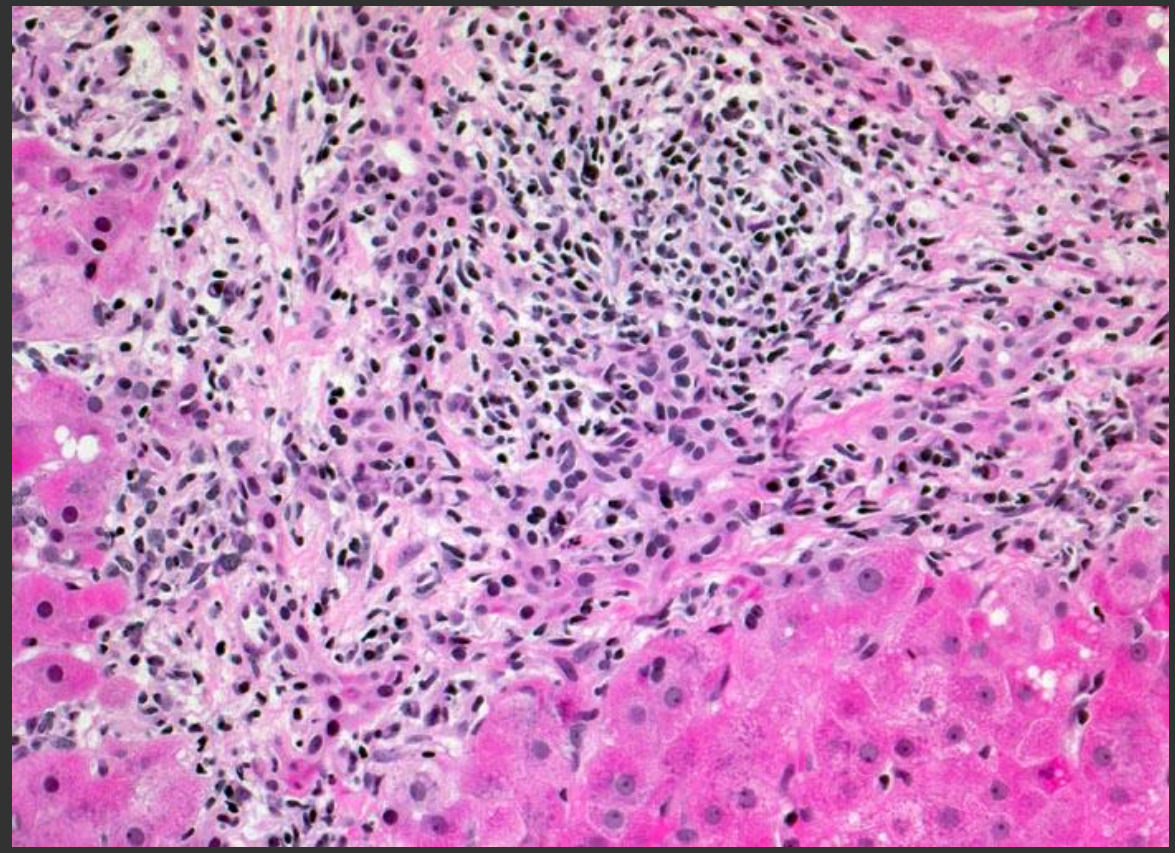

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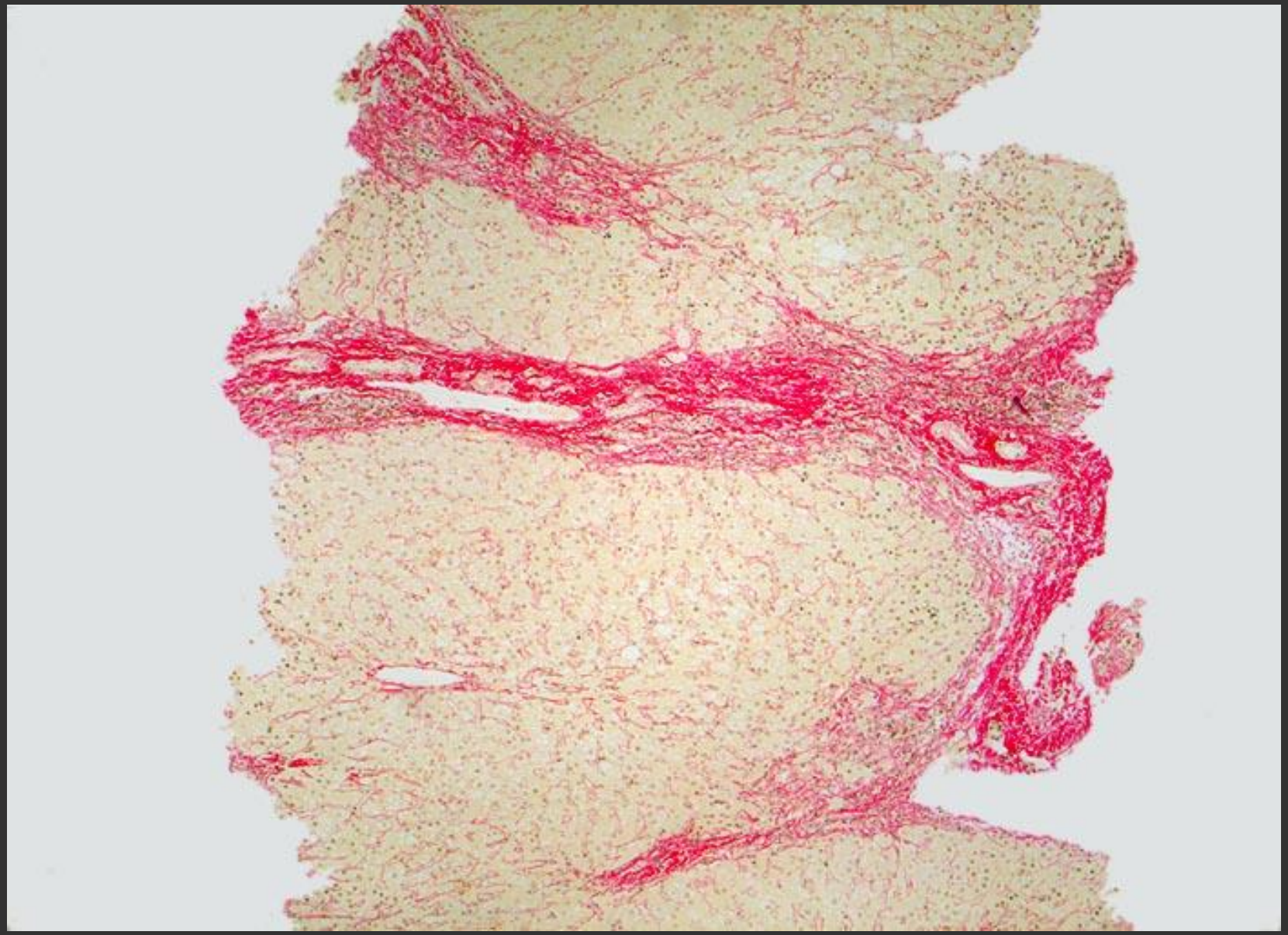


minimally active chronic hepatitis C with incomplete cirrhosis

http://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=4946

PathoPic
www.unibas.ch/patho

CIRRHOSIS

- the destruction of the normal hepatic architecture by fibrous septa that encompass regenerative nodules of hepatocytes
- end-stage of liver disease
- irreversible and progressive

Causes :

- alcoholic liver disease
- chronic active hepatitis
- primary biliary cirrhosis
- extrahepatic biliary obstruction
- hemochromatosis, heritable disorders, others

Four mechanisms

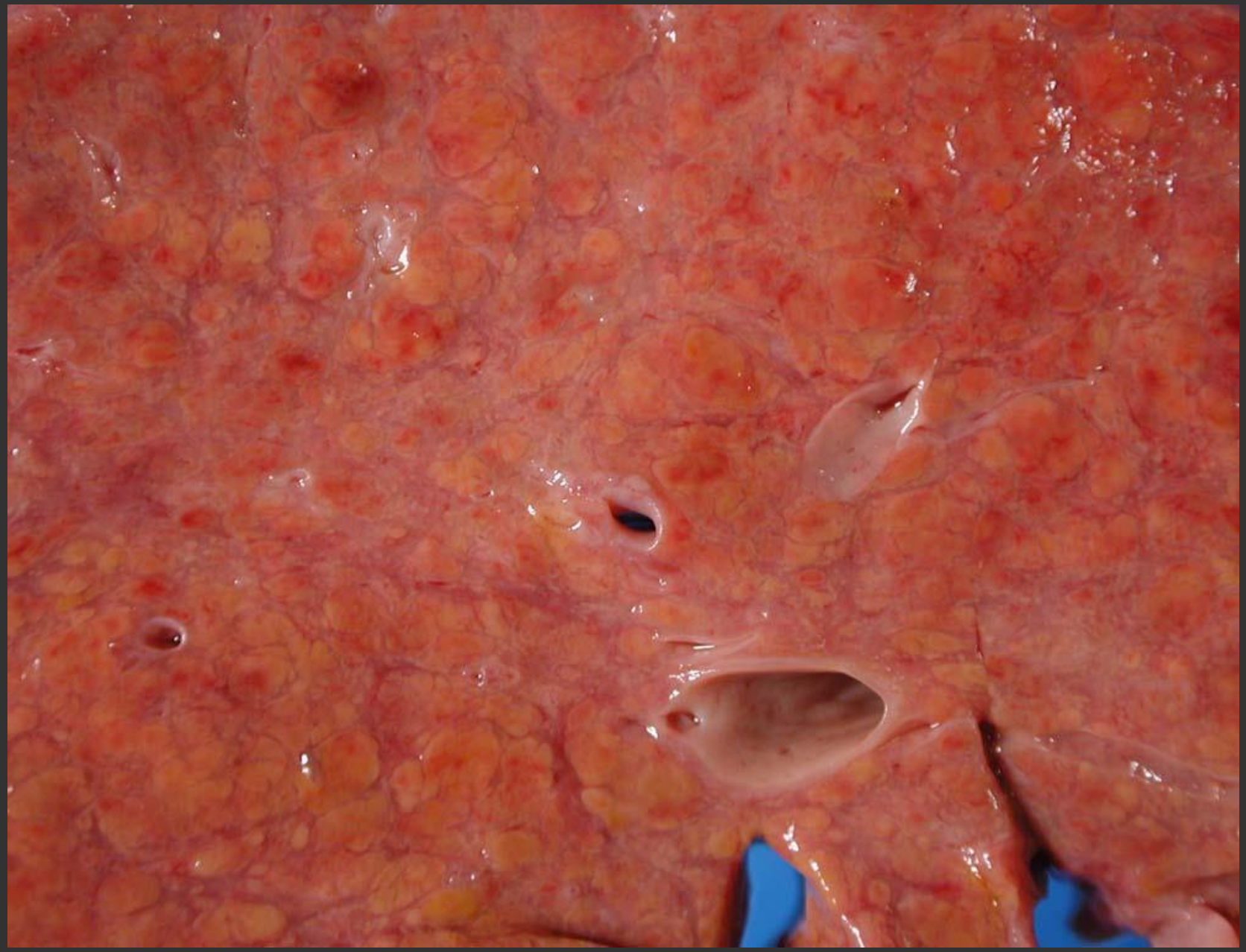
1. hepatocellular necrosis
2. replacement of the dead liver cells with fibrosis and inflammation
3. vascular derangement with impediment of flow
4. hyperplasia of surviving liver tissue

Gross examination :

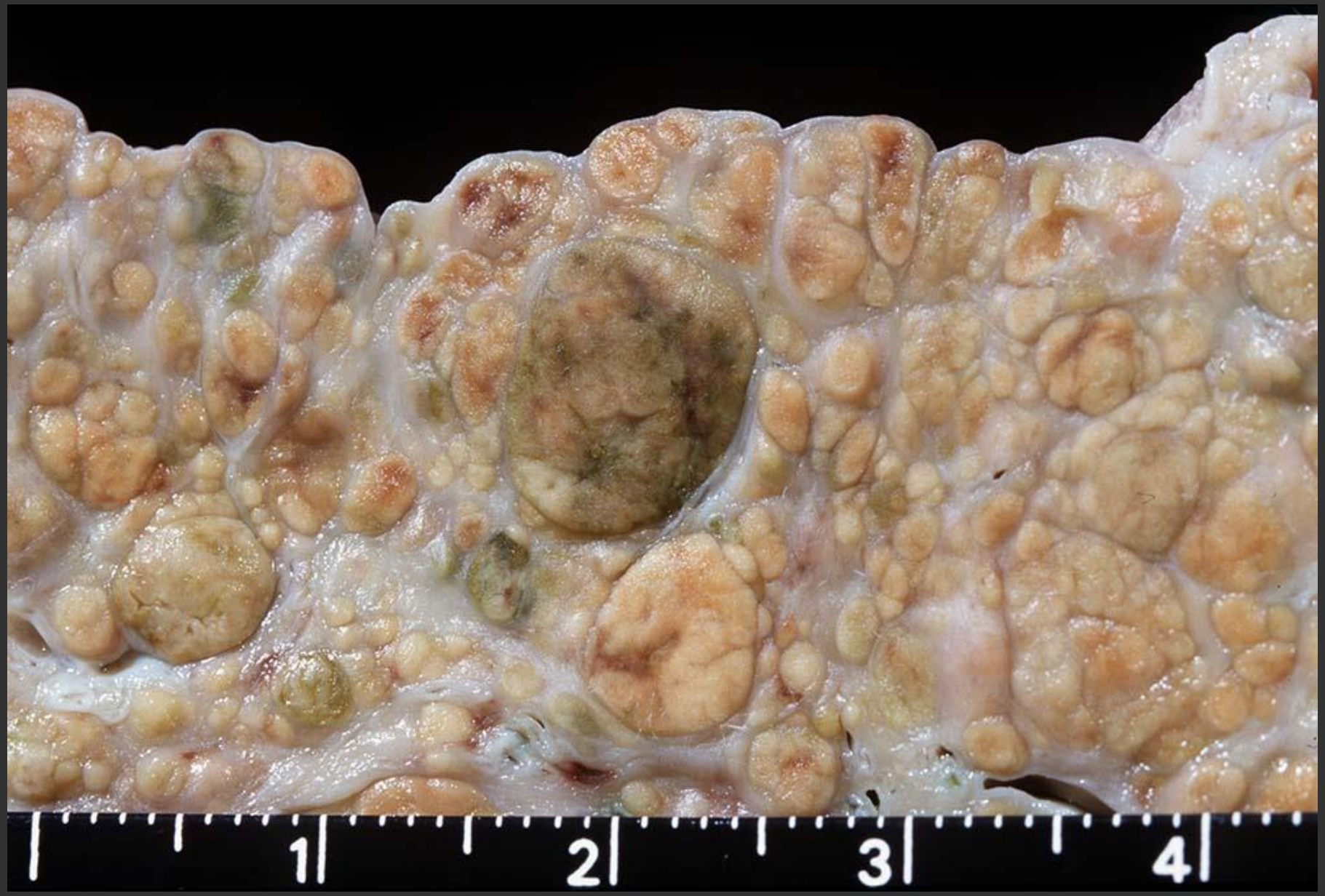
- shrunken, firm, with rough surface due to the nodules formation

Variants :

- micronodular type, with small, less than 3 mm in diameter nodules
- macronodular type, exhibits nodules of varying size
- mixed type

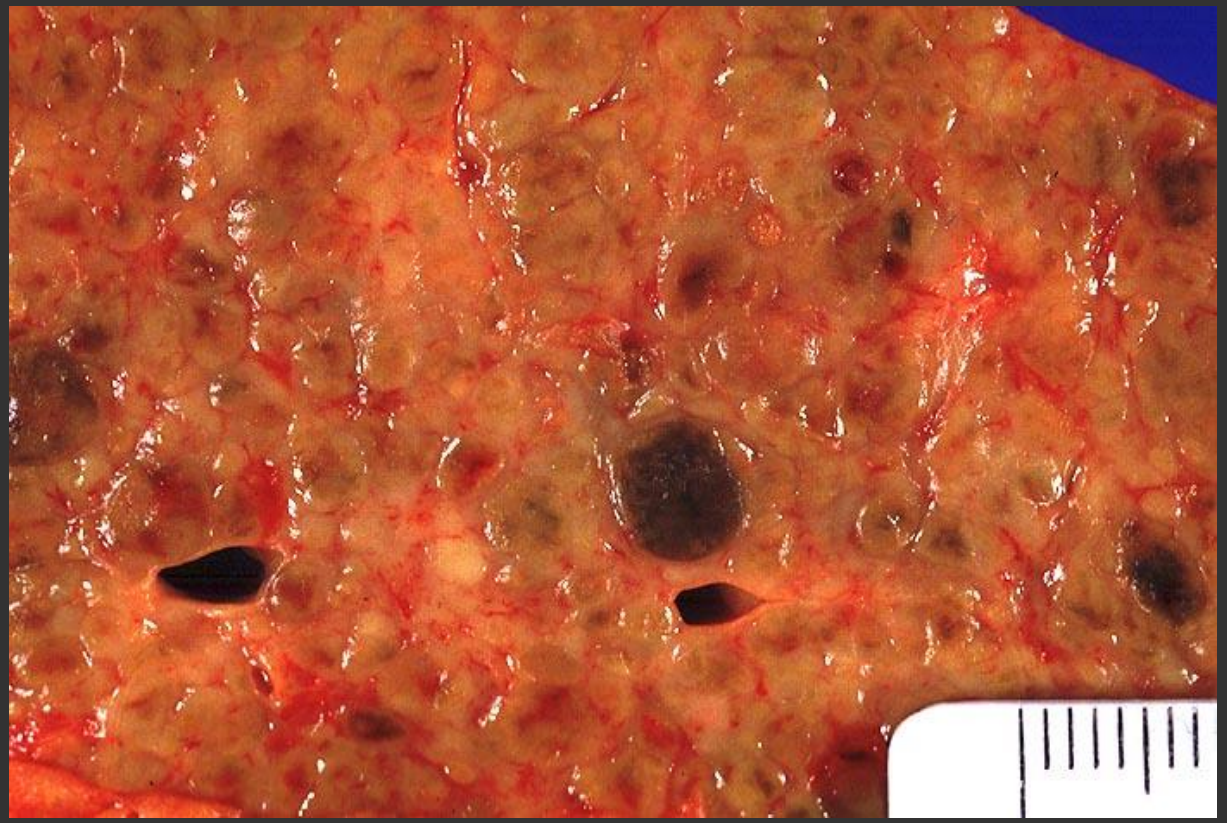


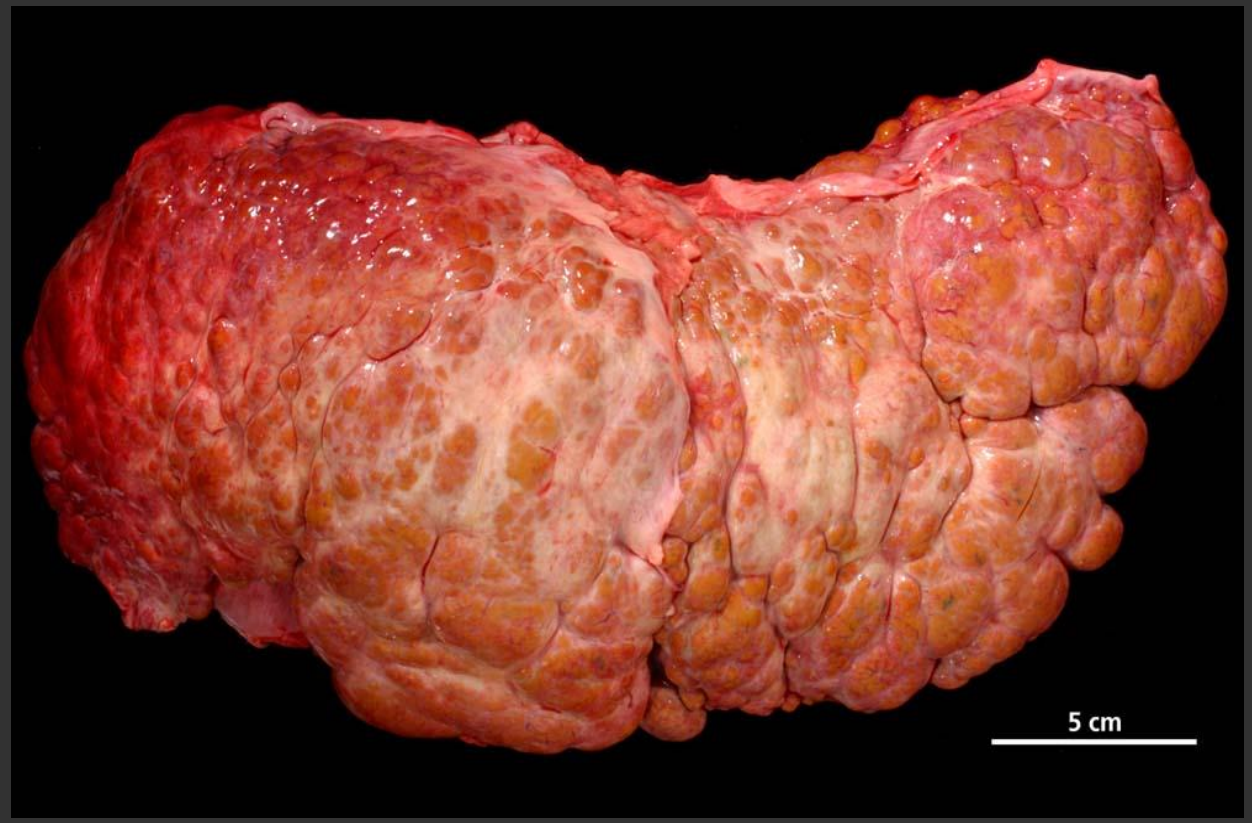
micronodular alcoholic liver cirrhosis



PathoPic
www.unibas.ch/patho

macronodular cirrhosis





mixed nodular liver cirrhosis

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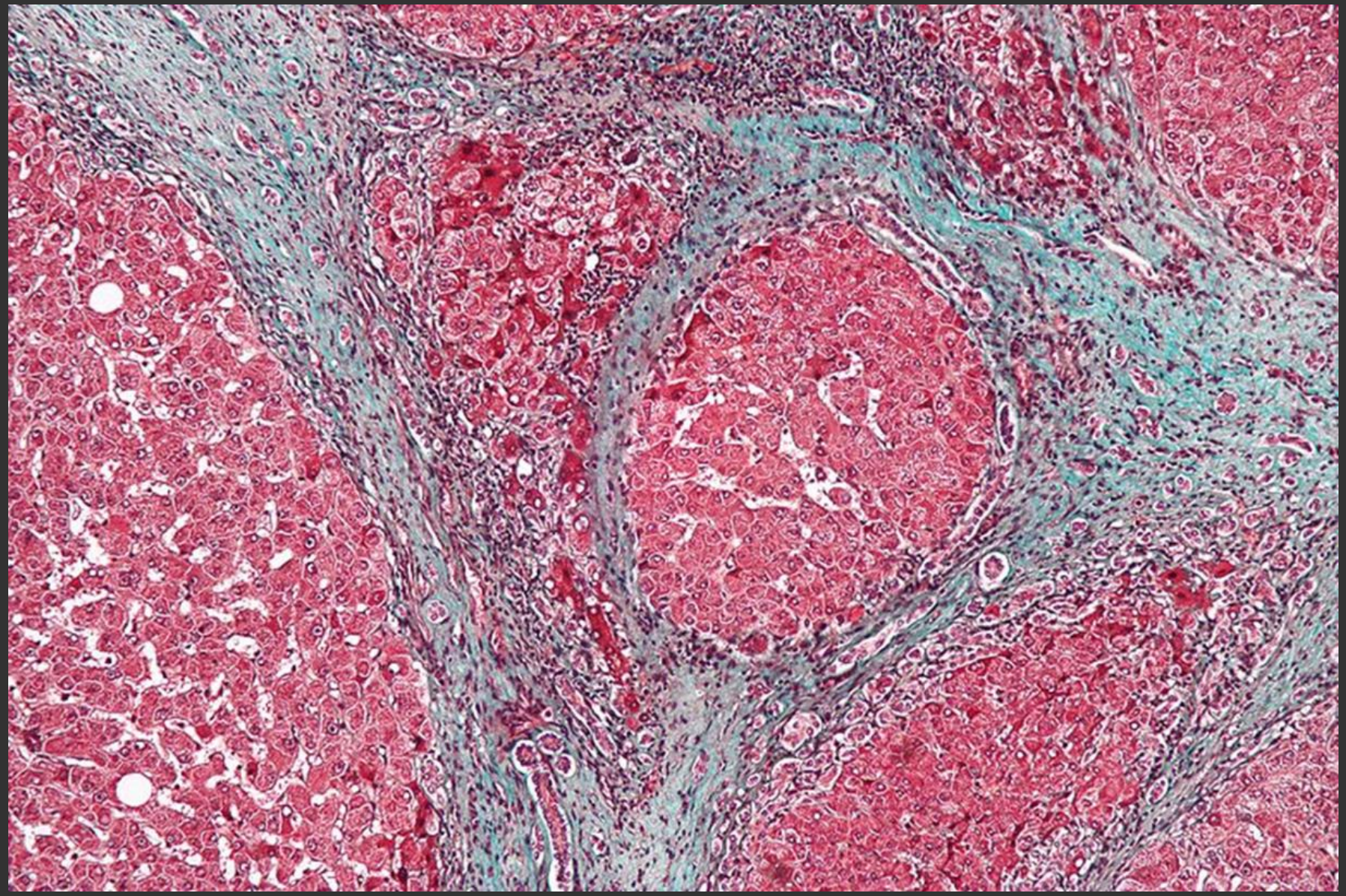


http://en.wikipedia.org

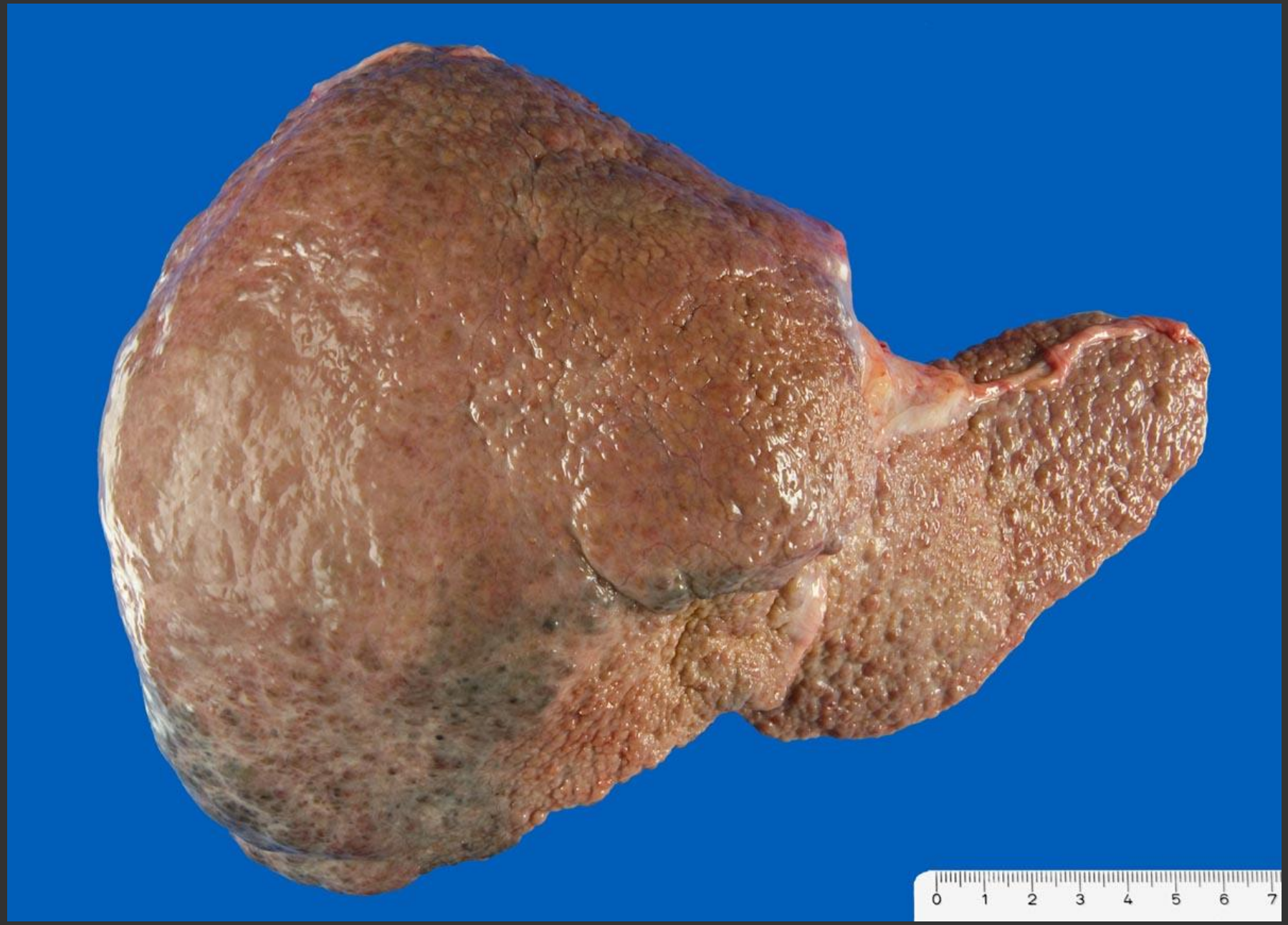
Alcoholic cirrhosis

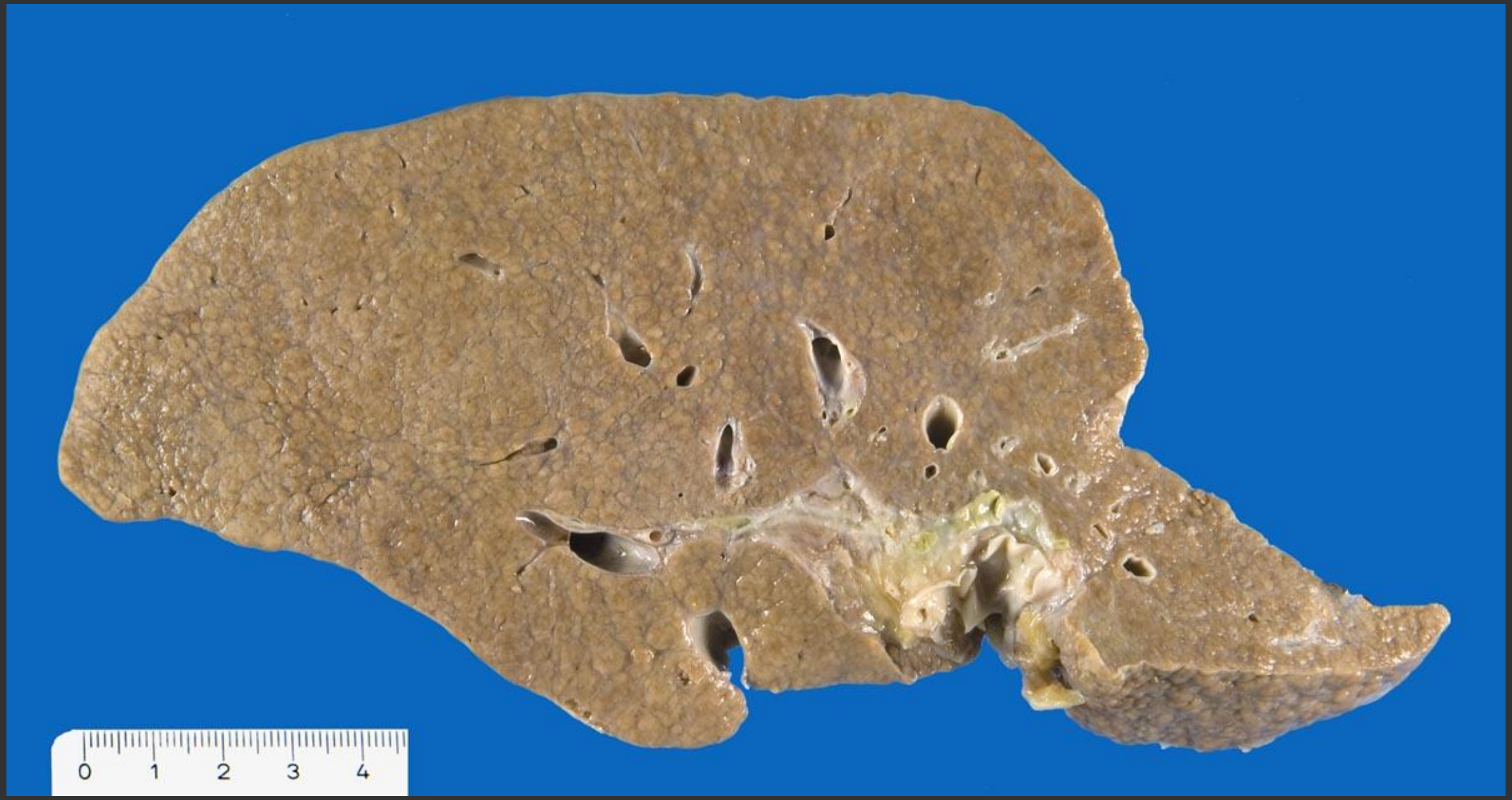
Macroscopy :

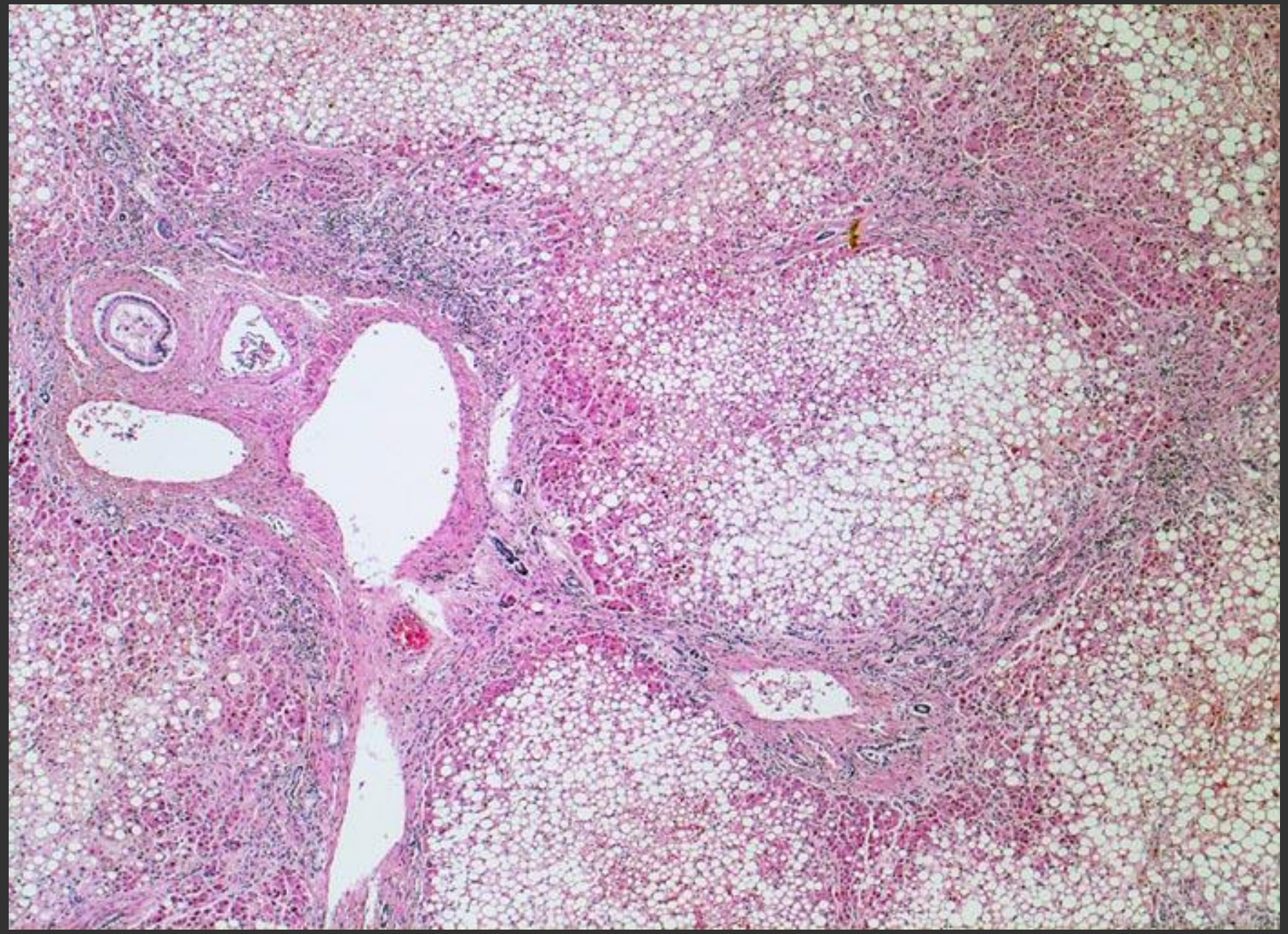
- at first : yellow tan, fatty, enlarged (>2kg)
- eventually : brown, non-fatty, shrunken (<1kg)
- micronodular surface – Laennec's cirrhosis

Microscopy :

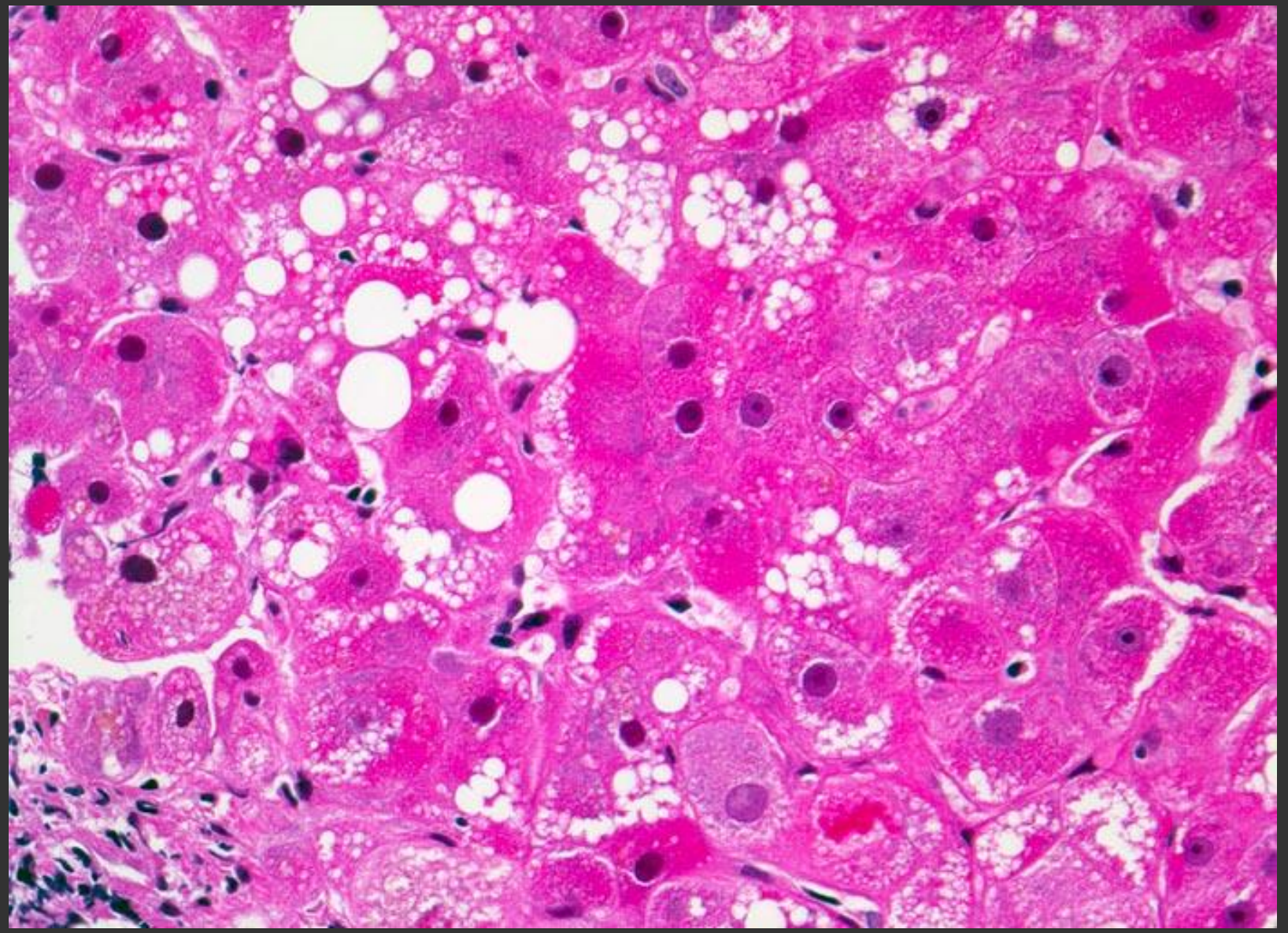
- thin connective tissue septa (portal tract to central vein, portal tract to portal tract) – may lead to thick septa
- +/- Mallory bodies
- +/- steatosis







alcoholic liver
cirrhosis + steatosis



cholestatic Mallory bodies

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PathoPic
www.unibas.ch/patho

Post-necrotic cirrhosis

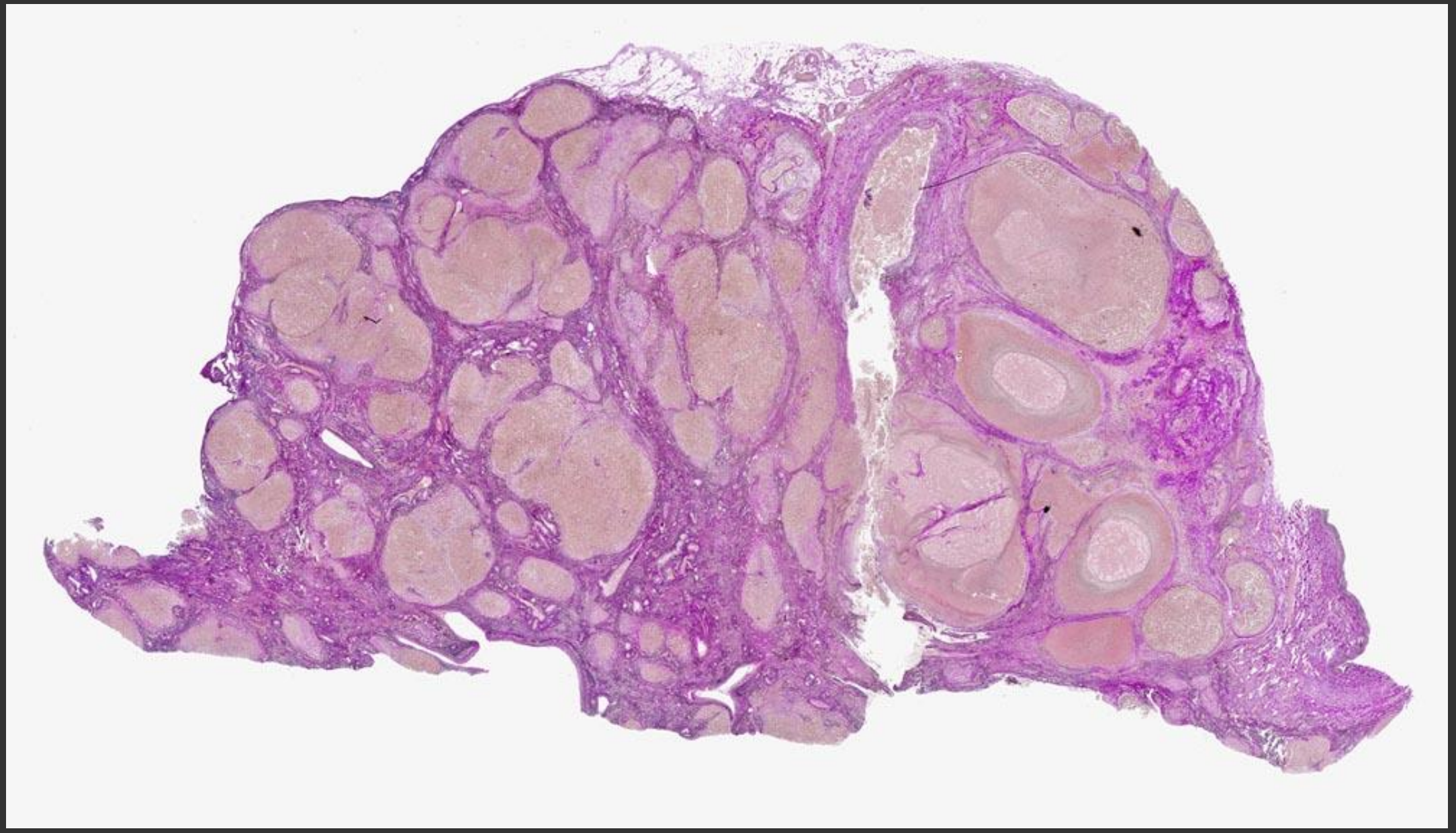
- post HBV, HCV

Macroscopy :

- large, irregularly sized nodules (>2 cm in diameter)
- broad bands of fibrosis

Microscopy :

- large scars surrounding more than a single lobule
- broad connective tissue septa, with proliferated bile ducts and elements of pre-existing portal tracts



Primary biliary cirrhosis

- chronic, progressive and often fatal cholestatic liver disease
- unknow etiology, most likely immunological

Defined by :

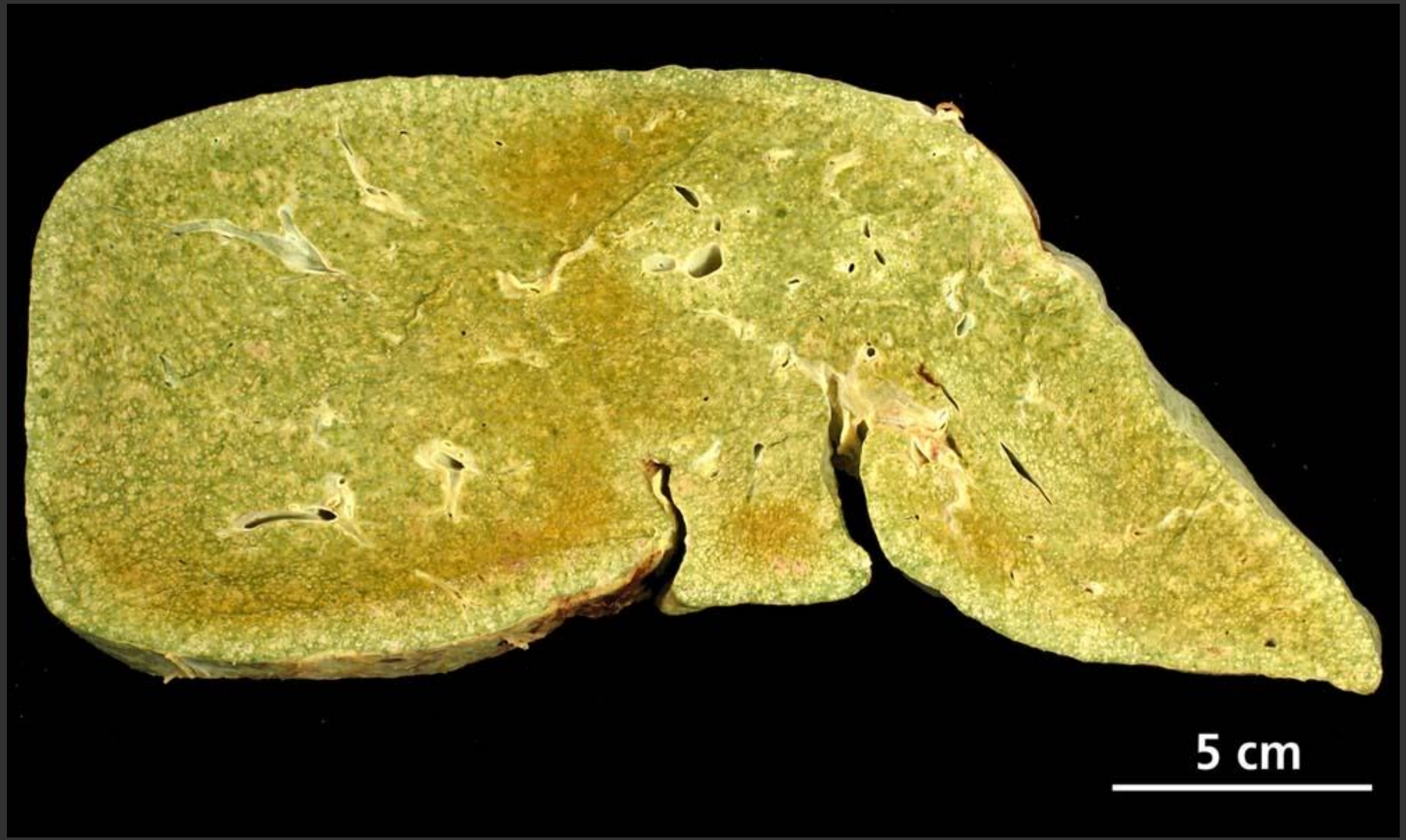
- non-suppurative destruction of intrahepatic bile ducts
- portal inflammation
- portal inflammation

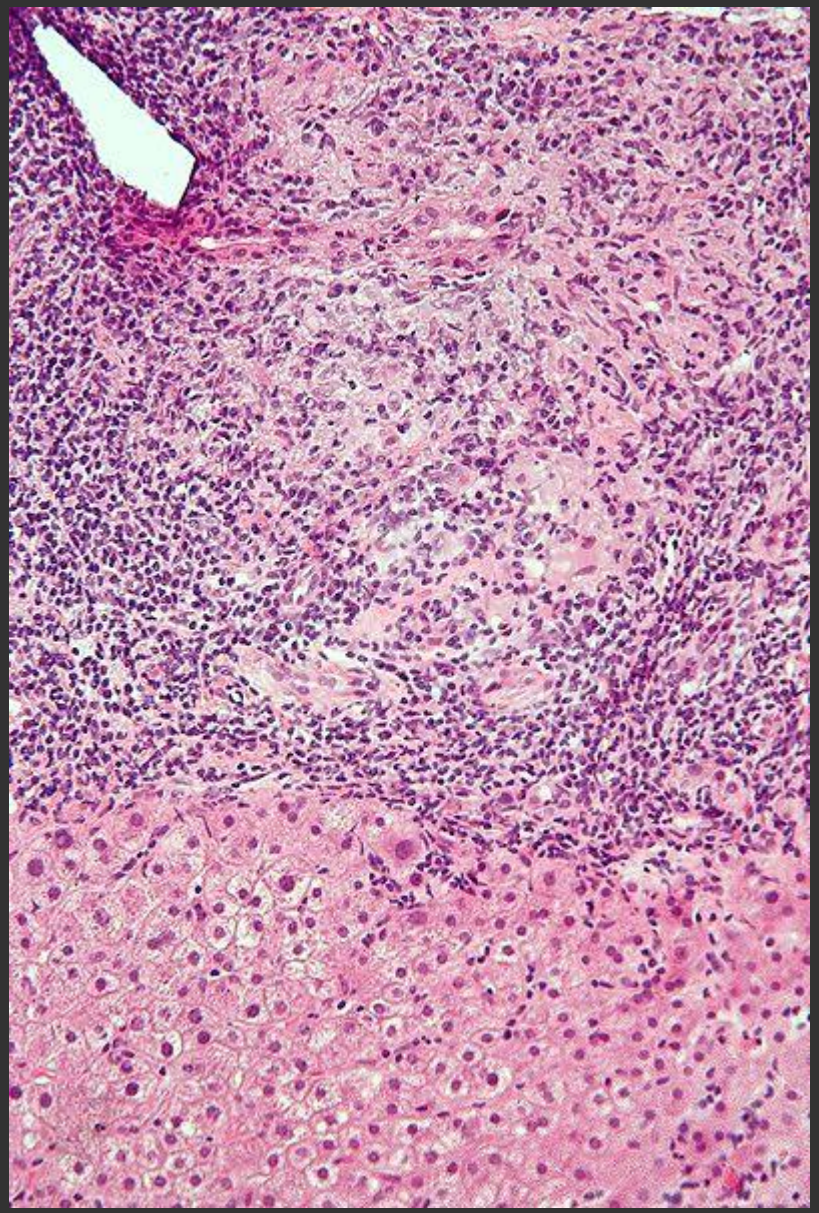
resulting in a *micronodular* pattern

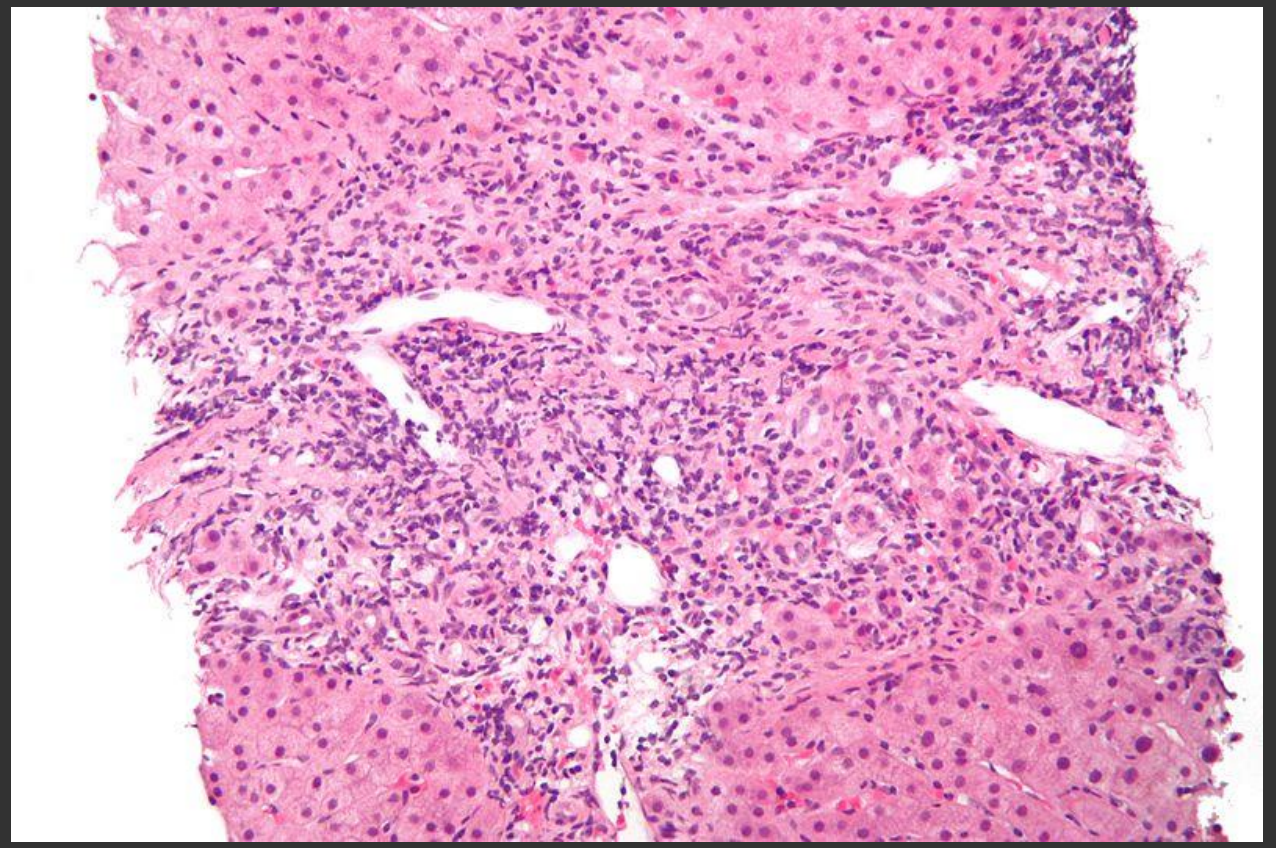
Primary biliary cirrhosis

Macroscopy :
- green appearance due to bile stasis
- micronodular pattern

Microscopy :
- chronic inflammation restricted, at first, to portal tracts, destroying the small intrahepatic bile ducts
- “florid duct lesion” (granulomatous inflammation)
- piecemeal necrosis







http://commons.wikimedia.org/wiki/File:Primary_biliary_cirrhosis_intermed_mag.jpg

http://commons.wikimedia.org/wiki/File:Primary_biliary_cirrhosis_intermed_mag_2.jpg

Secondary (obstructive) biliary cirrhosis

- the end result of prolonged obstruction of the extrahepatic biliary tree

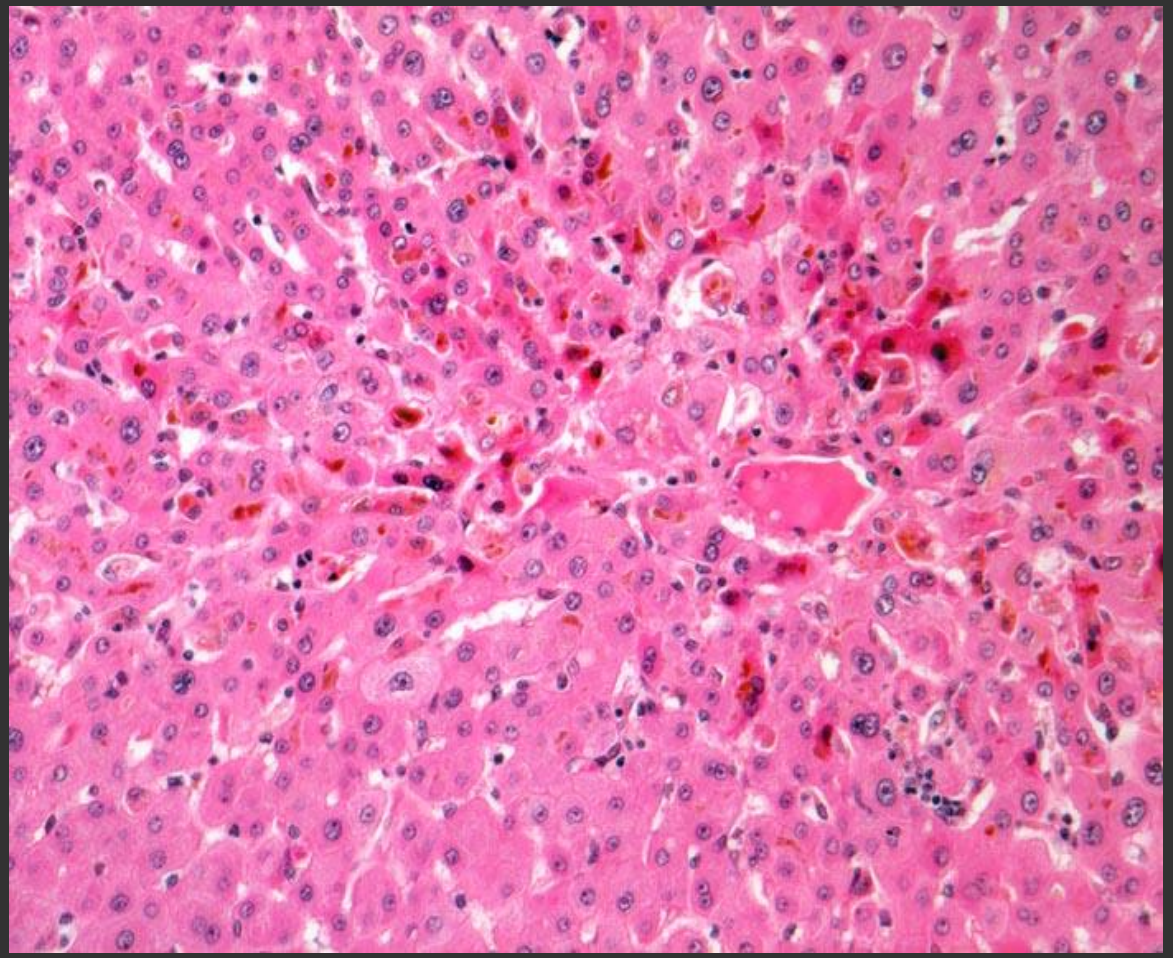
Produced by :

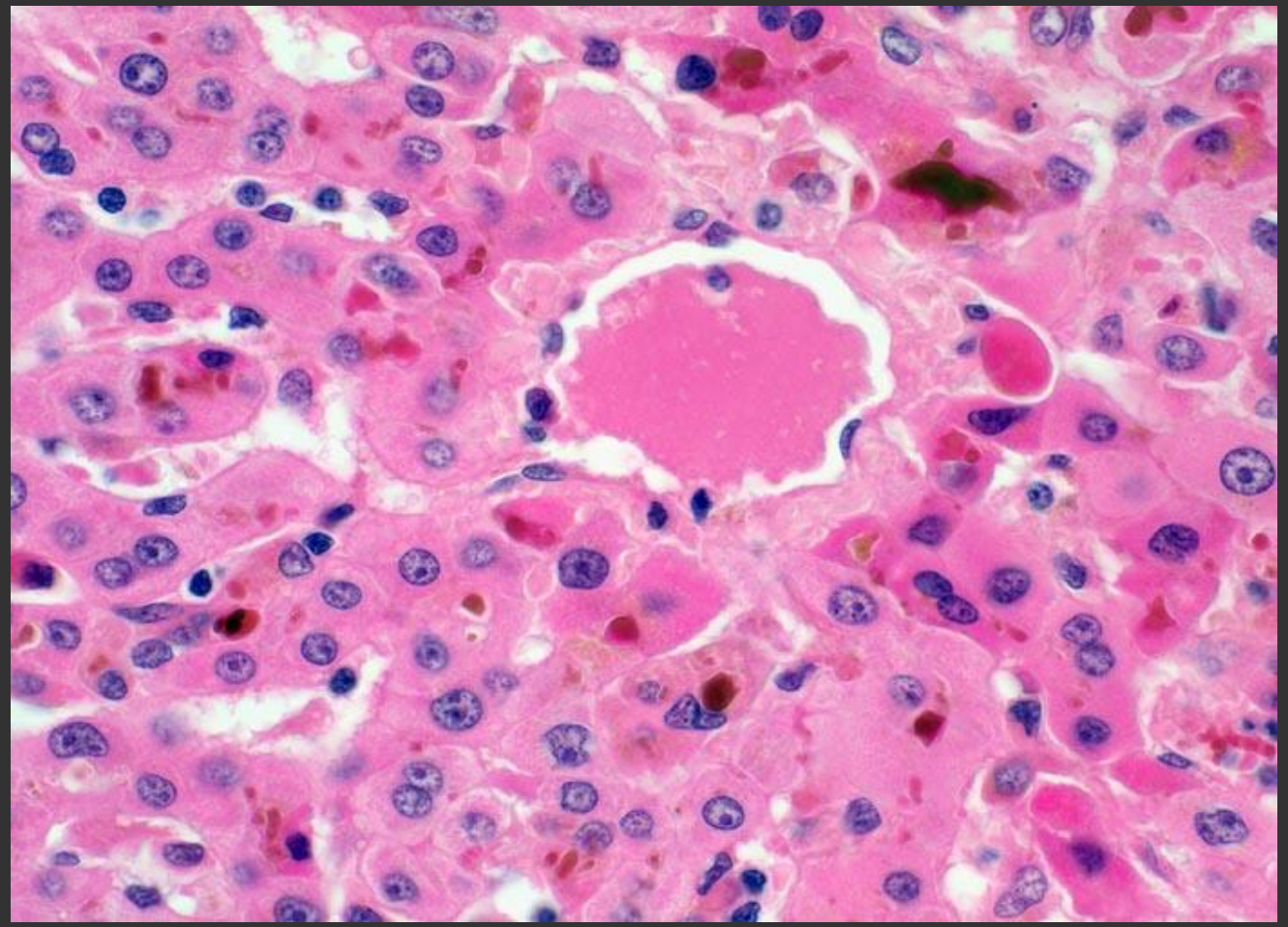
- impacted gallstones
- malignancy of the bile duct or surrounding tissues
- postoperative benign strictures
- congenital biliary atresia.

Secondary (obstructive) biliary cirrhosis

Macroscopy :
- striking yellow-green pigmentation
- marked icteric discoloration of body tissues and fluids

Microscopy :
- cholestasis
- hepatocytes contain large amounts of bile – “feathery degeneration”
- “bile lakes”
- biliary concretions within bile ducts and proliferated ductules
- chronic inflammation





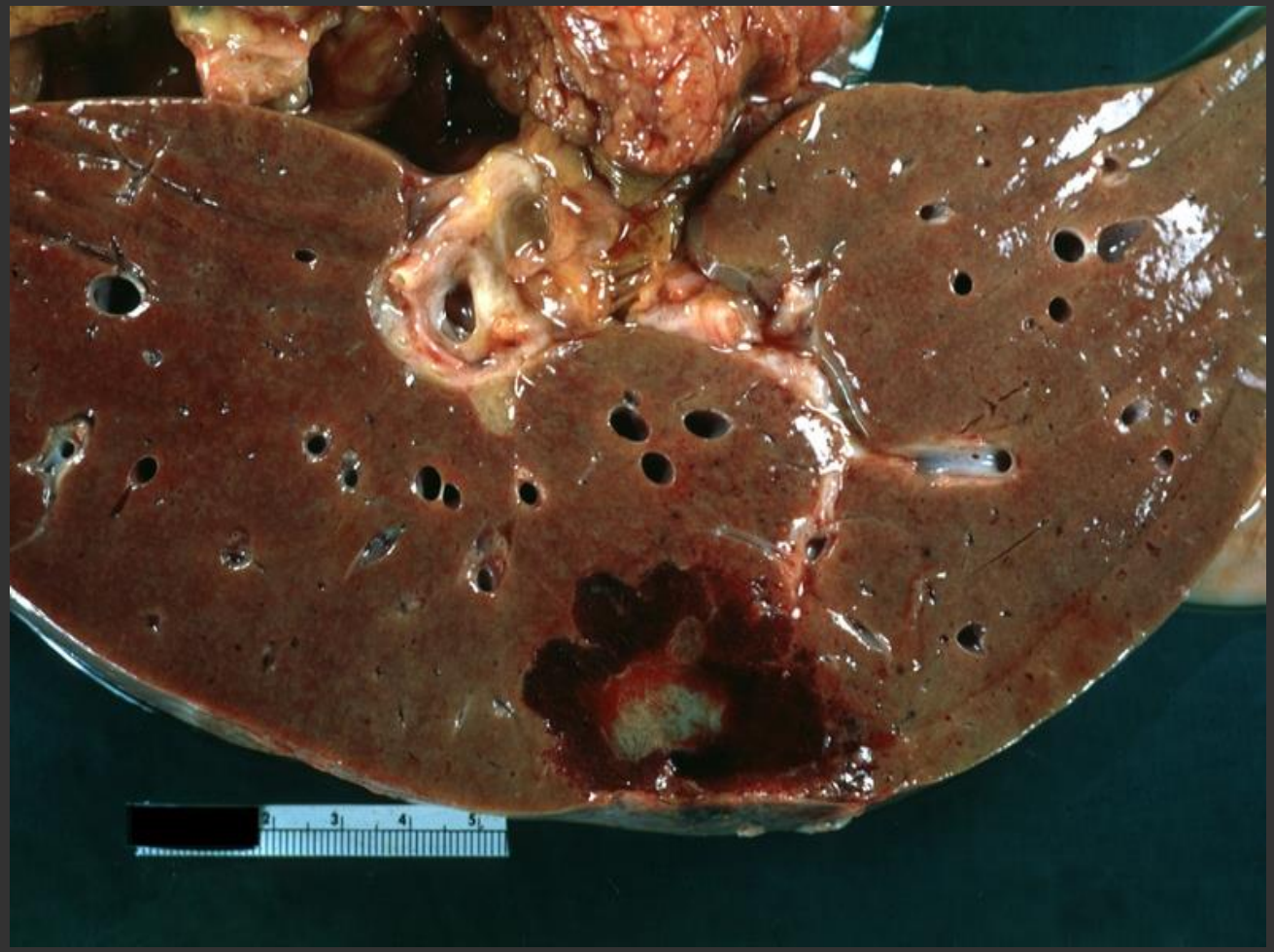
cholestasis + bile lakes

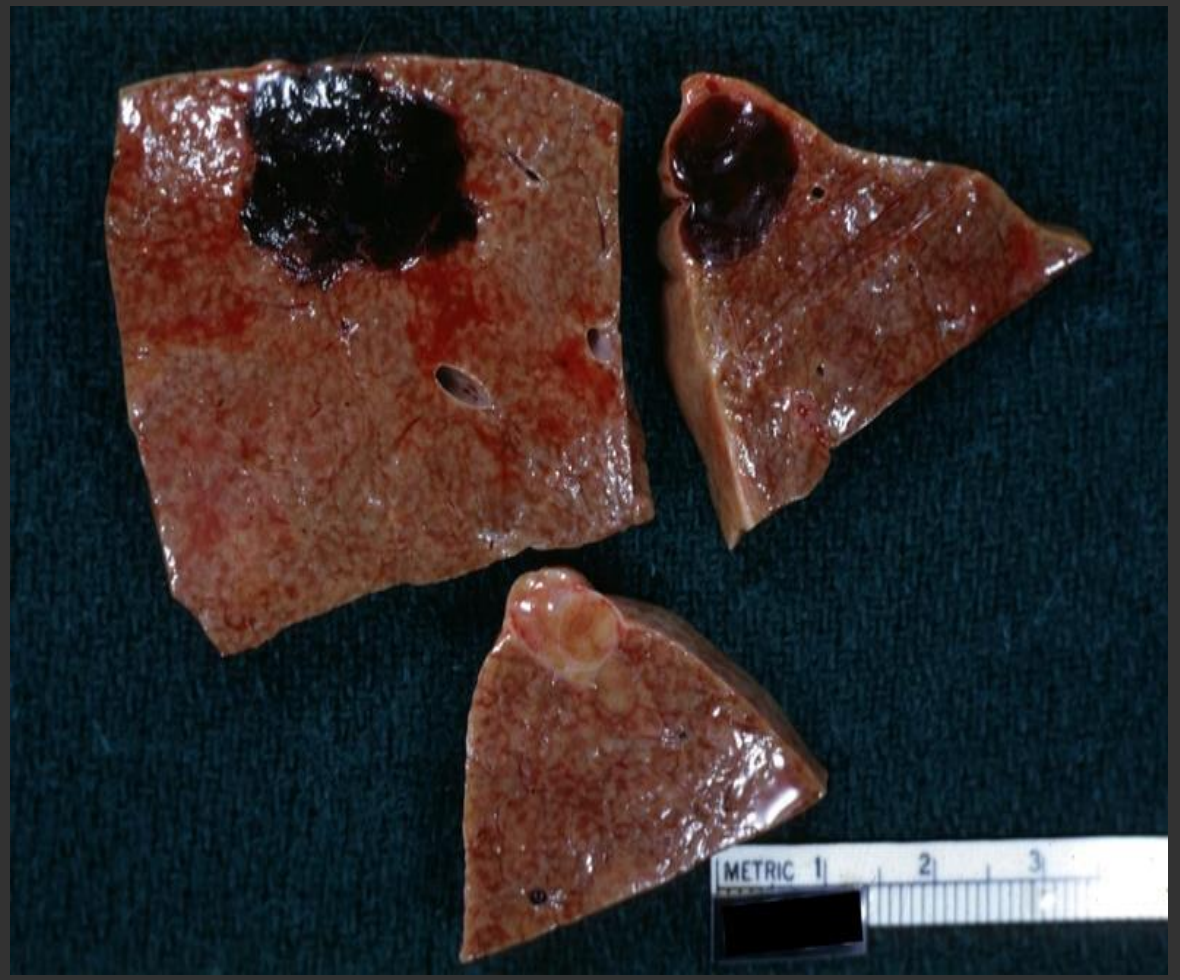
PathoPic
www.unibas.ch/patho

LIVER PRIMARY TUMORS

Benign

- cavernous hemangioma
- liver cell adenoma
- bile duct adenoma

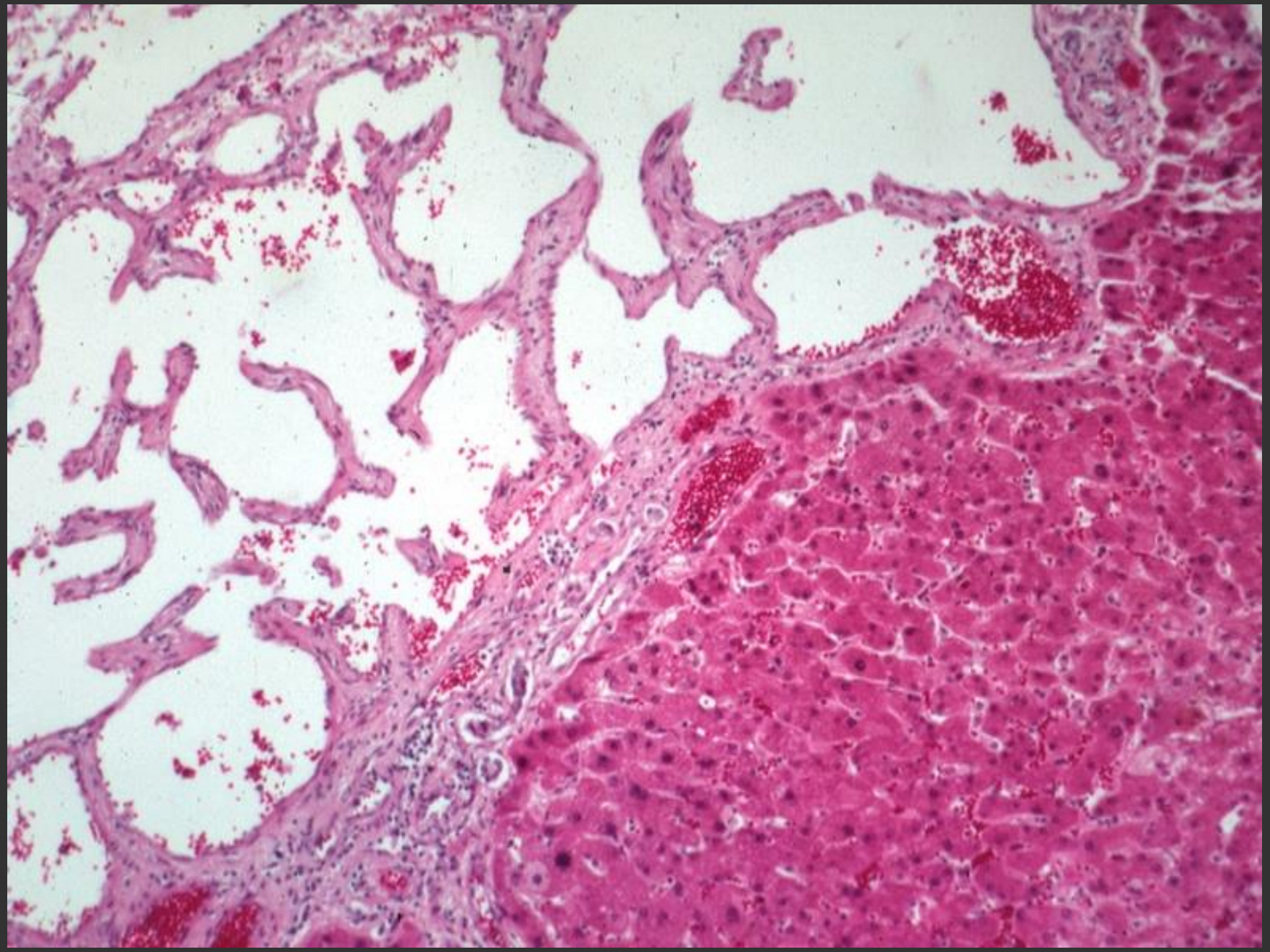




Cavernous hemangioma

https://peir.path.uab.edu/library/picture.php?/5698/search/1148

https://peir.path.uab.edu/library/picture.php?/8028/search/1148



Cavernous hemangioma

https://peir.path.uab.edu/library/picture.php?/8624/search/1148

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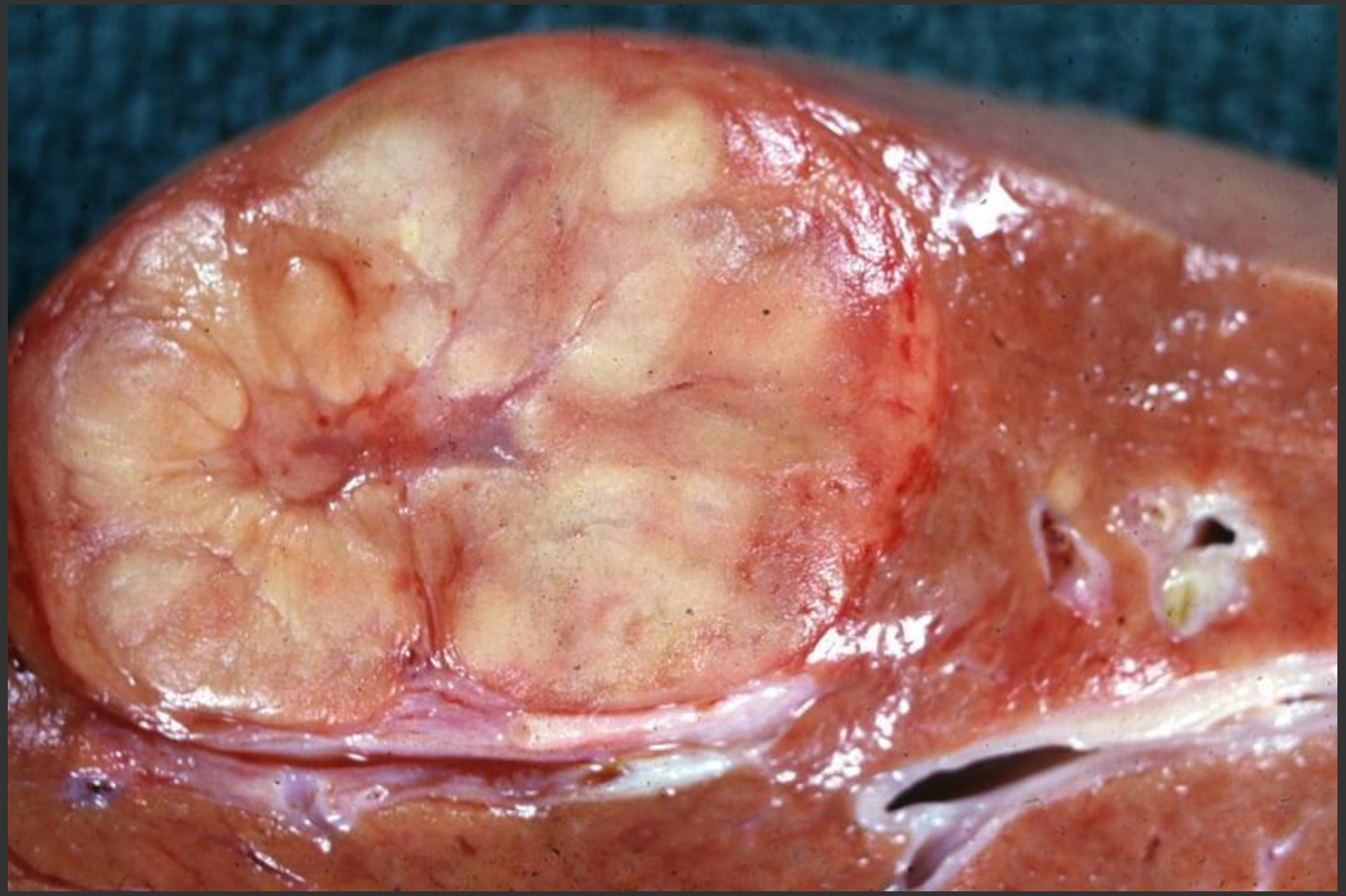
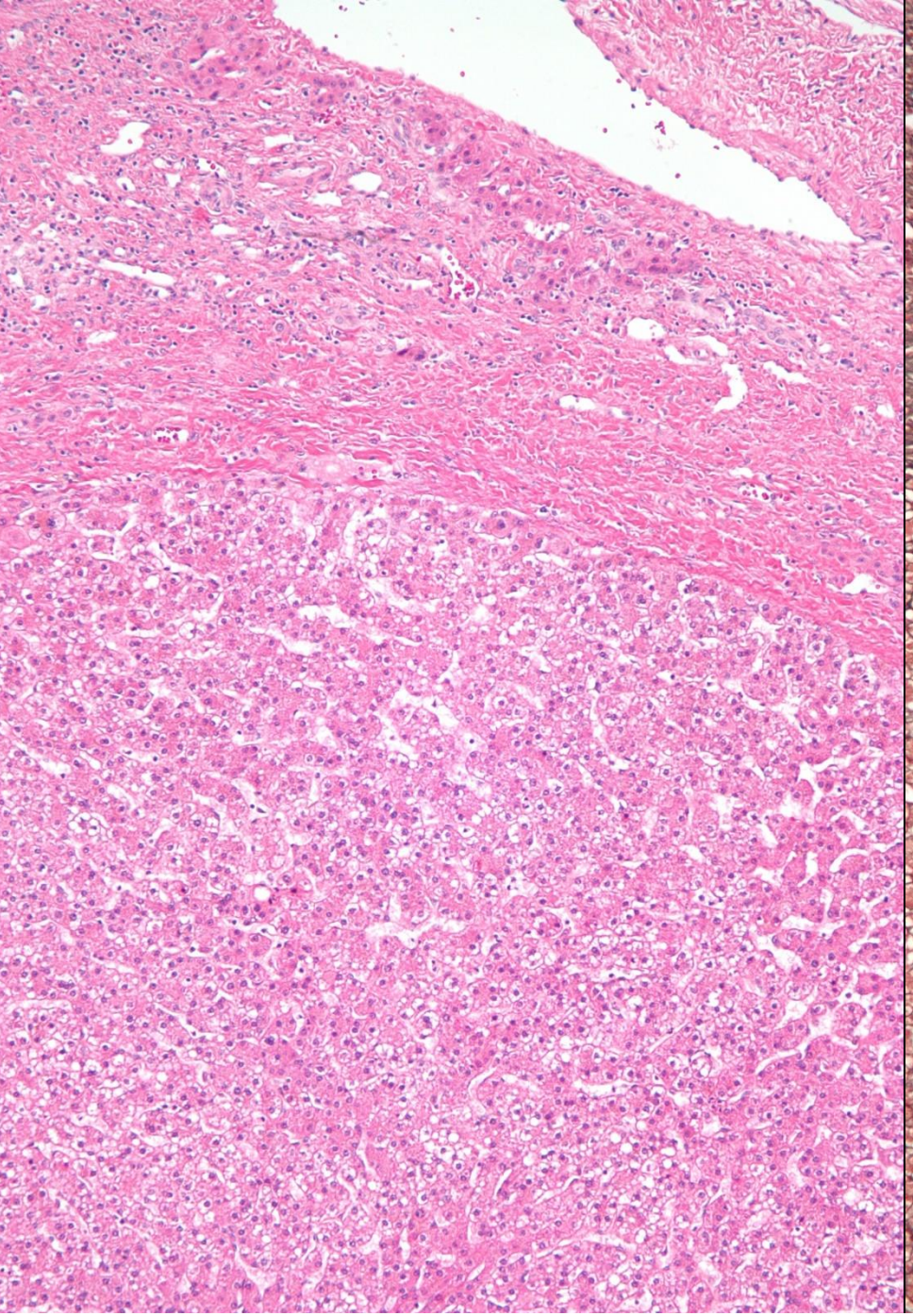


Hepatic adenoma

http://peir.path.uab.edu/library/picture.php?/8025/category/66



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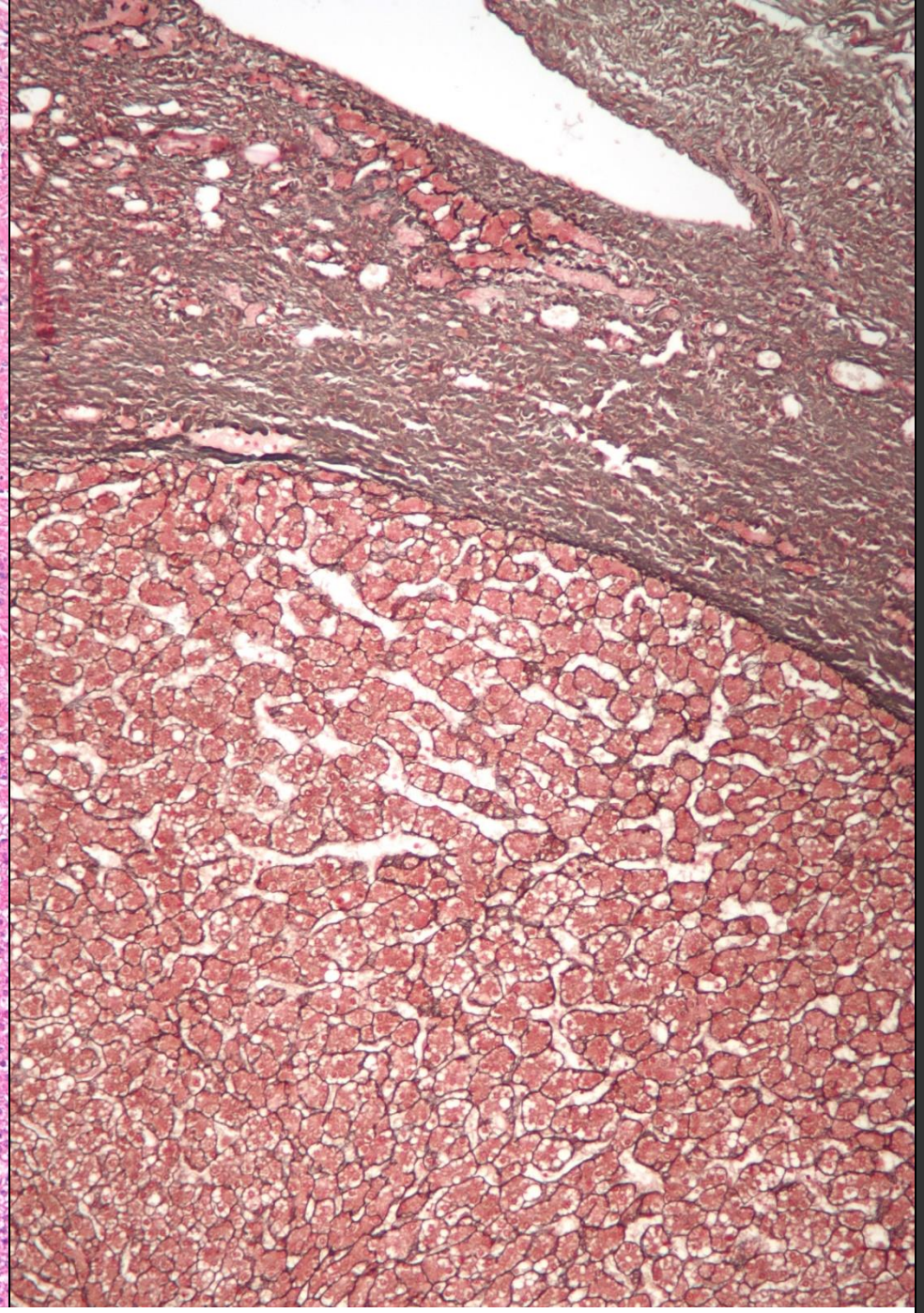

https://librepathology.org/wiki/File:Hepatic_adenoma_high_mag_reticulin.jpg

Hepatic adenoma
HE vs reticulin

LIVER PRIMARY TUMORS

Malignant

- hepatocellular carcinoma (HCC)
- cholangiocarcinoma
- hemangiosarcoma

Hepatocellular carcinoma

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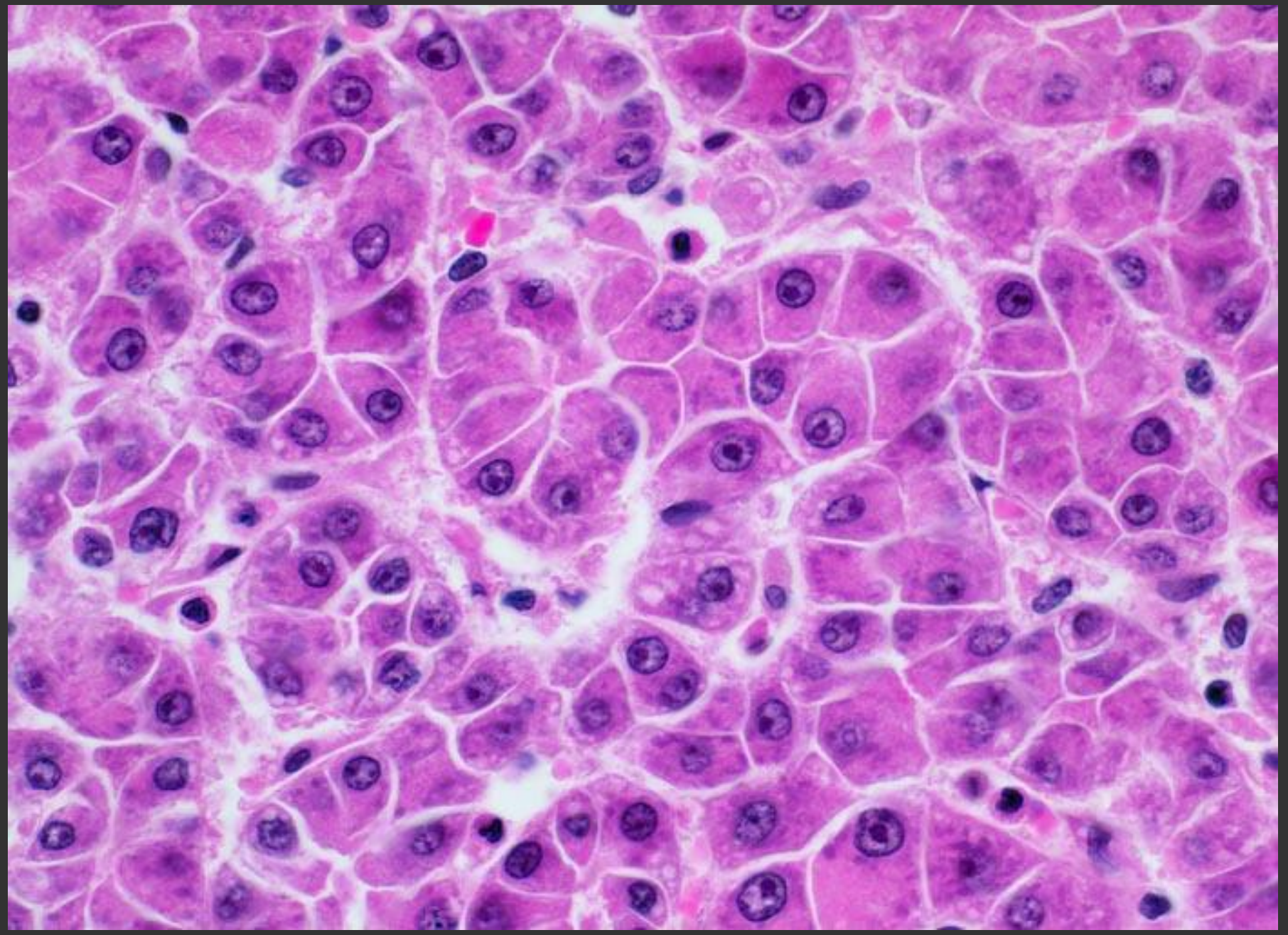
https://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=9579



Hepatocellular carcinoma

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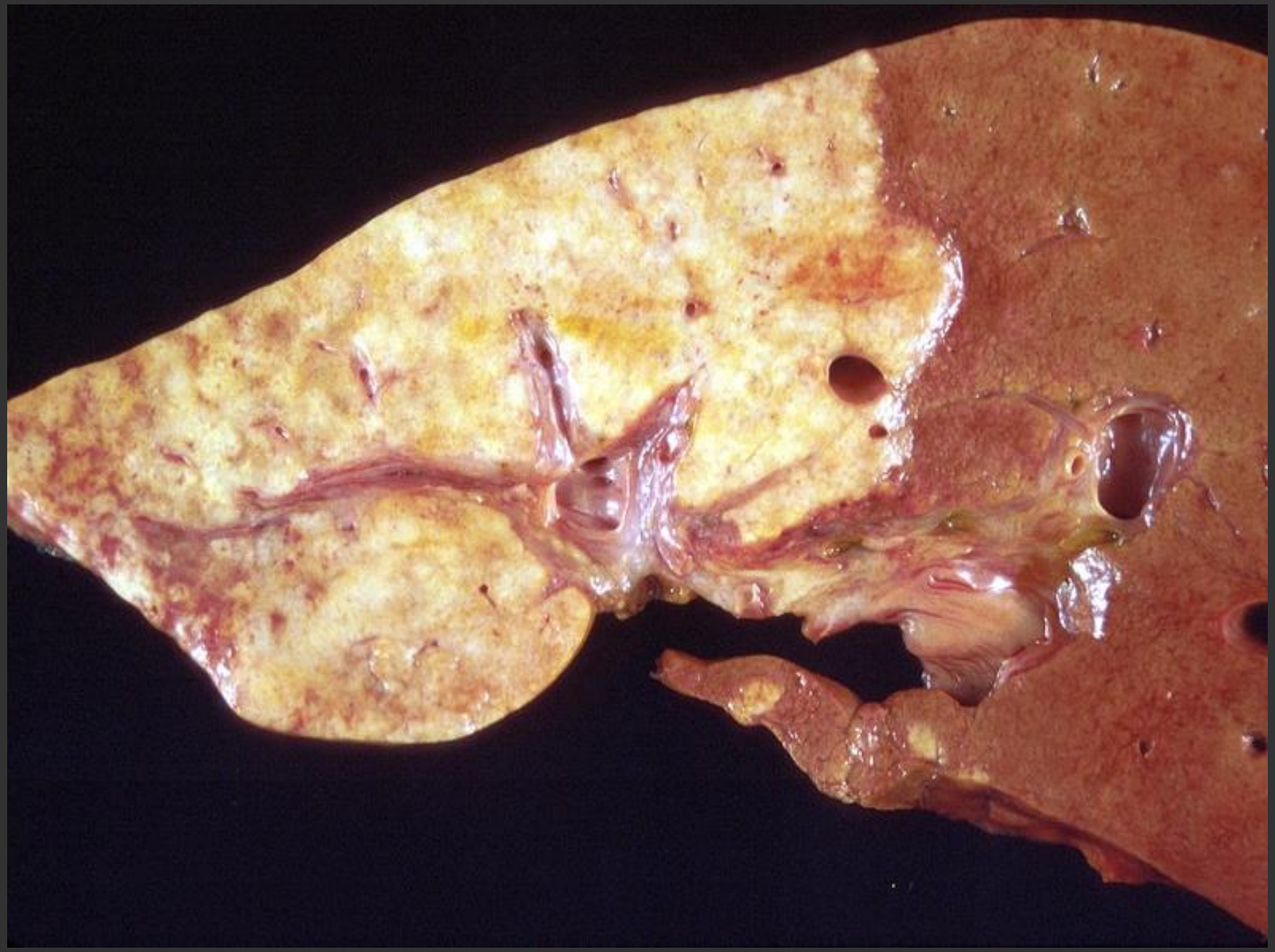
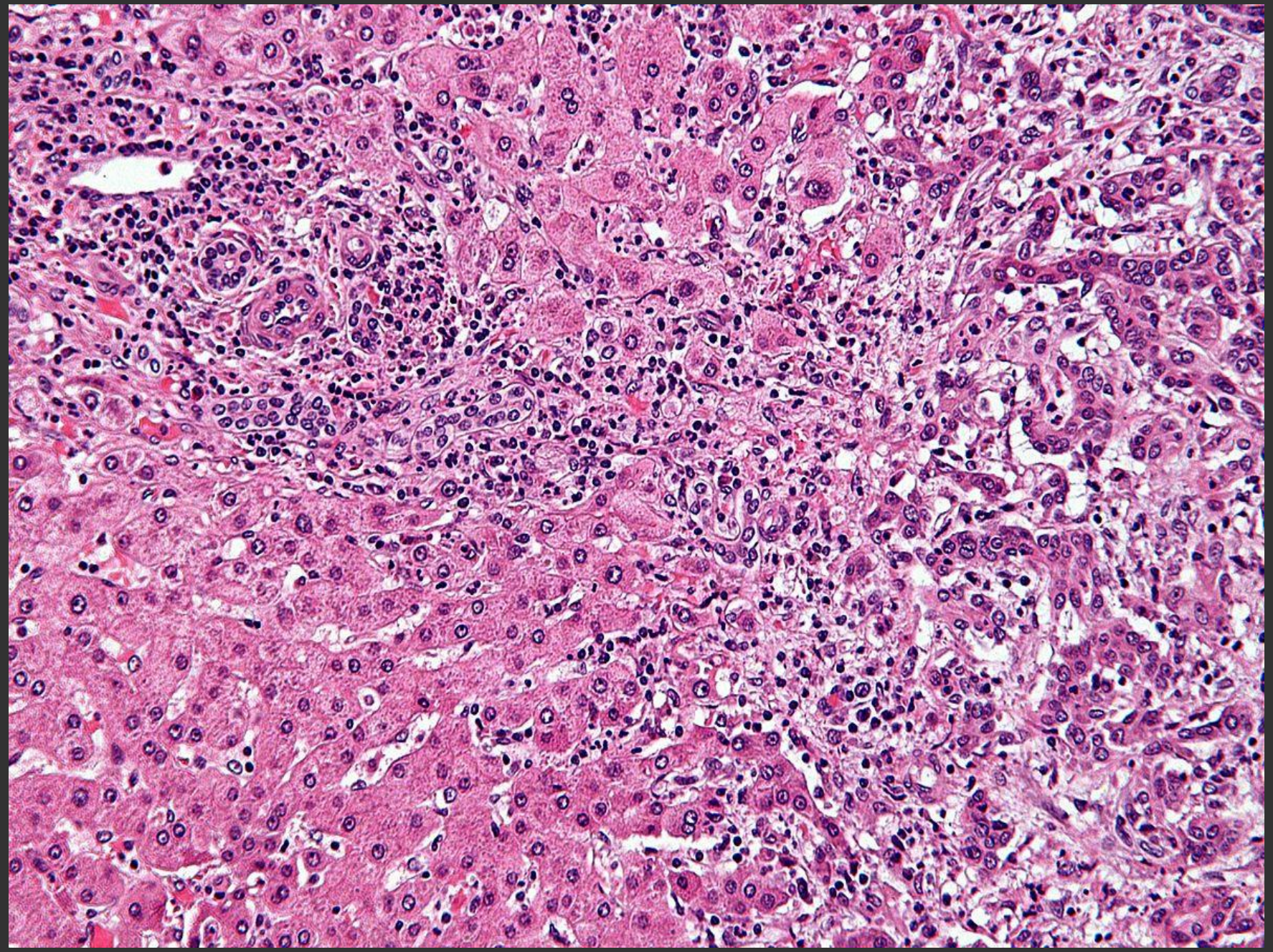


Cholangiocarcinoma



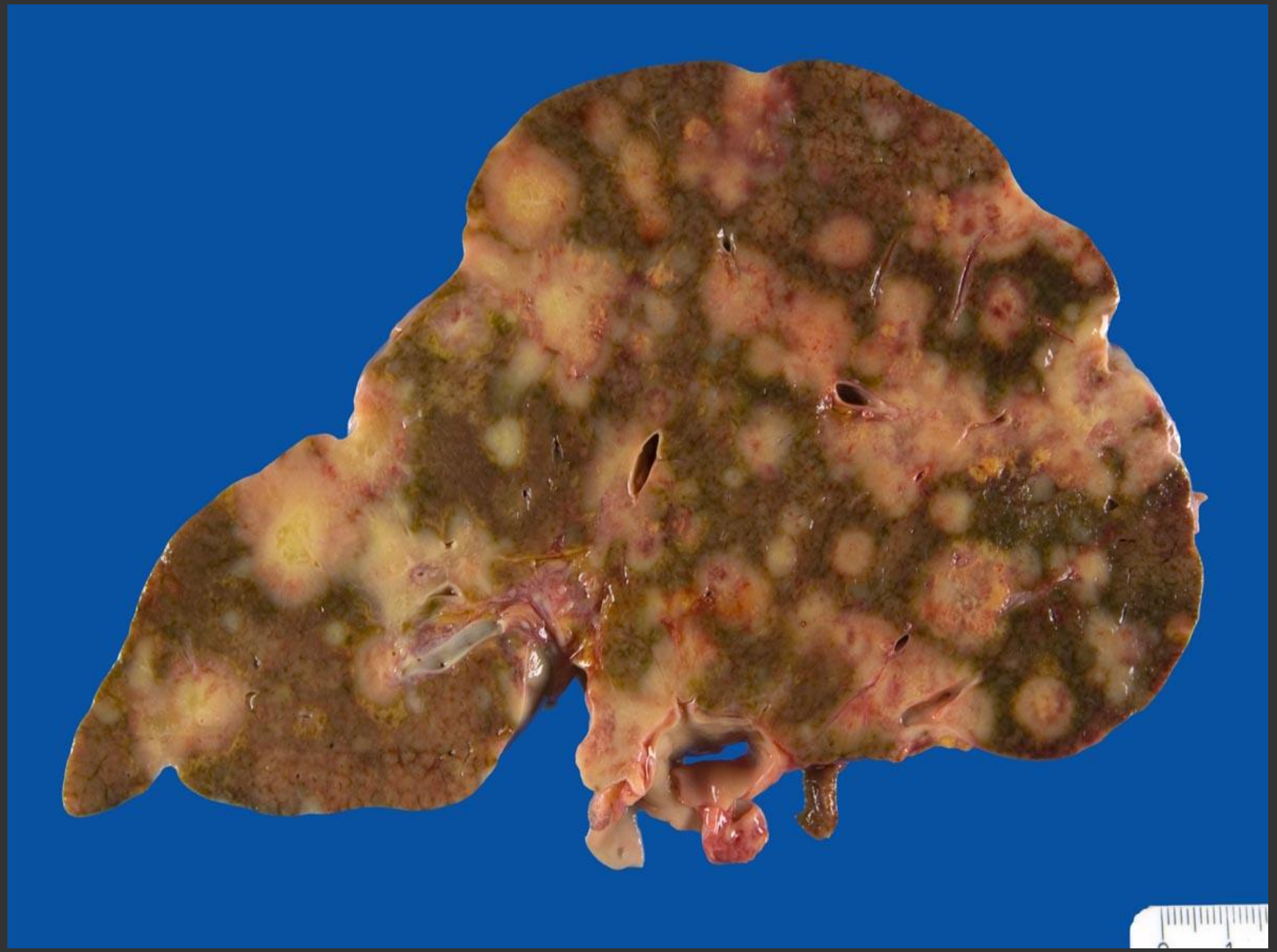
https://librepathology.org/wiki/File:Cholangiocarcinoma_-_high_mag.jpg

Cholangiocarcinoma

- resembles adenocarcinoma, often with a dense collagenous stroma

LIVER SECONDARY / METASTATIC TUMORS

- far more common than primary neoplasia
- multiple nodular implants
- gray-white
- found at the periphery of the circulation underneath the liver capsule
- cause striking hepatomegaly



Metastatic tumors

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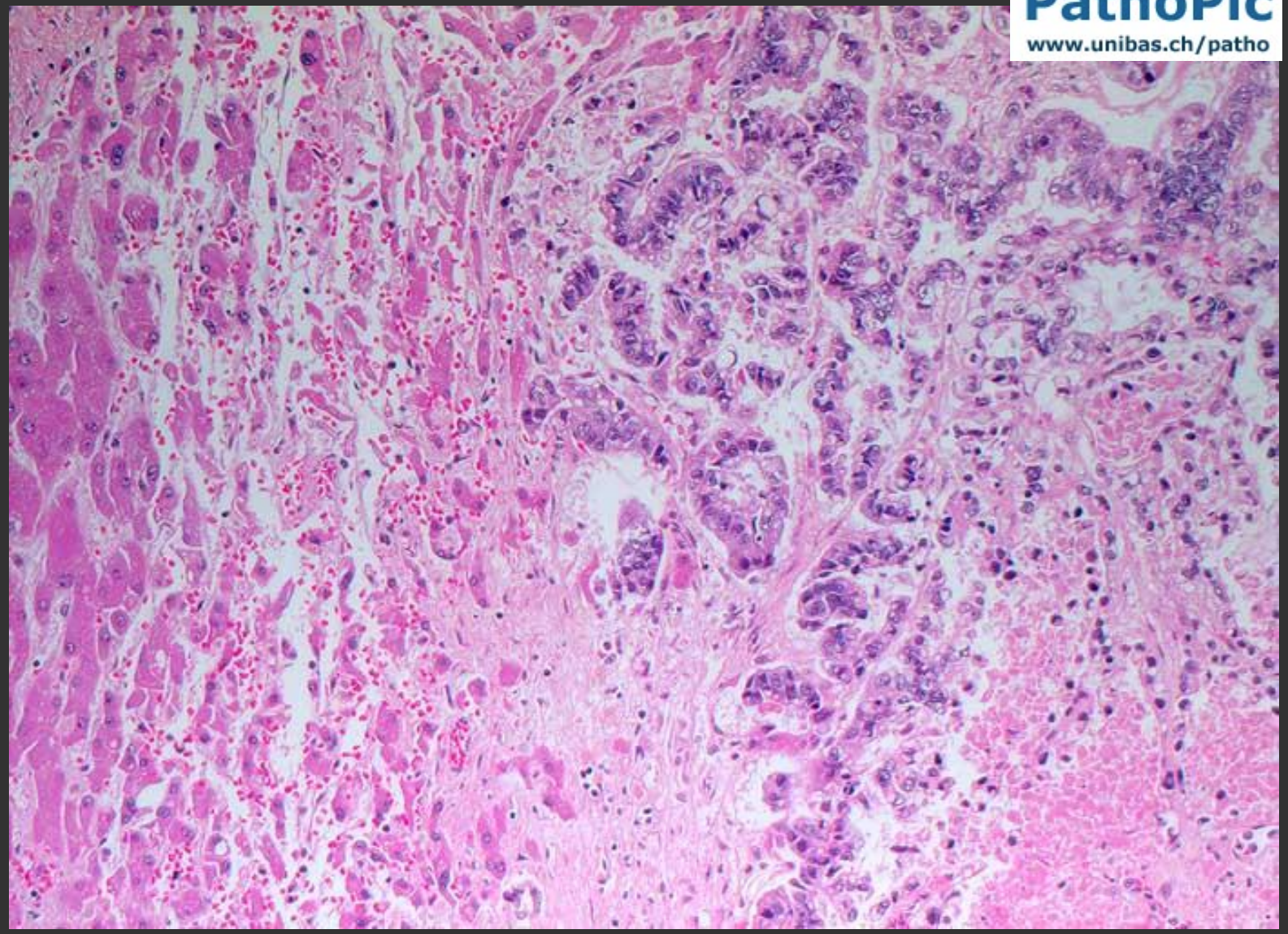


Liver adenocarcinomatous metastasis.

http://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=5606

GALLBLADDER PATHOLOGY

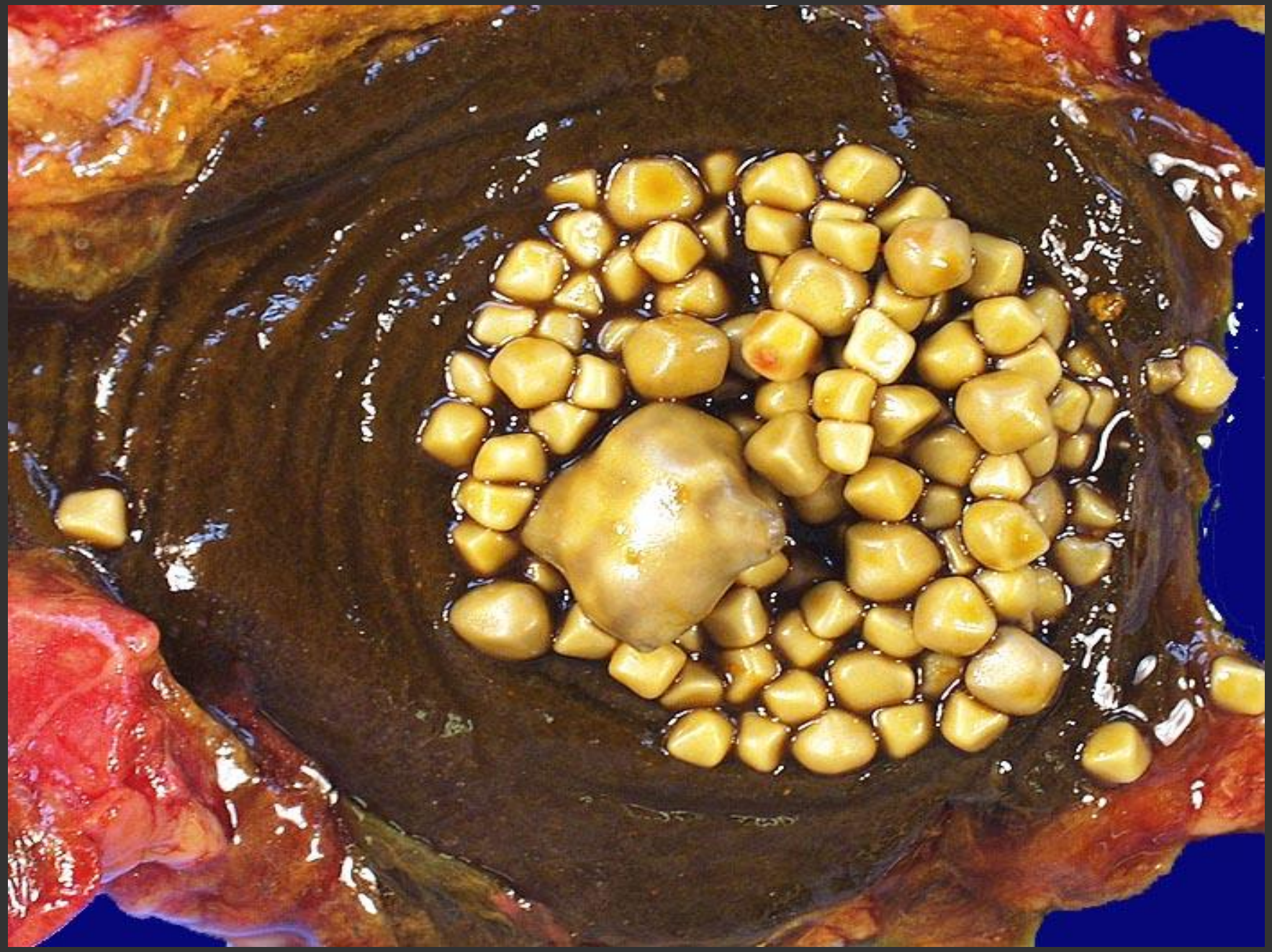
CHOLELITHIASIS

- the presence of stones within the lumen of the gallbladder or in the extrahepatic biliary tree

	Cholesterol stones	**Pigment (black or brown) stones**
Risk factors	- advancing age; - obesity + cholesterol rich diet; - female sex hormones; - gallbladder stasis; - hyperlipidemia; - disorders of bile metabolism.	- chronic hemolytic syndromes; - biliary infection; - gastrointestinal disorders (Crohn's disease, ileal resection, cystic fibrosis).
Pathogenesis	3 conditions must be met: (1) bile supersaturated with cholesterol, so it can no longer remain dispersed and nucleates into solid cholesterol monohydrate crystals; (2) bile' kinetic favorable for nucleation; (3) the persistence of cholester crystals within gallbladder long enough to aggregate into stones	Precipitation of abnormal insoluble calcium salts of unconjugated bilirubin. The presence of unconjugated bilirubin in the biliary tree is possible in some circumstances: (1) increased hemolysis; (2) infections of the biliary tract.

Cholesterol stones

- exclusive in the gallbladder
- 50-100% cholesterol
- hard external surface
- pale / yellow
- round / ovoid
- radiolucent if mostly cholesterol, radiopaque if sufficient calcium carbonate is found



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Pigment stones

- “black”
    - in sterile gallbladder bile
    - oxidized polymers of calcium salts of unconjugated bilirubin
    - < 1 cm in diameter
    - 50-75% radiopaque
- “brown”
    - in infected intrahepatic or extrahepatic ducts
    - pure calcium salts of unconjugated bilirubin
    - soap-like greasy consistence
    - radiolucent

http://www.med.umich.edu/lrc/coursepages/m1/anatomy2010/html/clinicalcases/cholelithiasis/cholelithiasis.html

CHOLECYSTITIS

- acute or chronic inflammation of the gallbladder

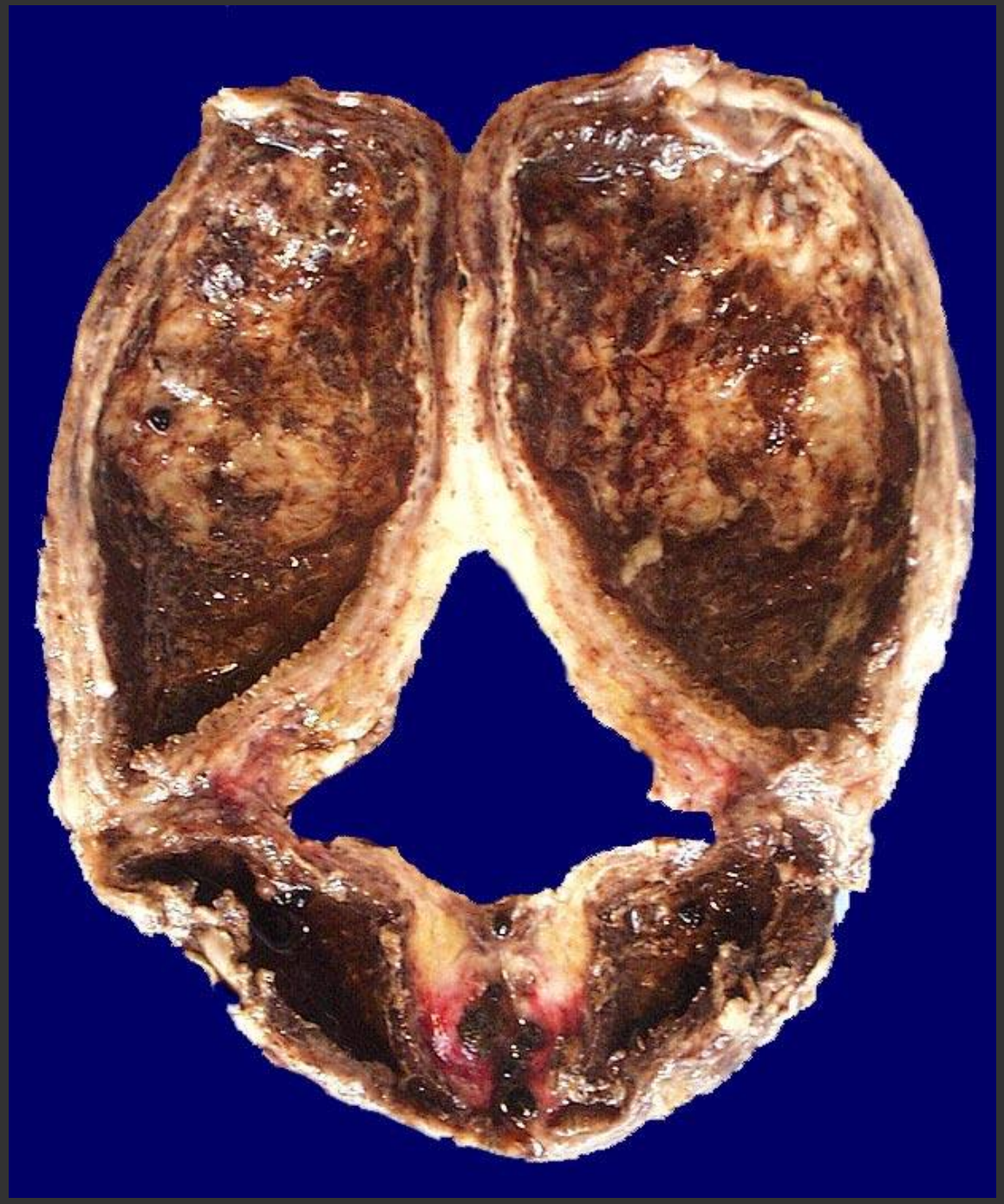
Acute cholecystitis

Macroscopy :

- enlarged, tense
- bright red or violaceus
- fibrinous / suppurative exudate on the serosa
- obstructive stones in the neck of the gallbladder or the cystic duct

Microscopy :

- covering epithelium is desquamated or severe ulcerated
- acute inflammatory reactions throughout the entire wall thickness



Acute cholecystitis

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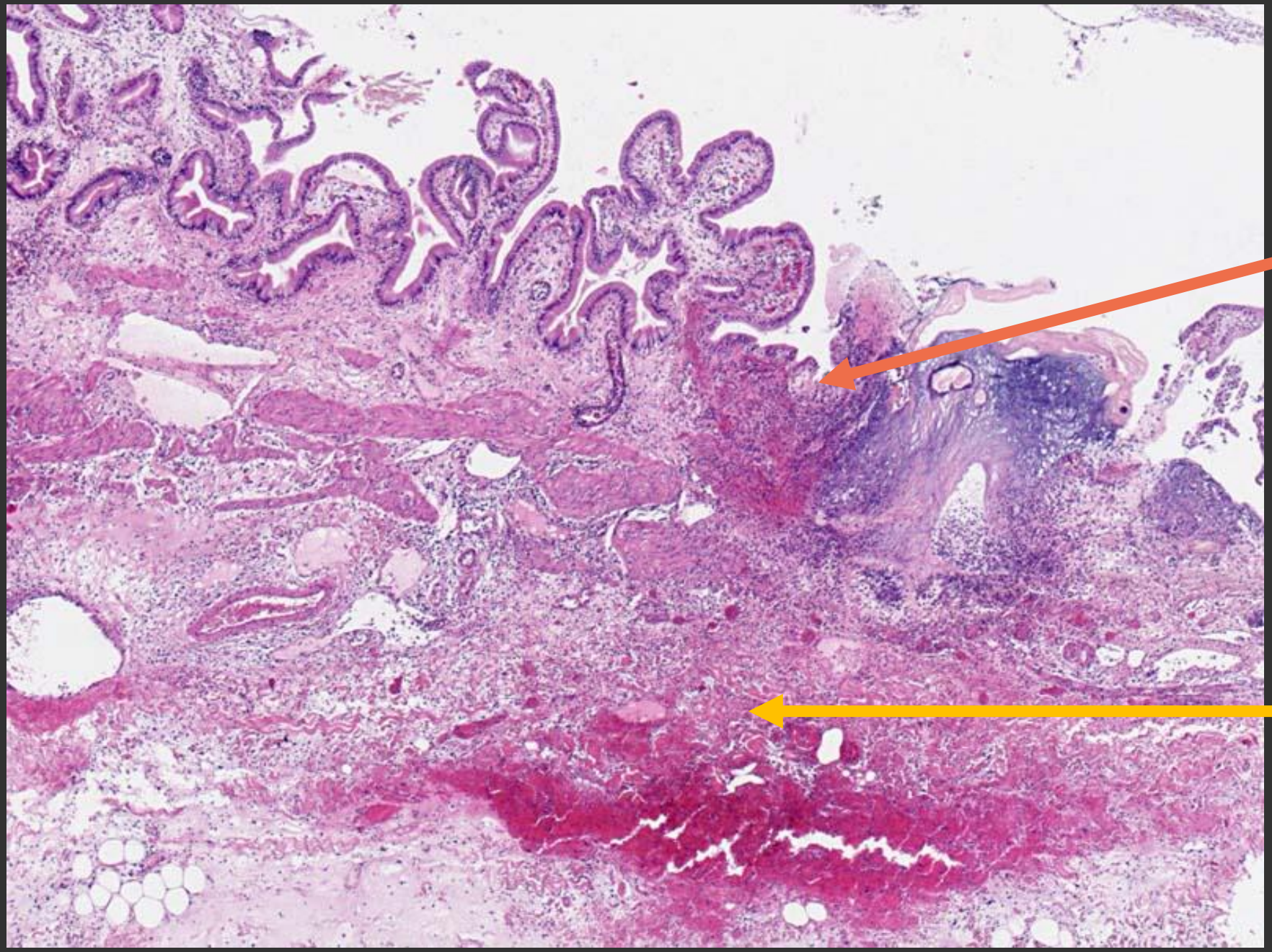

ulceration of the mucosae

edema + hemorrhage

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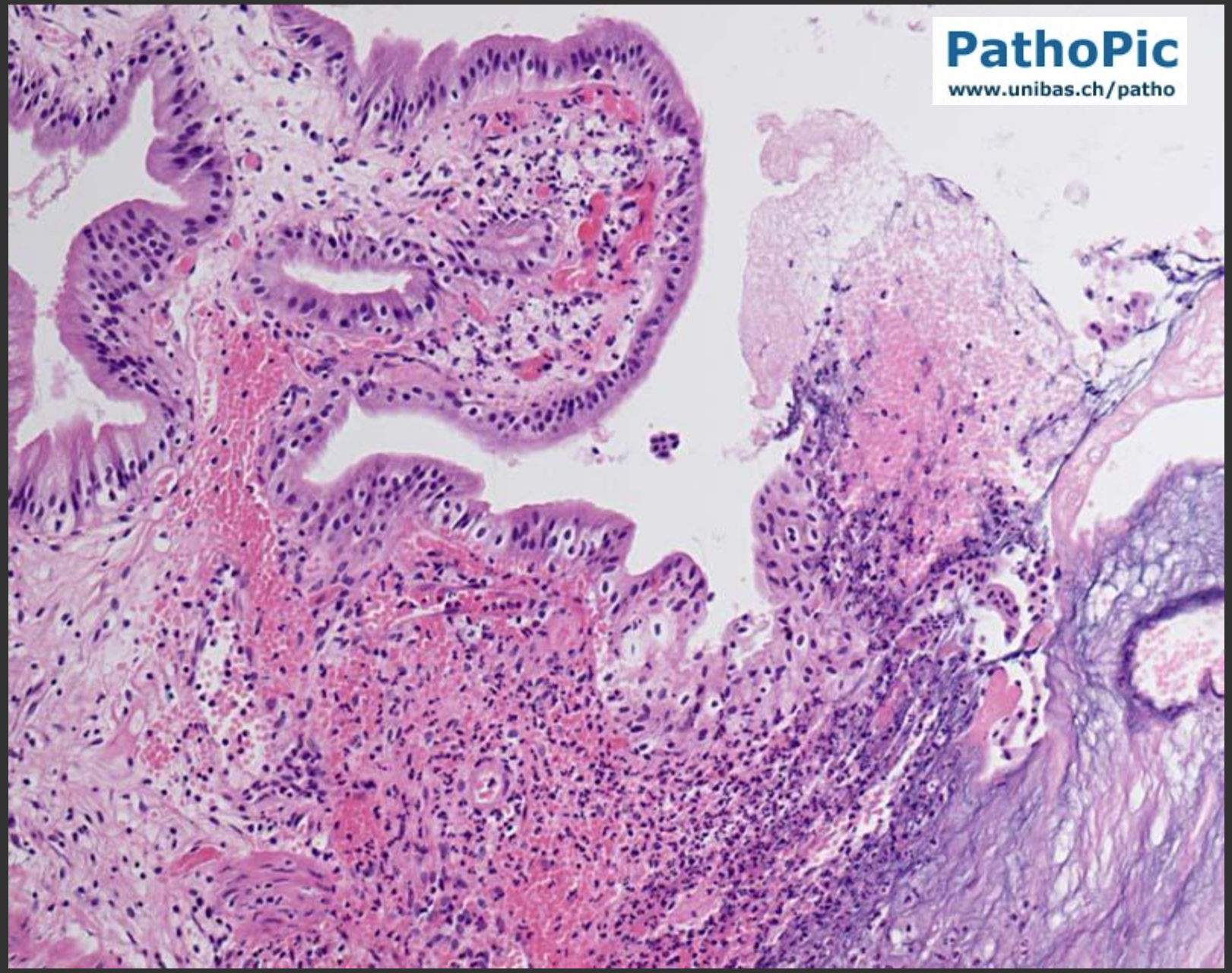

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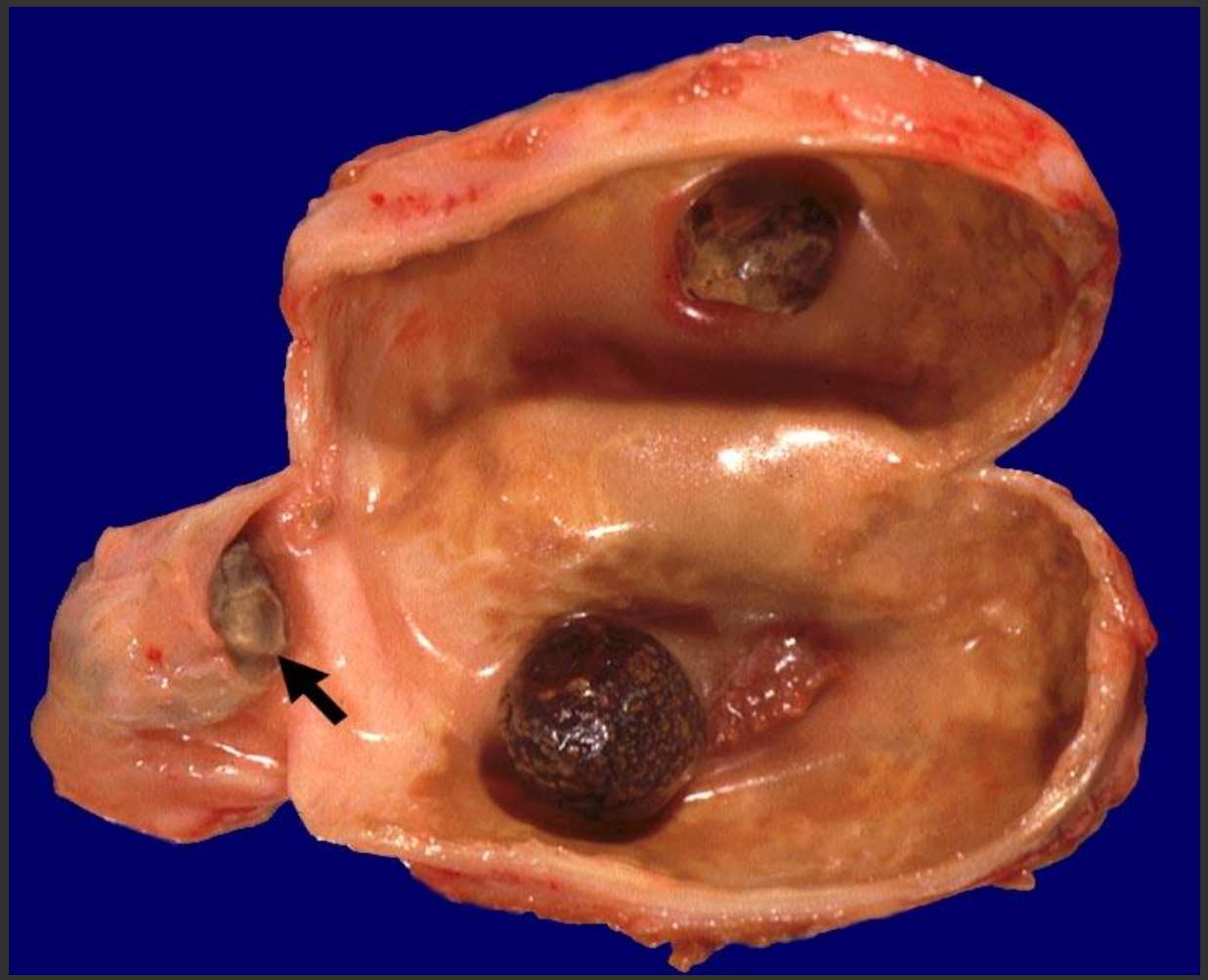
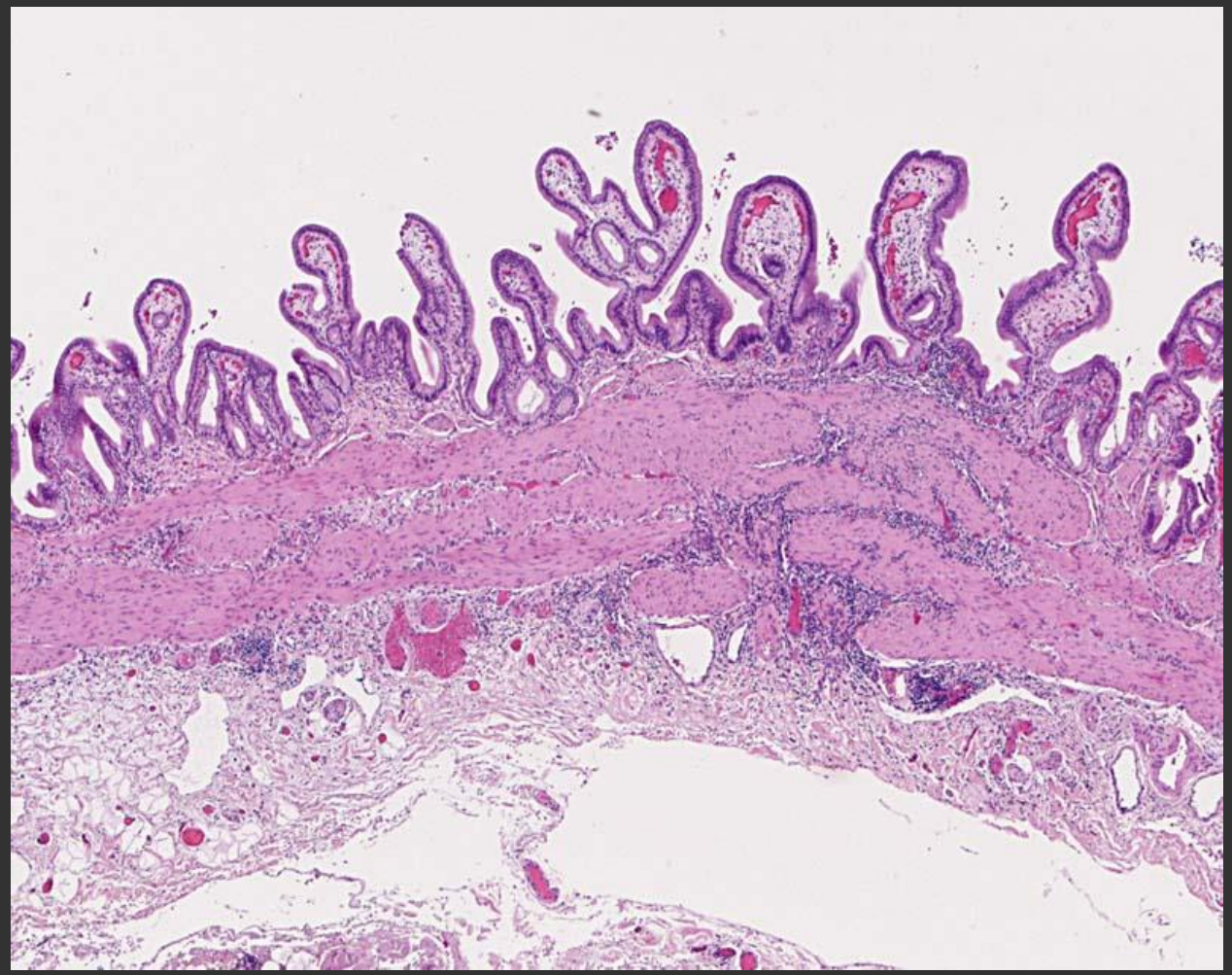
Chronic cholecystitis

- 90% of cases associated with gallstones
- two variants :
  - Hypertrophic chronic cholecystitis
  - Atrophic chronic cholecystitis

- Hypertrophic chronic cholecystitis
  - wall is thickened, firm
  - intact epithelium, Rokitansky-Aschoff sinuses
  - cholesterol foci in the submucosa
  - muscle bundles are hypertrophied, fibrosis is present

- Atrophic chronic cholecystitis
  - following the complete blockage of the cystic duct by an impacted stone
  - thin walls
  - flattened mucosa
  - content distends the wall (mucocele)
  - muscle is almost absent, replaced by fibrosis





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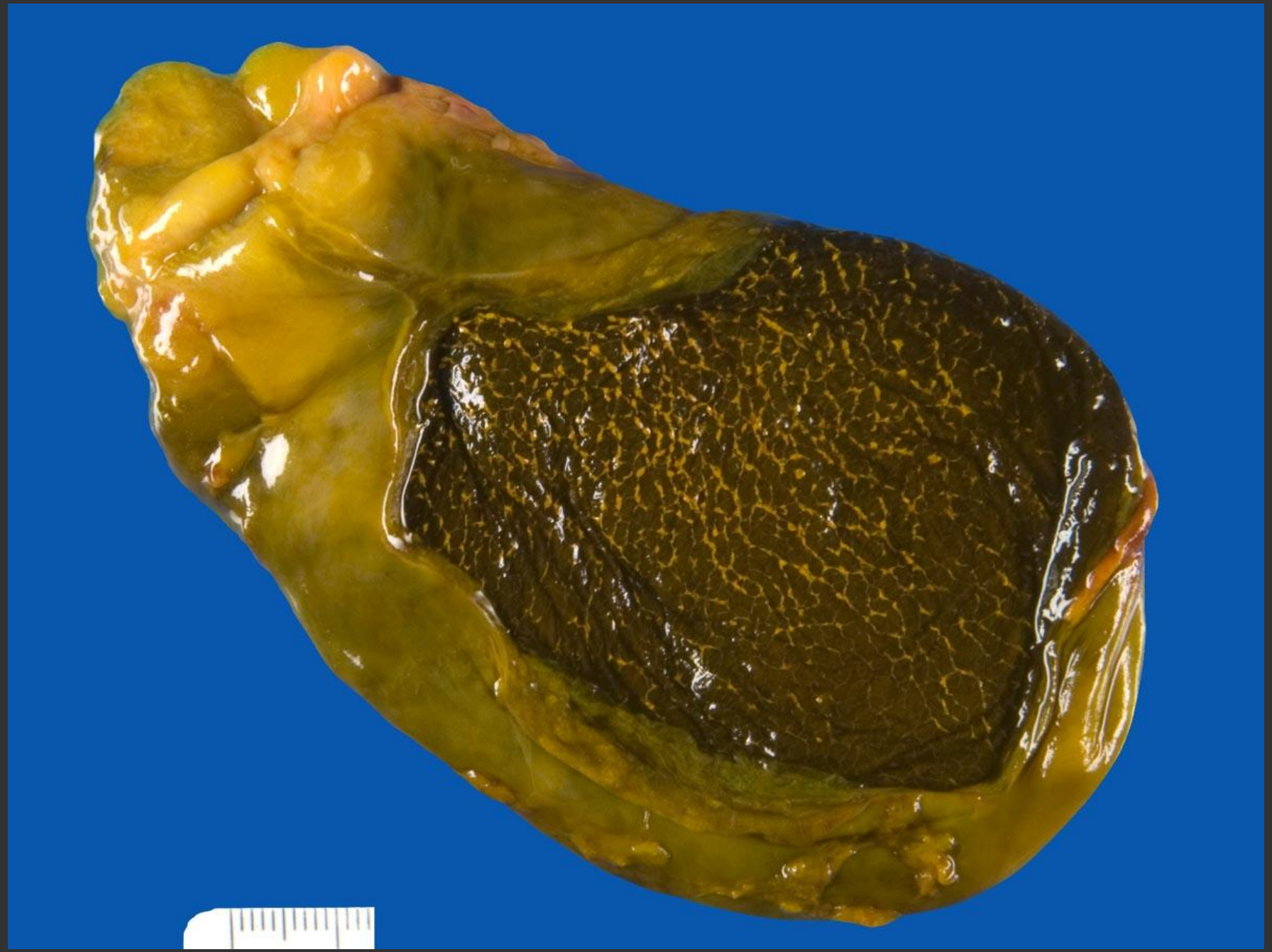
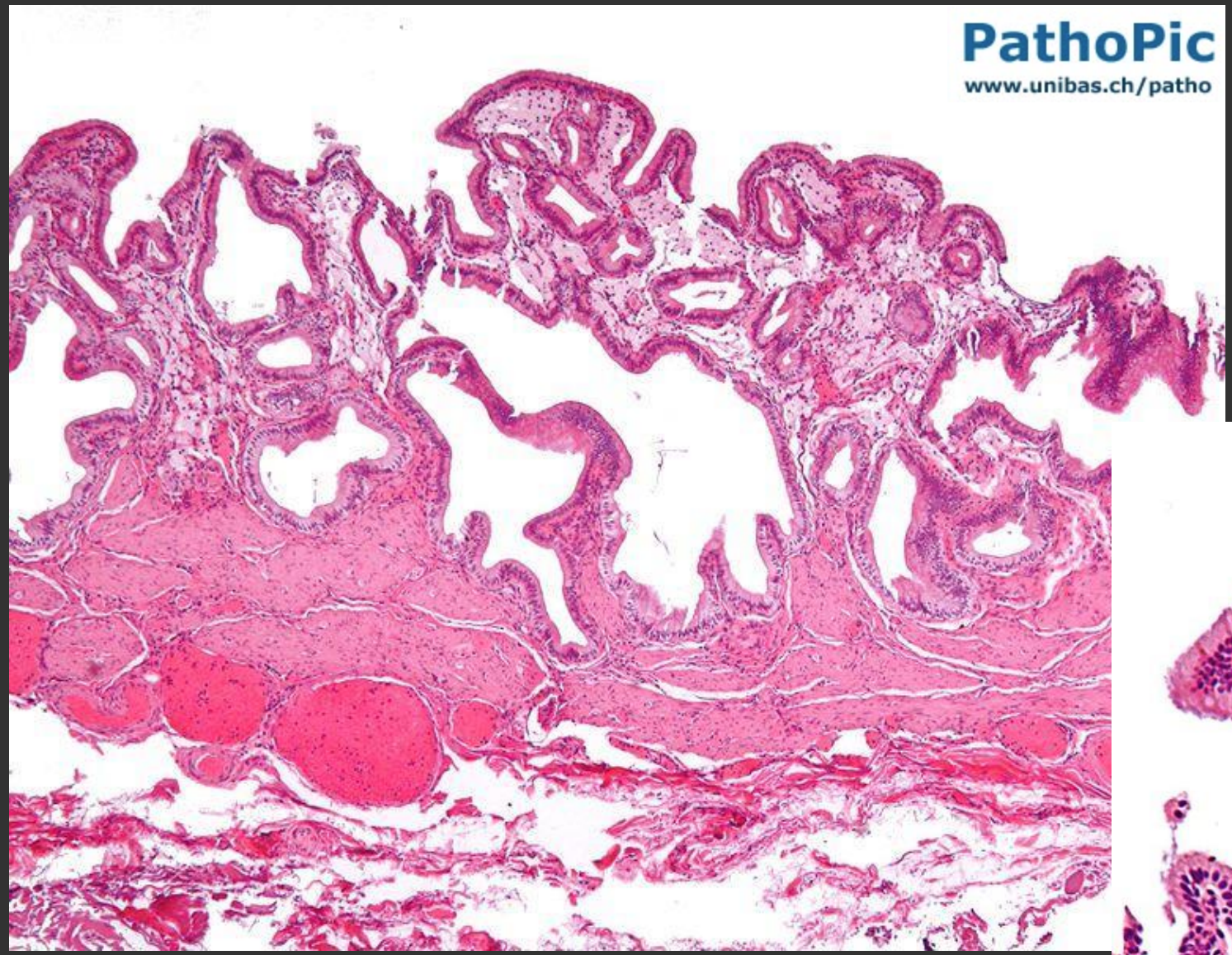
Sometimes, the dystrophic changes of the gallbladder wall predominate:

- *"strawberry gallbladder"*
    - mucosa surface presents scattered, yellow flecks
    - extensive cholesterol-laden macrophage accumulations
- *"porcelain gallbladder"*
    - extensive dystrophic calcification within the gallbladder wall
    - markedly increase incidence of associated cancer.

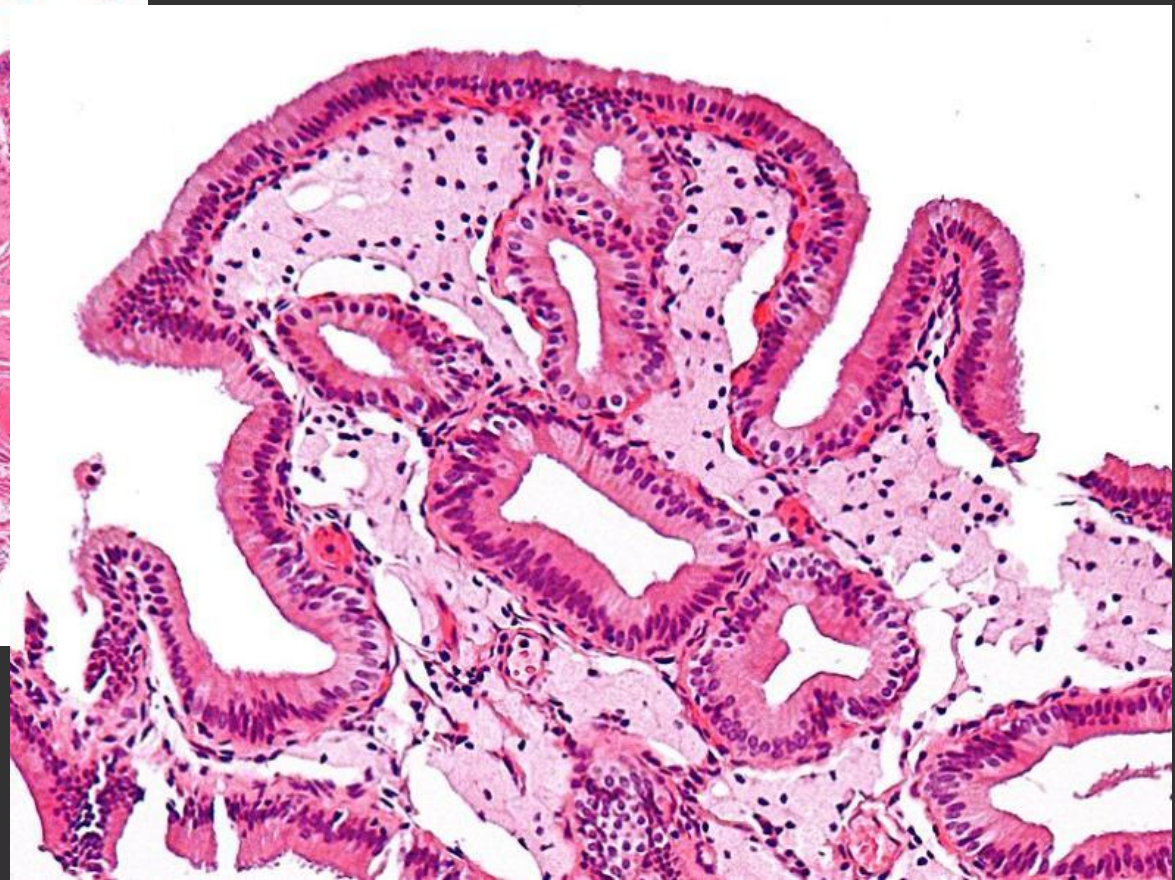


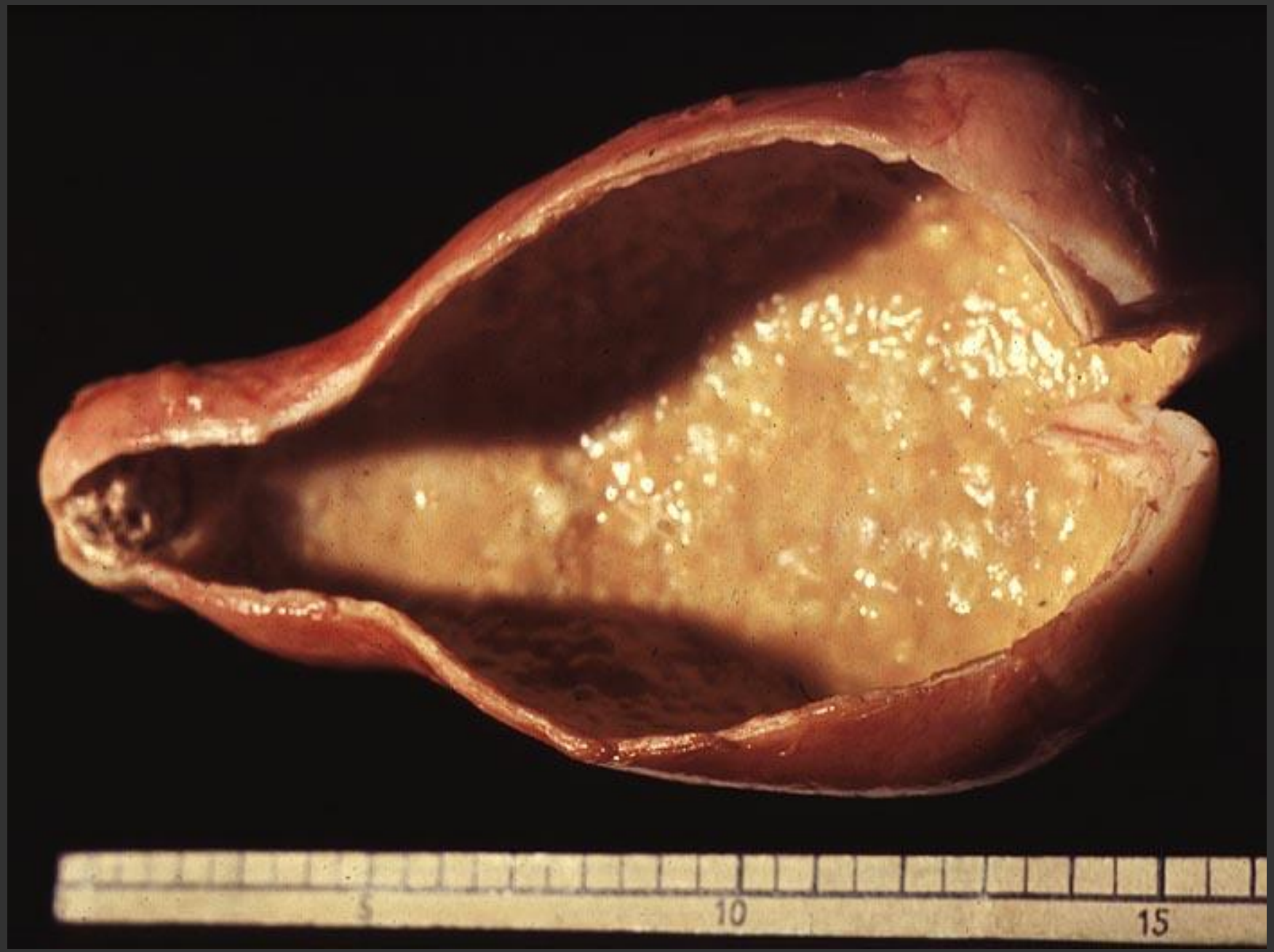
"strawberry gallbladder"

http://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=9884



Strawberry gallbladder extensive cholesterol-laden macrophage accumulations within mucosa – the yellowish flecks grossly.





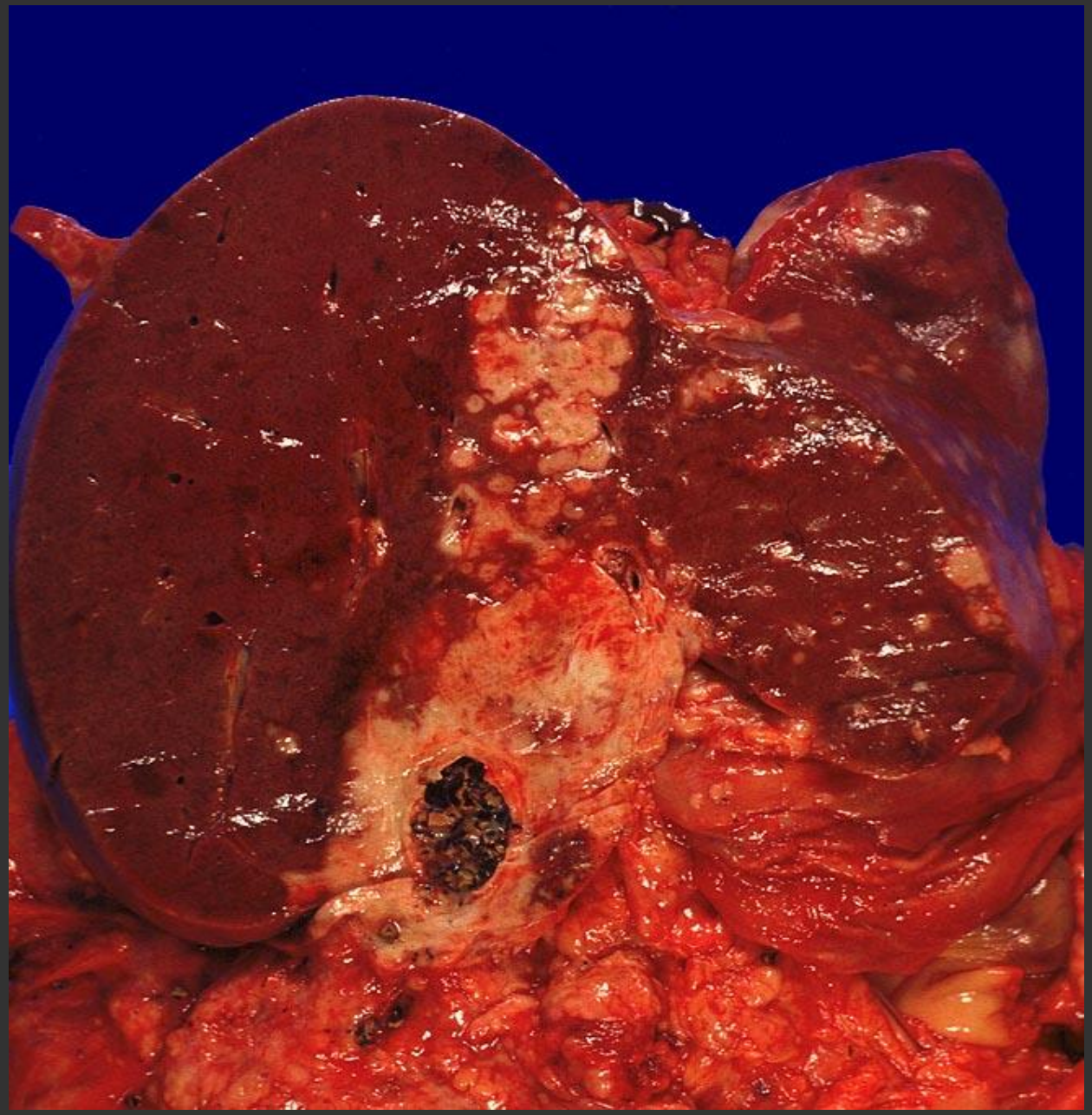
"porcelain gallbladder"

http://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=003606

GALLBLADDER TUMORS

Adenocarcinoma

- most common tumor
- 80% associated with gallstones
- usually well differentiated
- similar symptoms as gallstone disease
- poor prognosis : tumor often advanced when found



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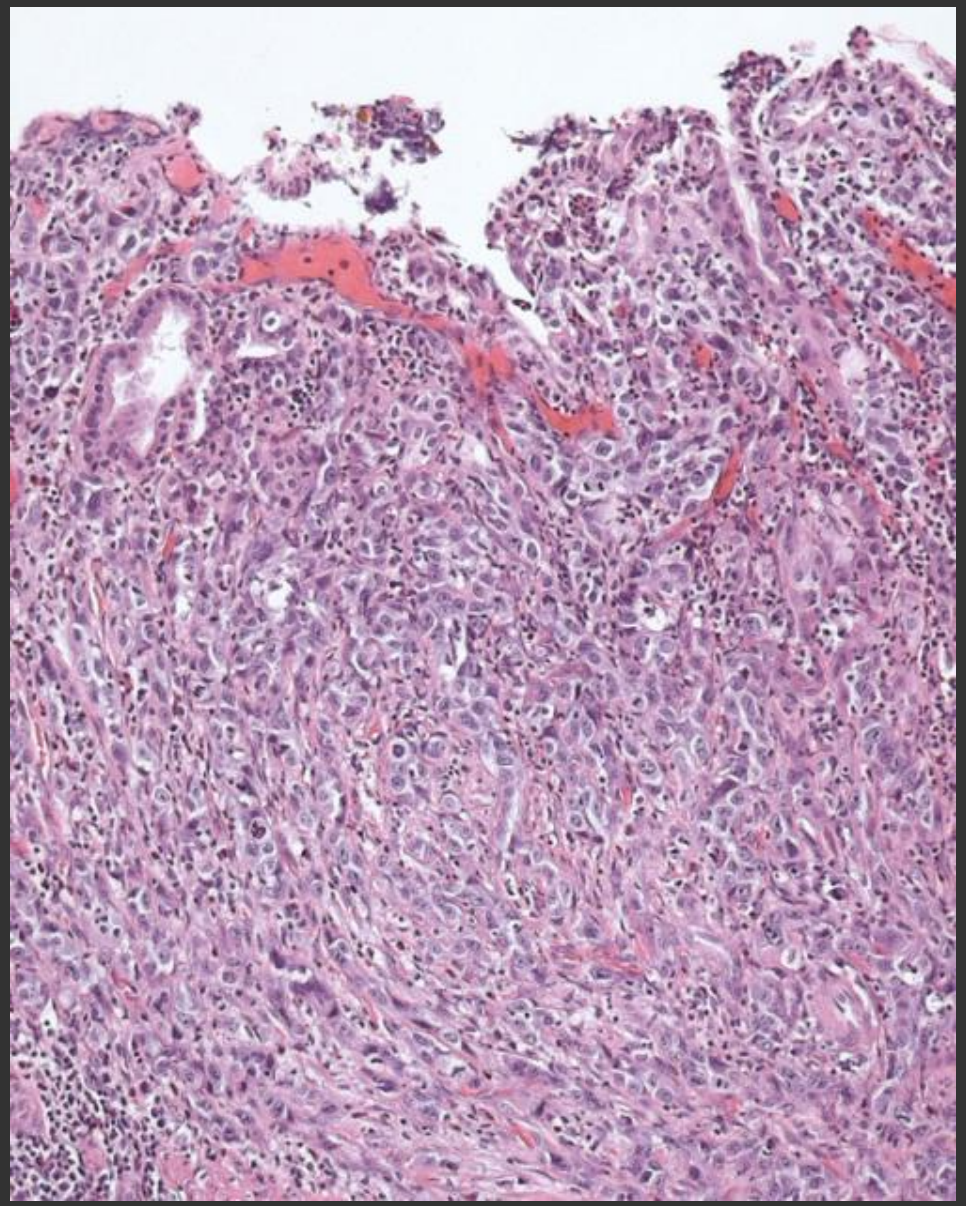
Gallbladder adenocarcinoma, infiltrating the liver



PathoPic
www.unibas.ch/patho

Poorly differentiated gallbladder adenocarcinoma.

http://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=10993

PANCREAS PATHOLOGY

PANCREATITIS

- inflammatory condition the results from injury of acinar cells

Variants :

- acute pancreatitis (self limited disease)
- acute hemorrhagic pancreatitis
- chronic pancreatitis

Acute hemorrhagic pancreatitis (“necrotizing pancreatitis”)

- extensive fat necrosis in and about the pancreas
- hemorrhage into the parenchyma

Associated with alcoholism (men) and cholelithiasis (women)

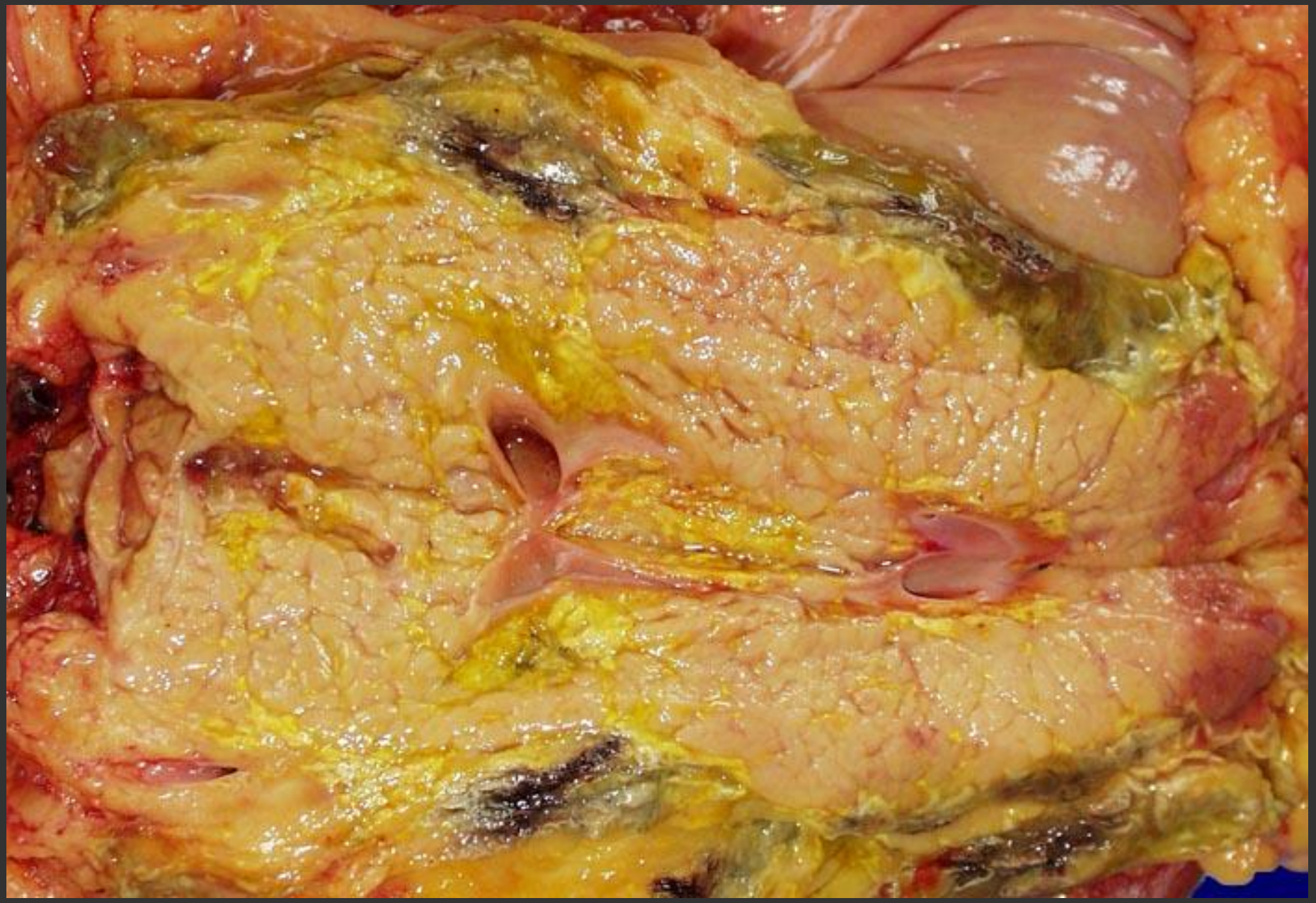
Mechanisms :

- main pancreatic duct obstruction (gallstones)
- acinar cell injury (alcohol)
- deranged intracellular transport of pancreatic enzymes

Acute hemorrhagic pancreatitis (“necrotizing pancreatitis”)

Macroscopy :
- initially edematous and hyperemic
- progressing into a large retroperitoneal hematoma
- yellow-white areas of fat necrosis -> saponification
- occasionally, liquefied areas are walled off (“pancreatic abscesses”)

Microscopy :
- fat necrosis
- inflammatory reaction
- necrosis of the blood vessels, with hemorrhage



Acute pancreatitis

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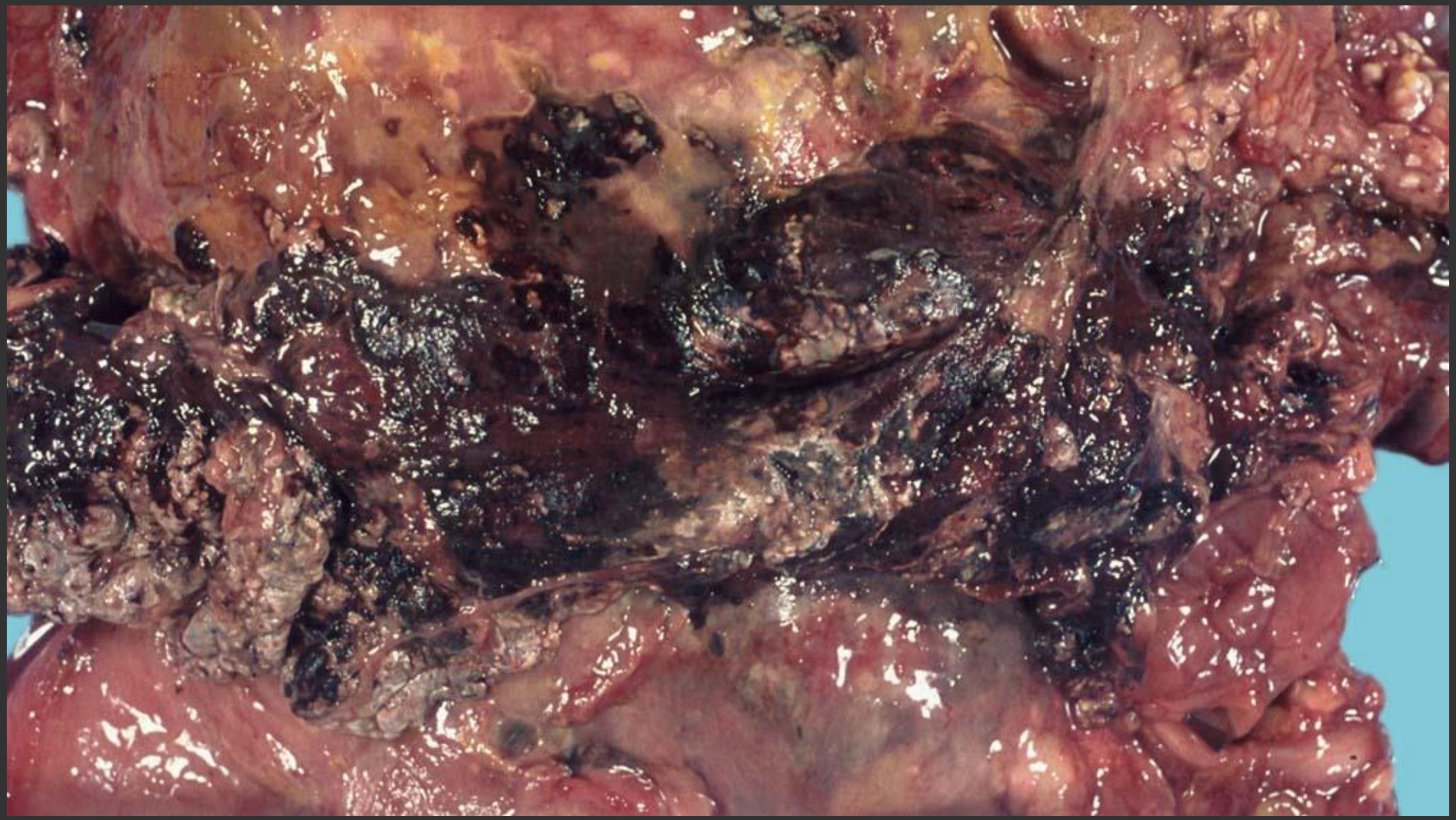
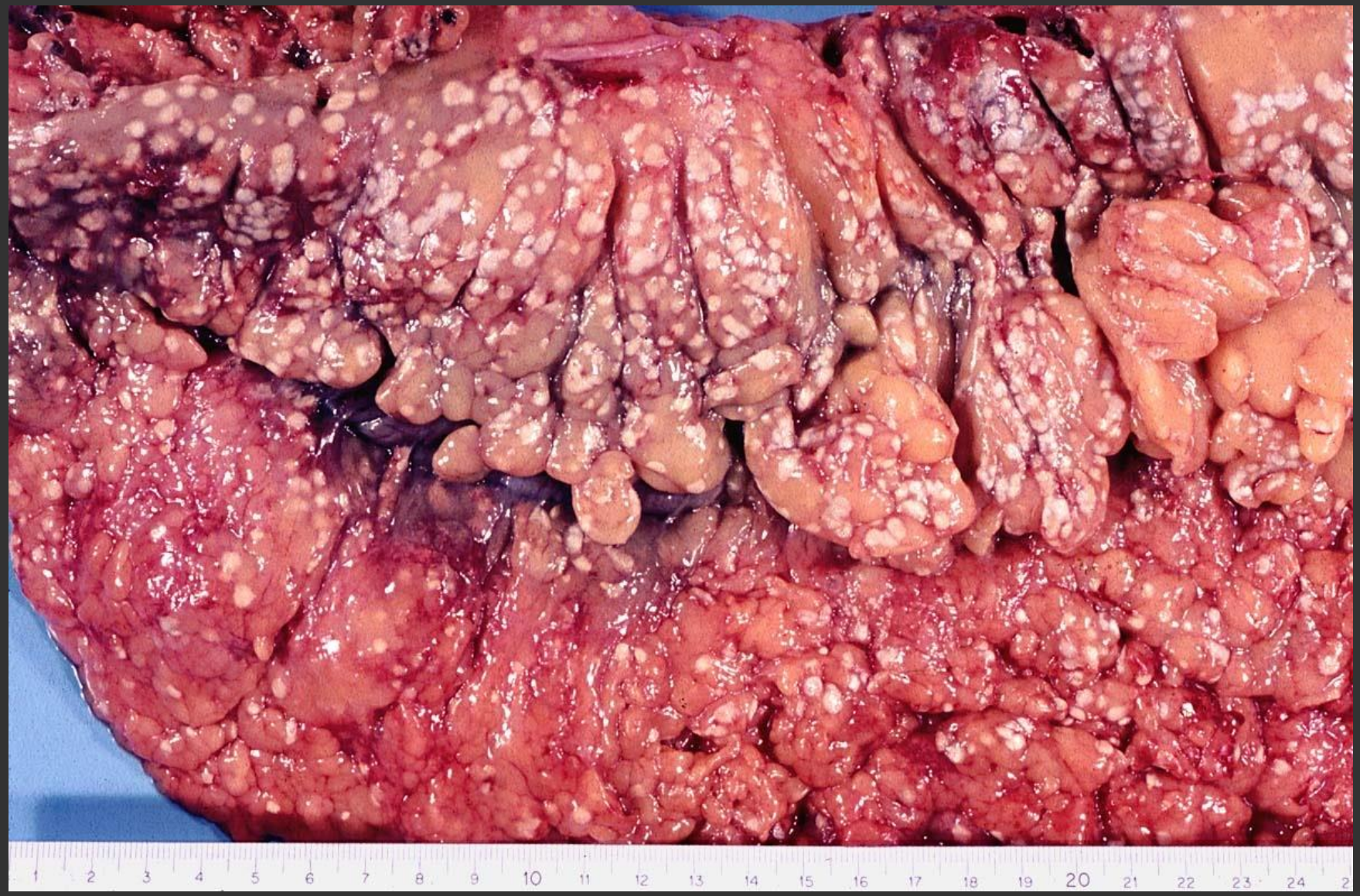


Acute pancreatitis with hemorrhage and necrosis



Fat necrosis of the mesentery

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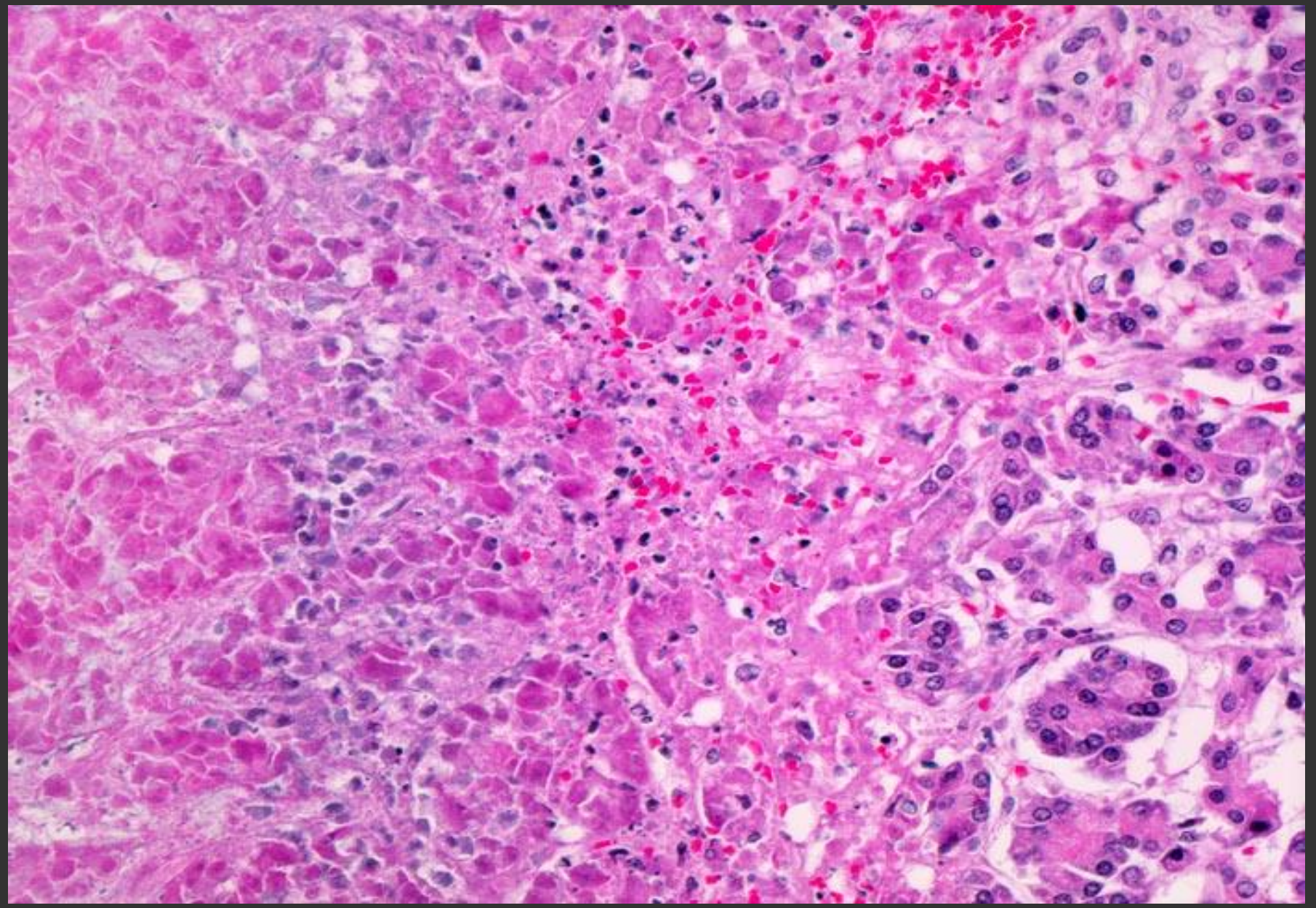


Necrosis

Viable parenchyma

Chronic pancreatitis

- progressive destruction of the pancreas with accompanying irregular fibrosis and chronic inflammation
- mostly in alcoholic, middle-aged males

Pathogenesis

- ductal obstruction by concretions
- interstitial fat necrosis and hemorrhage

Chronic pancreatitis

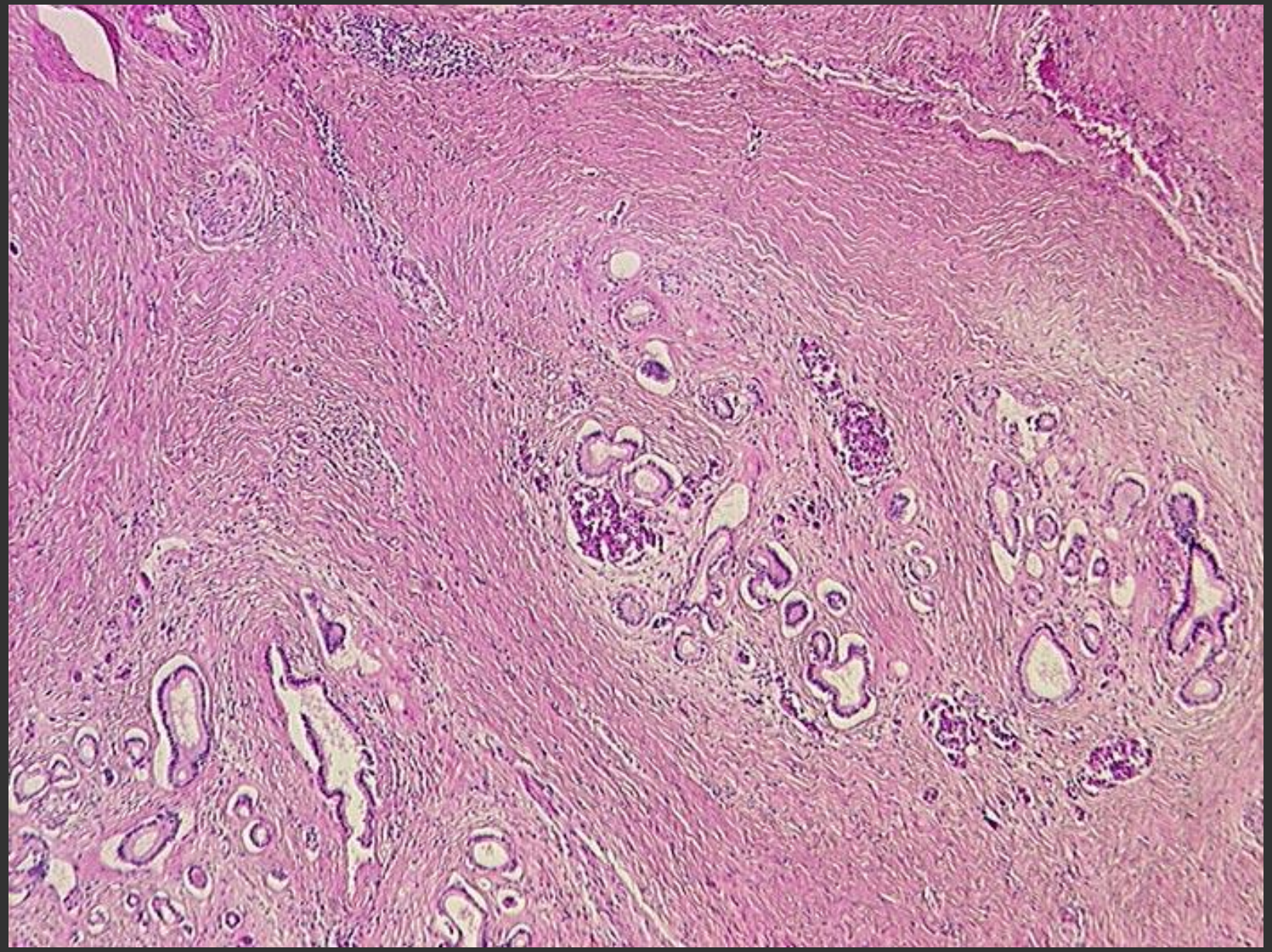
Macroscopy :

- hard consistency, with calcifications and calculi
- cut surface lacks the usual lobular appearance
- true cysts / pseudocysts

Microscopy :

- exocrine and endocrine components reduced in area
- large areas of fibrosis
- ducts contain calcified proteinaceous material
- ductal epithelium may exhibit squamous metaplasia

Chronic sclerosing pancreatitis



http://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=001526

CARCINOMA OF THE PANCREAS

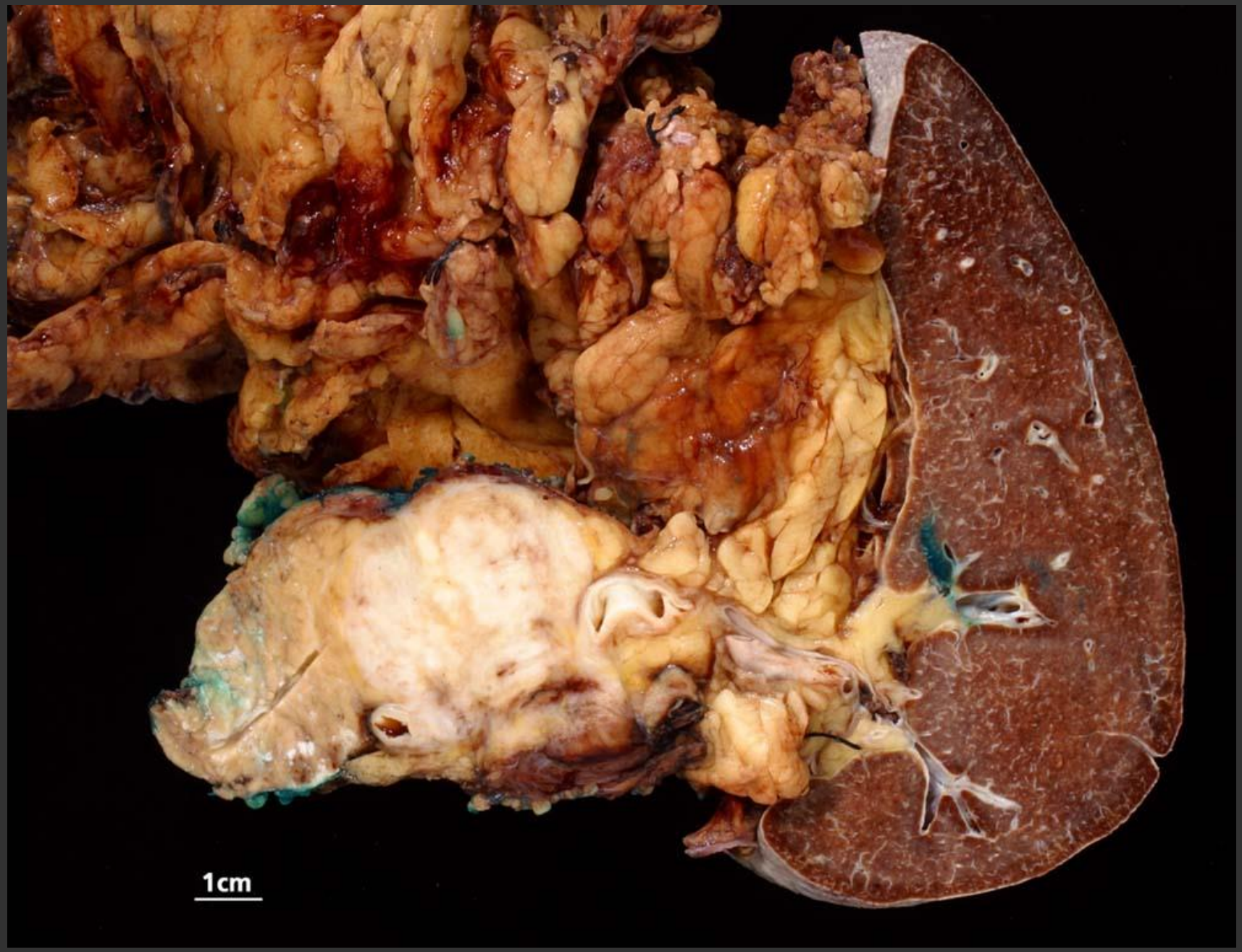
- adenocarcinoma, in almost all cases
- mostly arising from the head of the pancreas (60%)

Macroscopy :

- firm, gray, poorly demarcated multinodular mass
- often embedded in a dense connective tissue (scirrhous tumor)
- duodenal, bile duct invasion (carcinoma of the head)
- vertebral column, retroperitoneal, spleen invasion (carcinoma of the body and tail)

Microscopy :

- well differentiated to poorly differentiated carcinoma
- infiltrative growth
- desmoplastic reaction / perineural invasion



Carcinoma of the pancreatic tail

PathoPic
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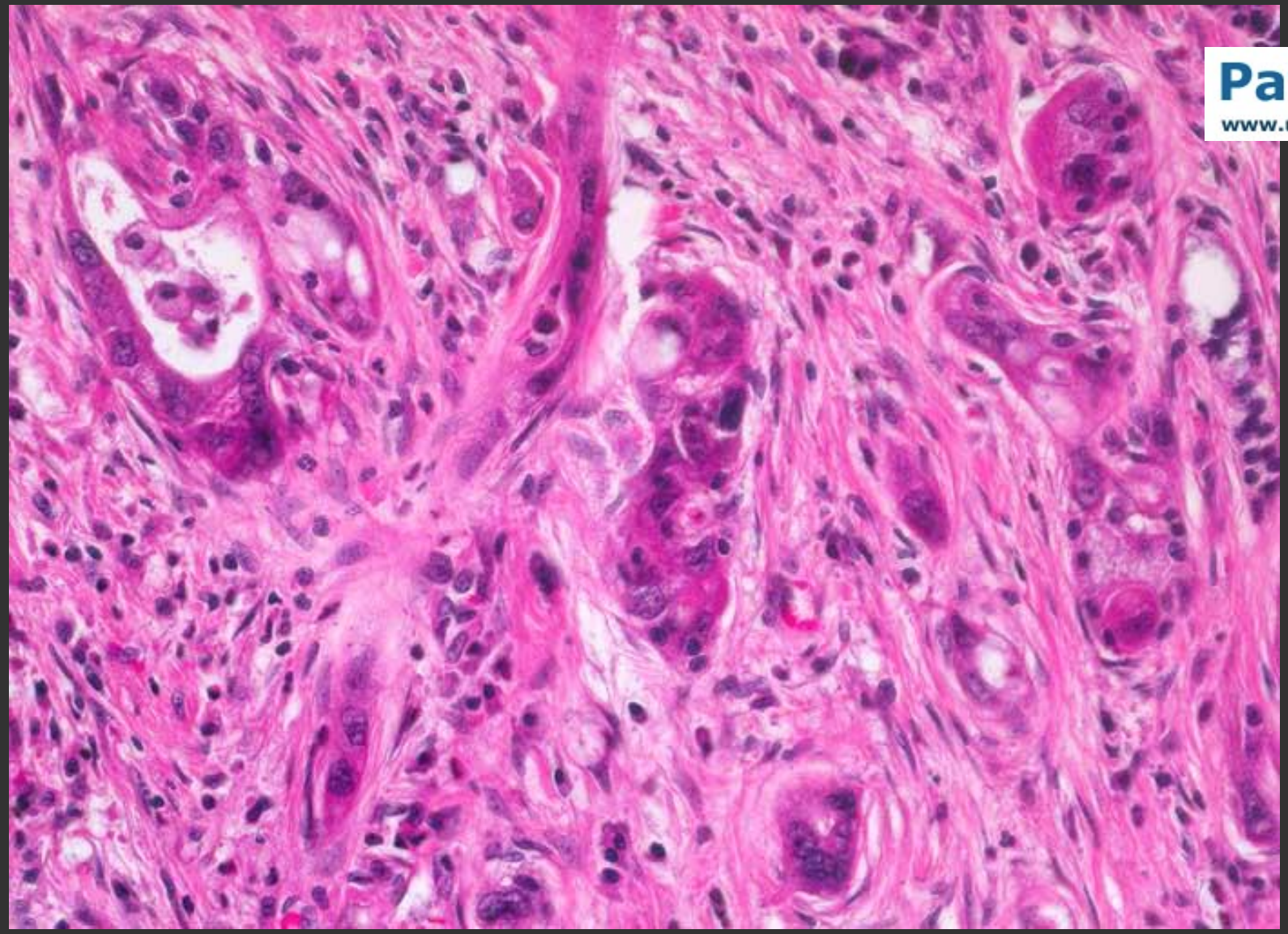

Pancreatic carcinoma inducing dense stromal fibrosis (desmoplastic reaction).

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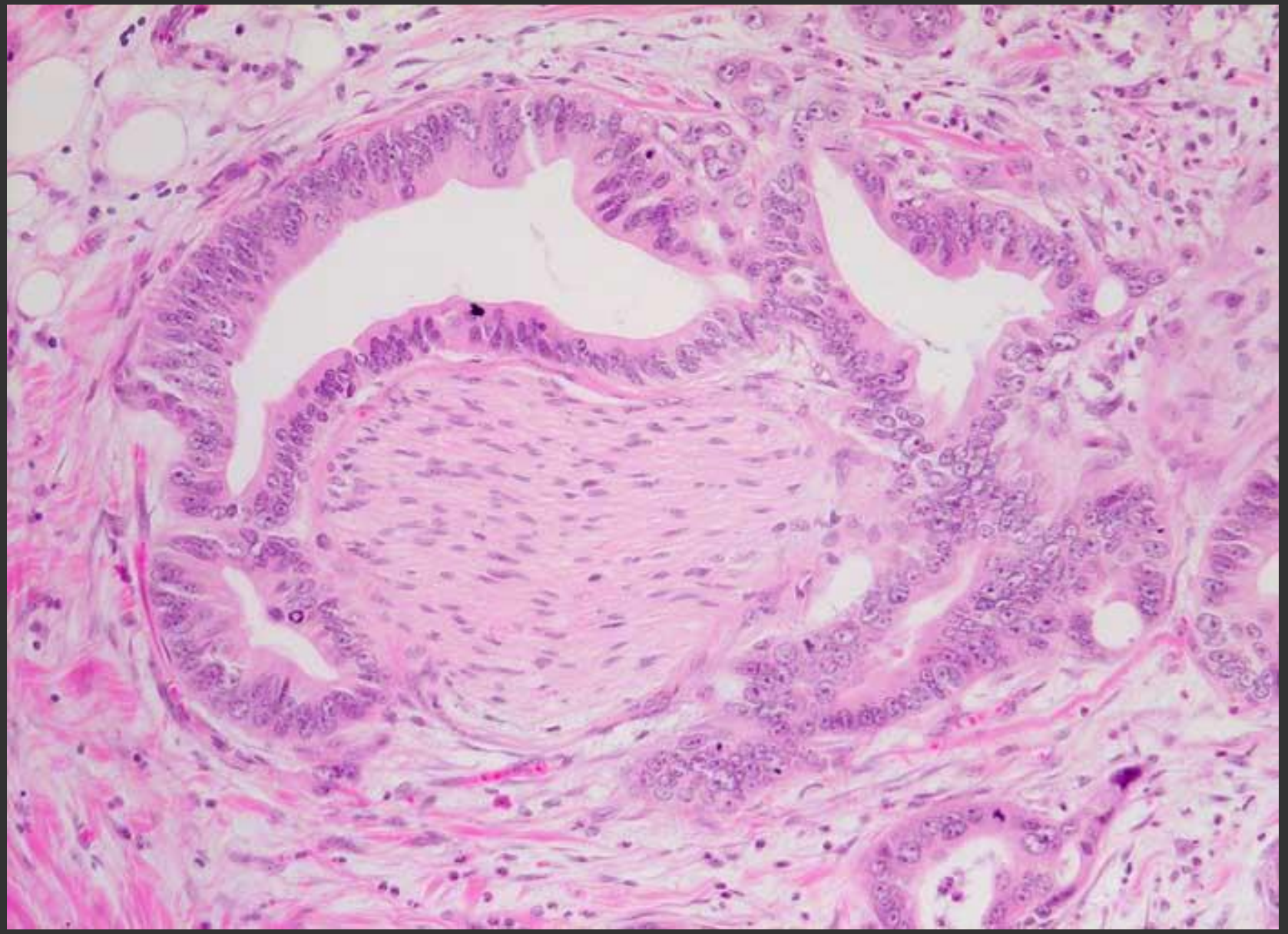


Pancreatic adenocarcinoma with perineural invasion

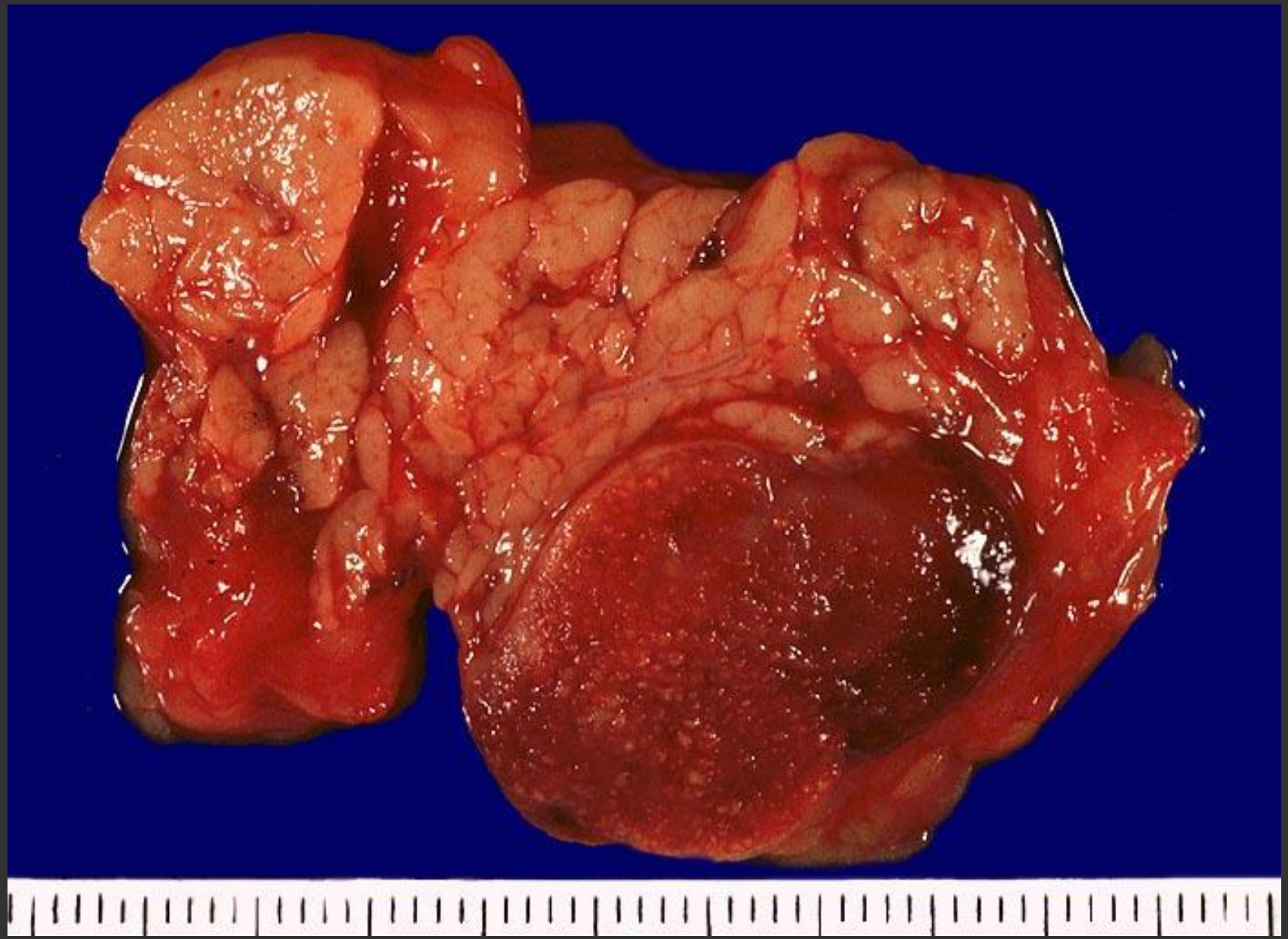
http://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=005884

ISLET CELL TUMORS

- 10% of pancreatic tumors
- mostly non-functional, discovered incidentally

- insulinoma
- glucagonoma
- pancreatic gastrinoma
- somatostastinoma
- VIPoma
- enterochromaffin cell tumors

- difficult to distinguish between benign and malignant on the basis of histology alone



Insulinoma

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PathoPic
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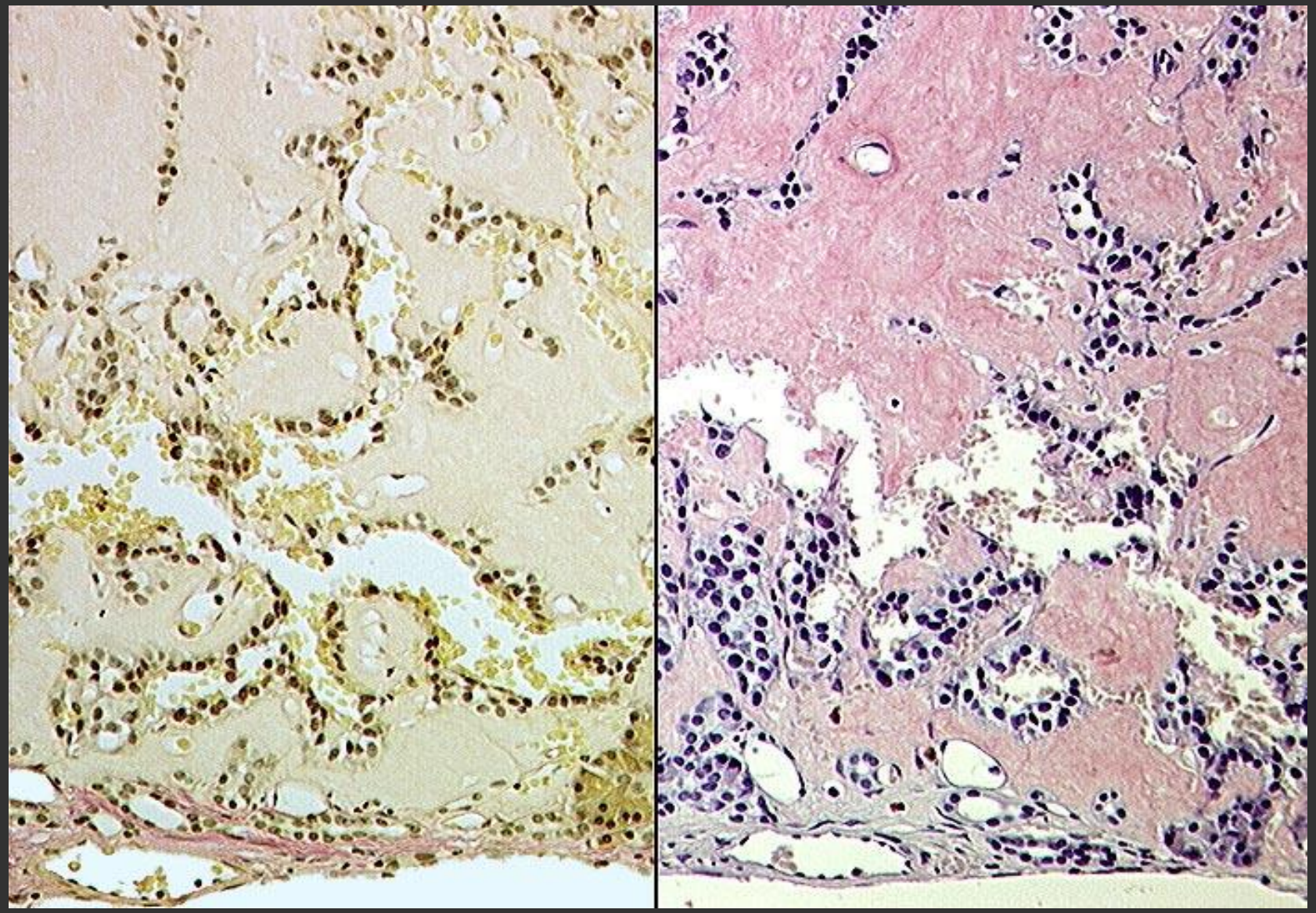

Insulinoma
- stroma containing amyloid (yellow in the van Gieson stain)

http://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=1497

PathoPic
www.unibas.ch/patho