

Harvard-MIT Division of Health Sciences and Technology

HST.121: Gastroenterology, Fall 2005

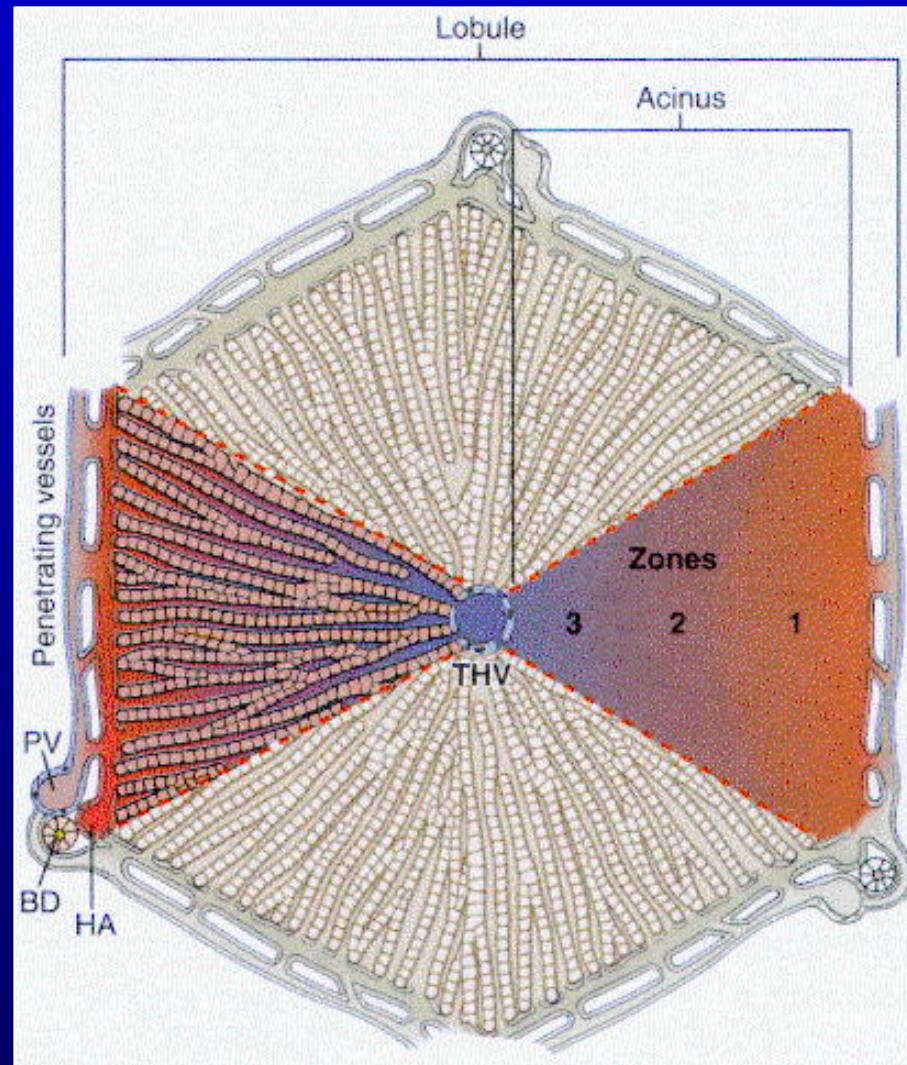
Instructors: Dr. Martin Carey, Dr. Raymond Chung, and Dr. Jonathan Glickman

# The Normal Liver

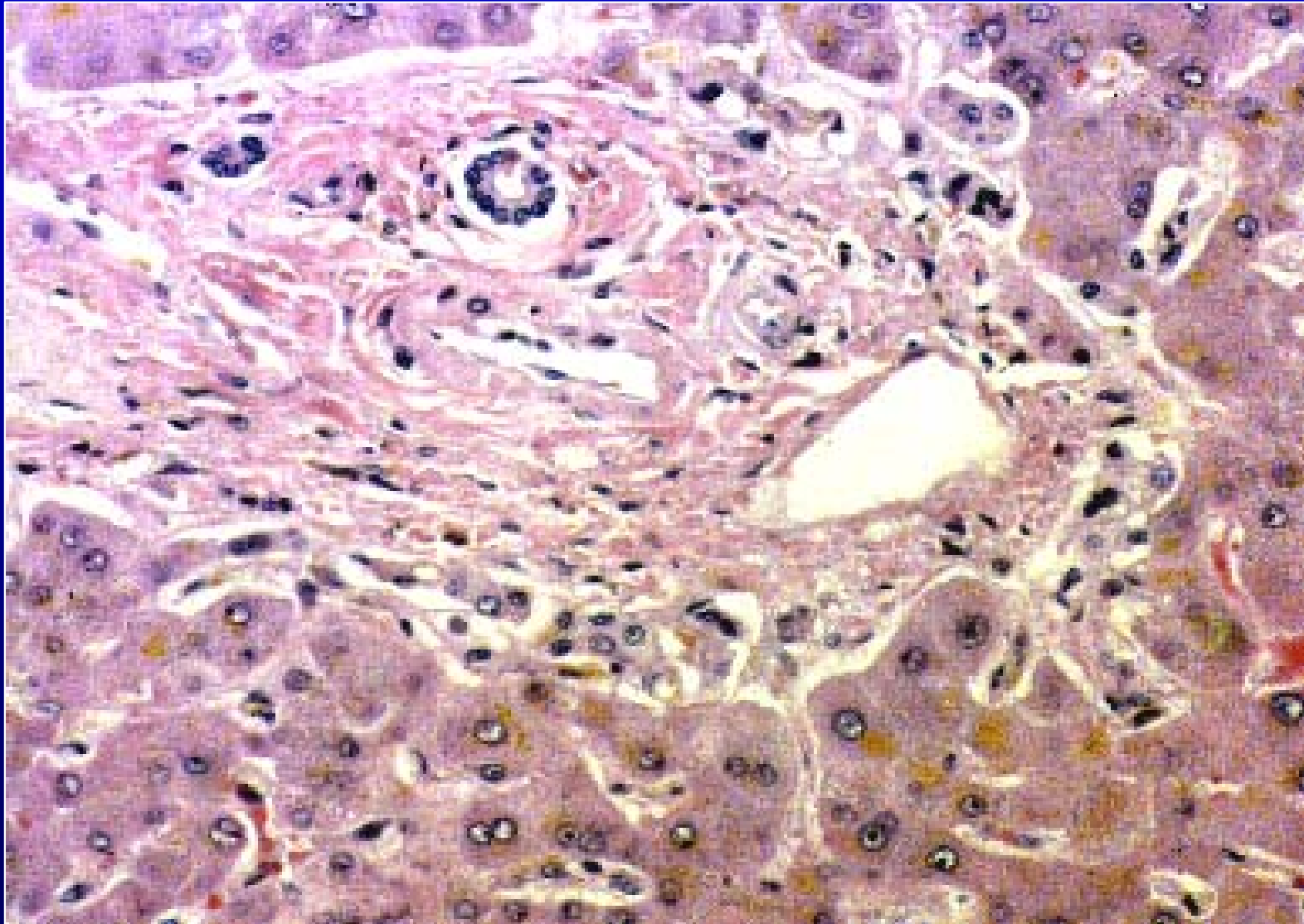
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- Acinar/lobular architecture
- Portal tracts
- Hepatic plates & sinusoids
- Central veins

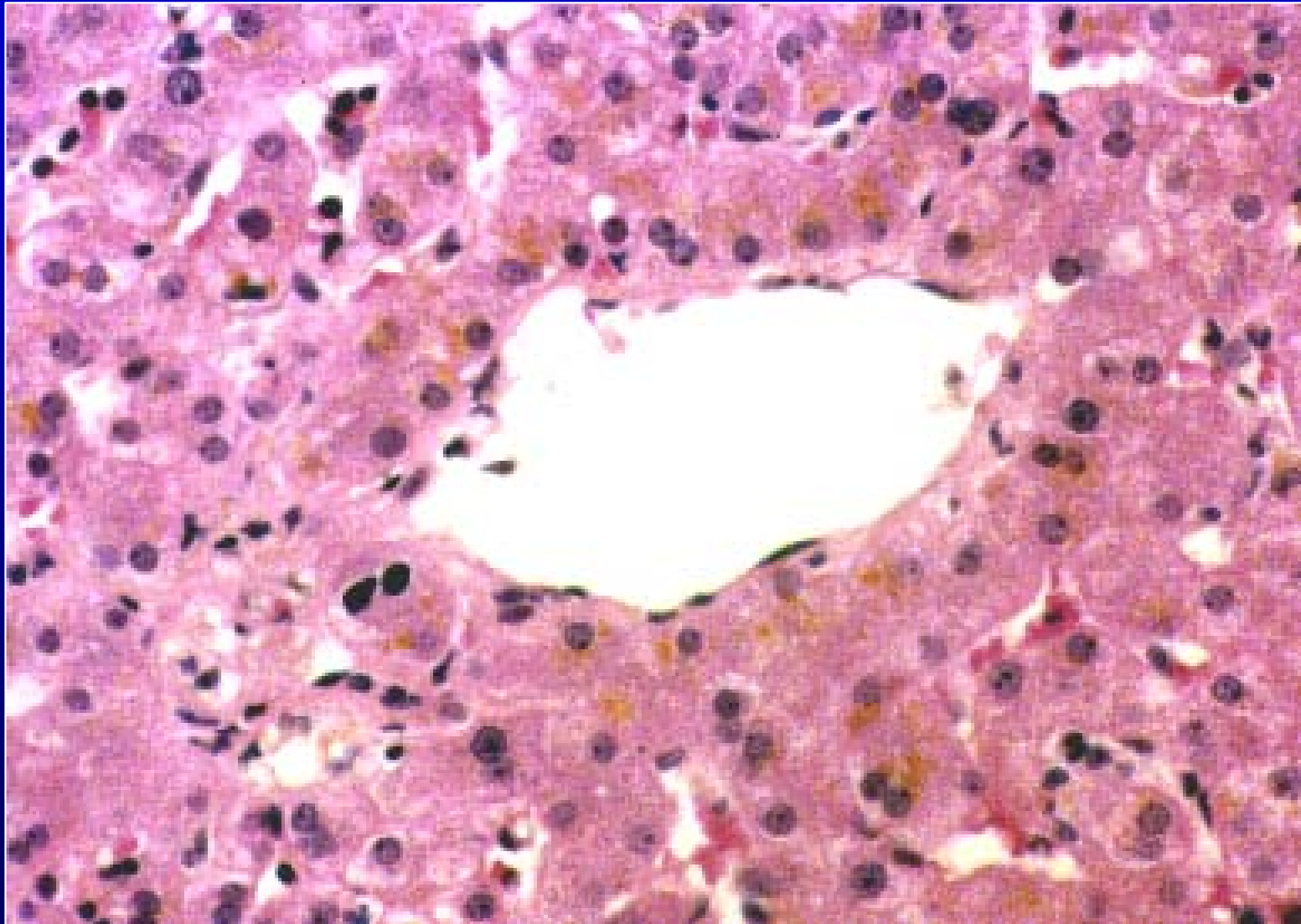
# Normal liver architecture



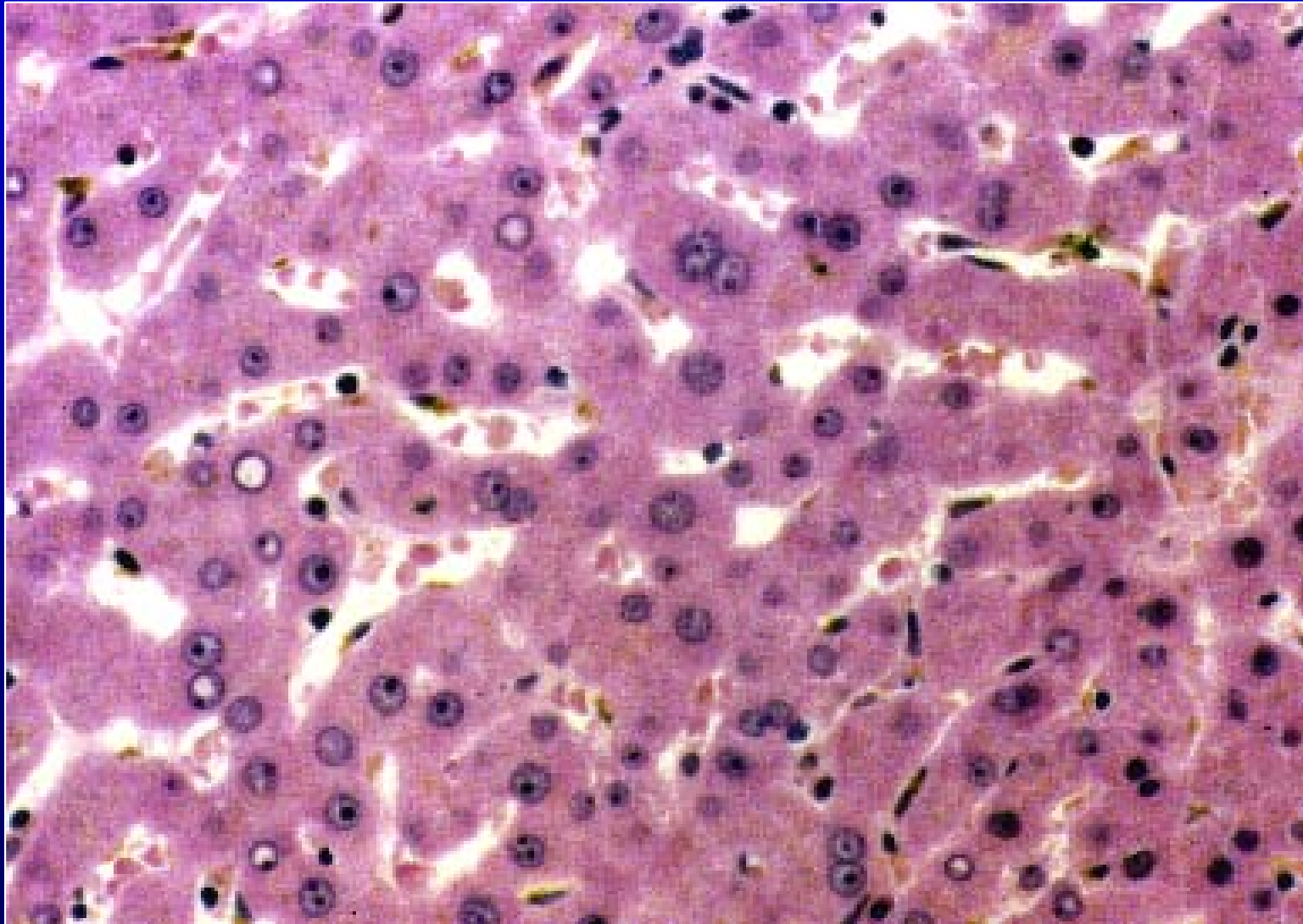
# Normal portal tract



# Normal Central Vein

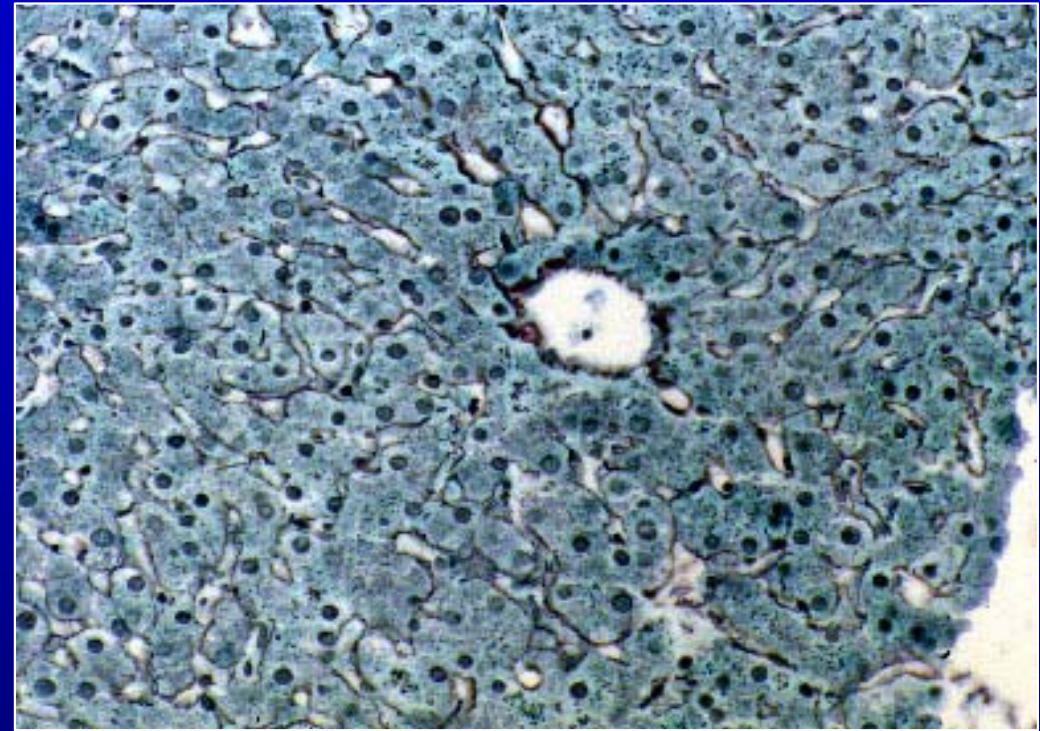
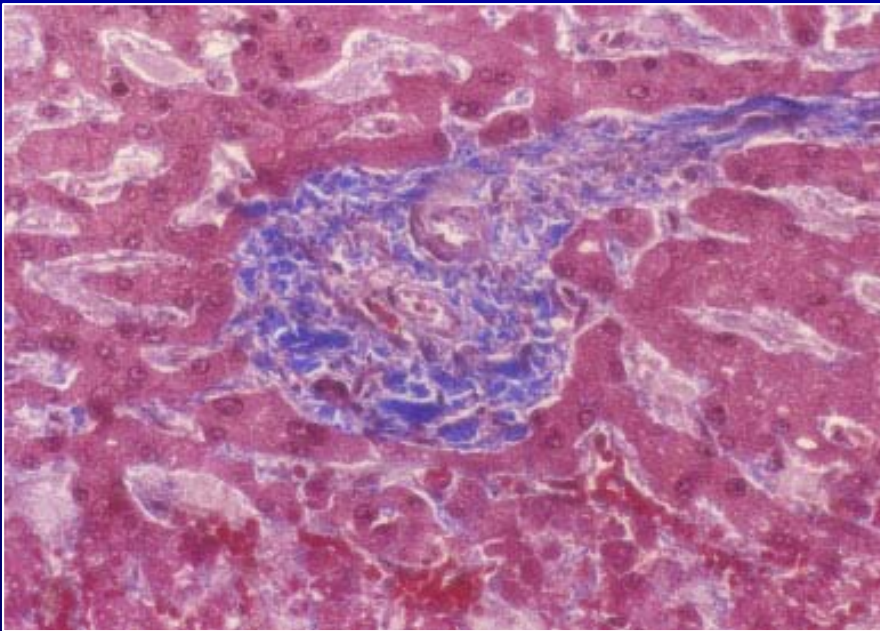


# Normal hepatic plates



# Special stains

**Trichrome**



**Reticulin**

# Histologic Types of Liver Injury

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- Necrosis
- Hepatocyte degeneration/regeneration
- Hepatitis (acute and chronic)
- Steatosis (fatty change)/steatohepatitis
- Cholestasis (bile accumulation)
- Fibrosis and cirrhosis

# Chronic Hepatitis

## Key Histologic Features

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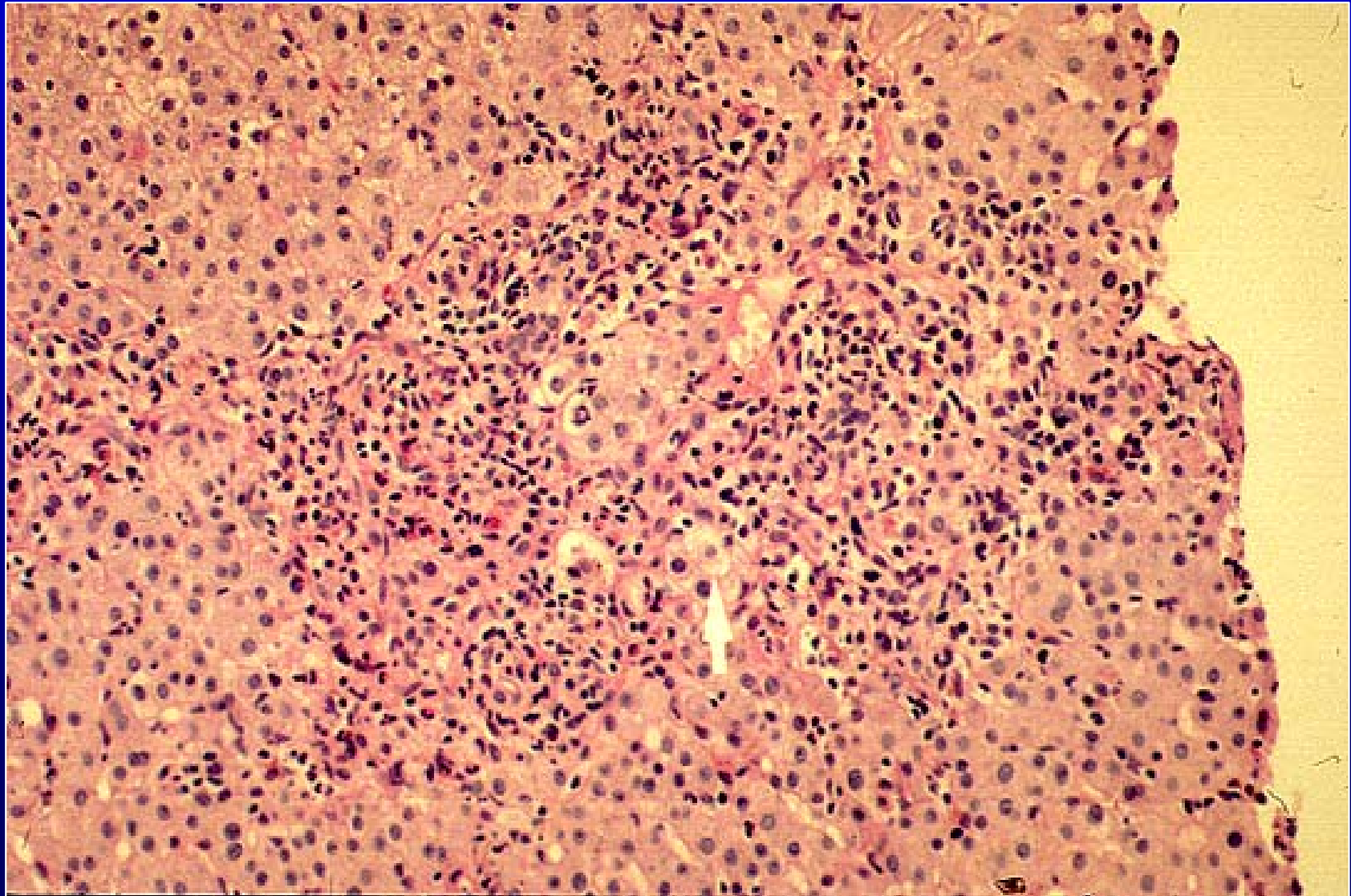
- Portal tract mononuclear inflammation
- Periportal activity
  - Extension beyond limiting plate (“piecemeal necrosis”)
- Lobular Activity
  - Lobular mononuclear inflammation
  - Lobular hepatocyte necrosis
- Fibrosis, Cirrhosis



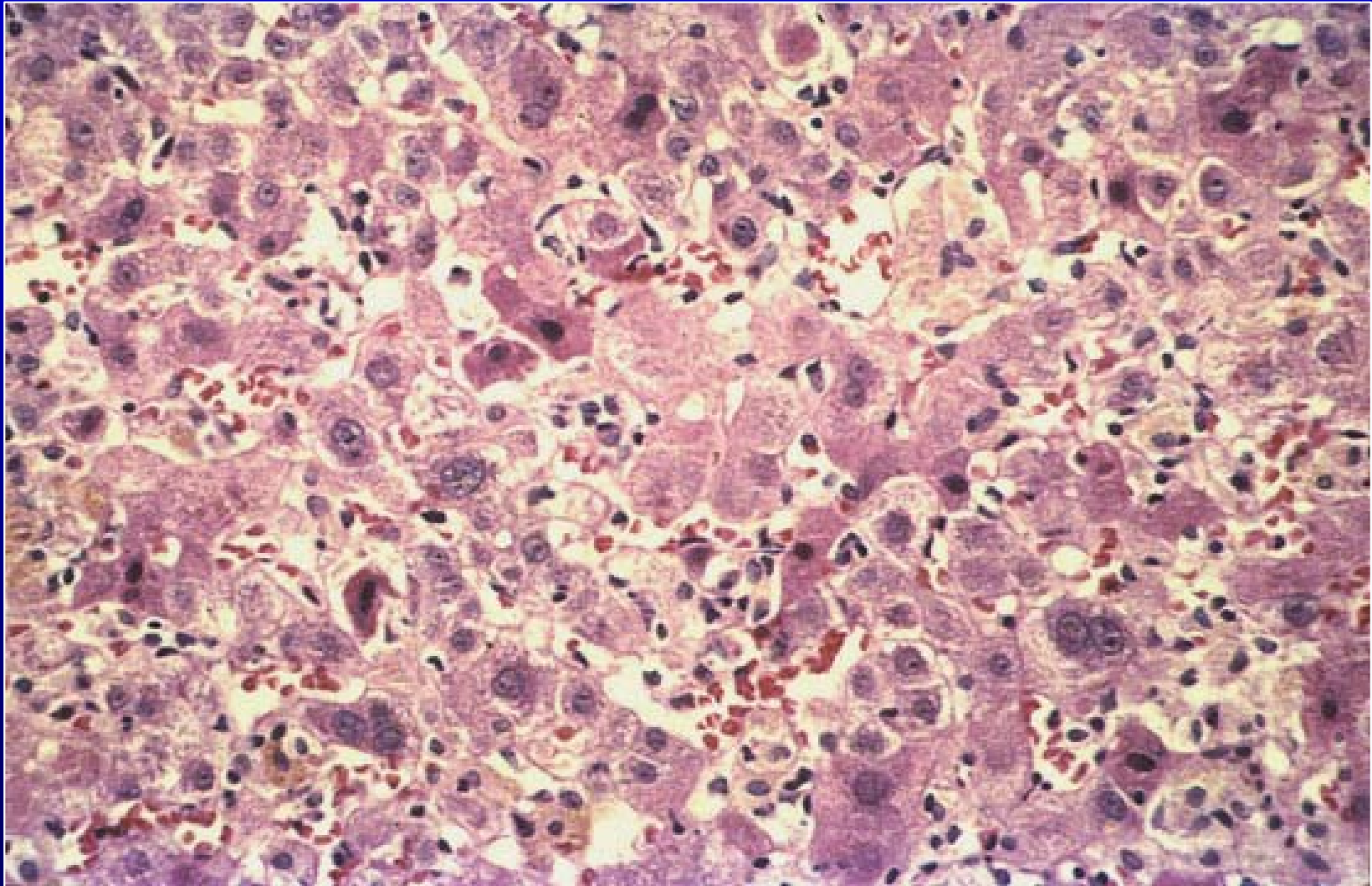
# Acute vs. Chronic Viral Hepatitis

	<u>Acute</u>	<u>Chronic</u>
<b>Causes</b>	<b>HAV,HBV,HCV</b>	<b>HBV,HCV</b>
<b>Inflamm-distrib</b>	<b>Lobular</b>	<b>Portal+lobular</b>
<b>Inflamm-cells</b>	<b>Lymphocytes Macrophages</b>	<b>Lymphocytes Plasma cells</b>
<b>Necrosis</b>	<b>+ - +++</b>	<b>-/+</b>
<b>Sequelae</b>	<b>Resolution Chronic hepatitis Post-hepatitic scarring</b>	<b>Chronic carrier Cirrhosis</b>

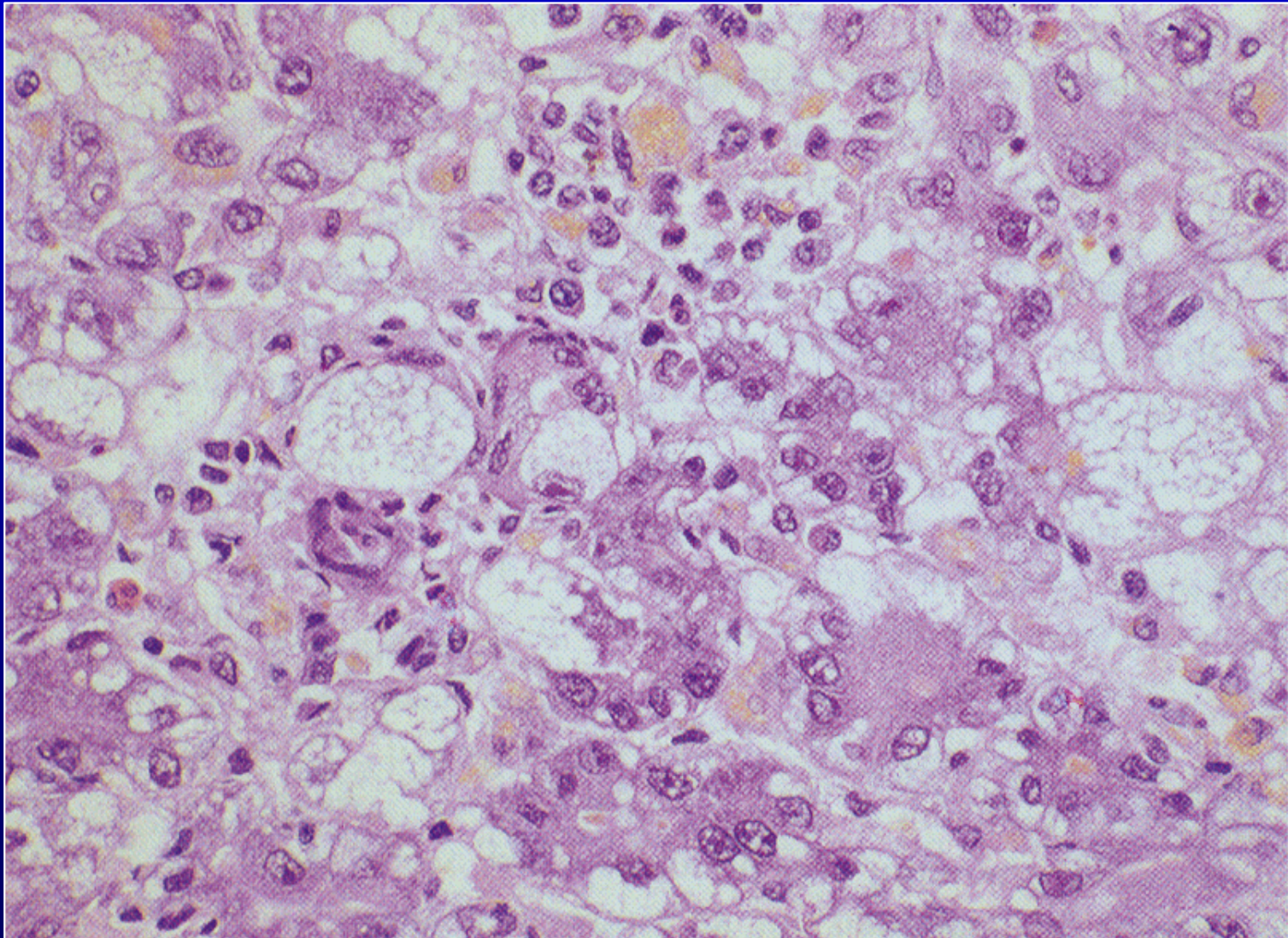
# Acute viral hepatitis



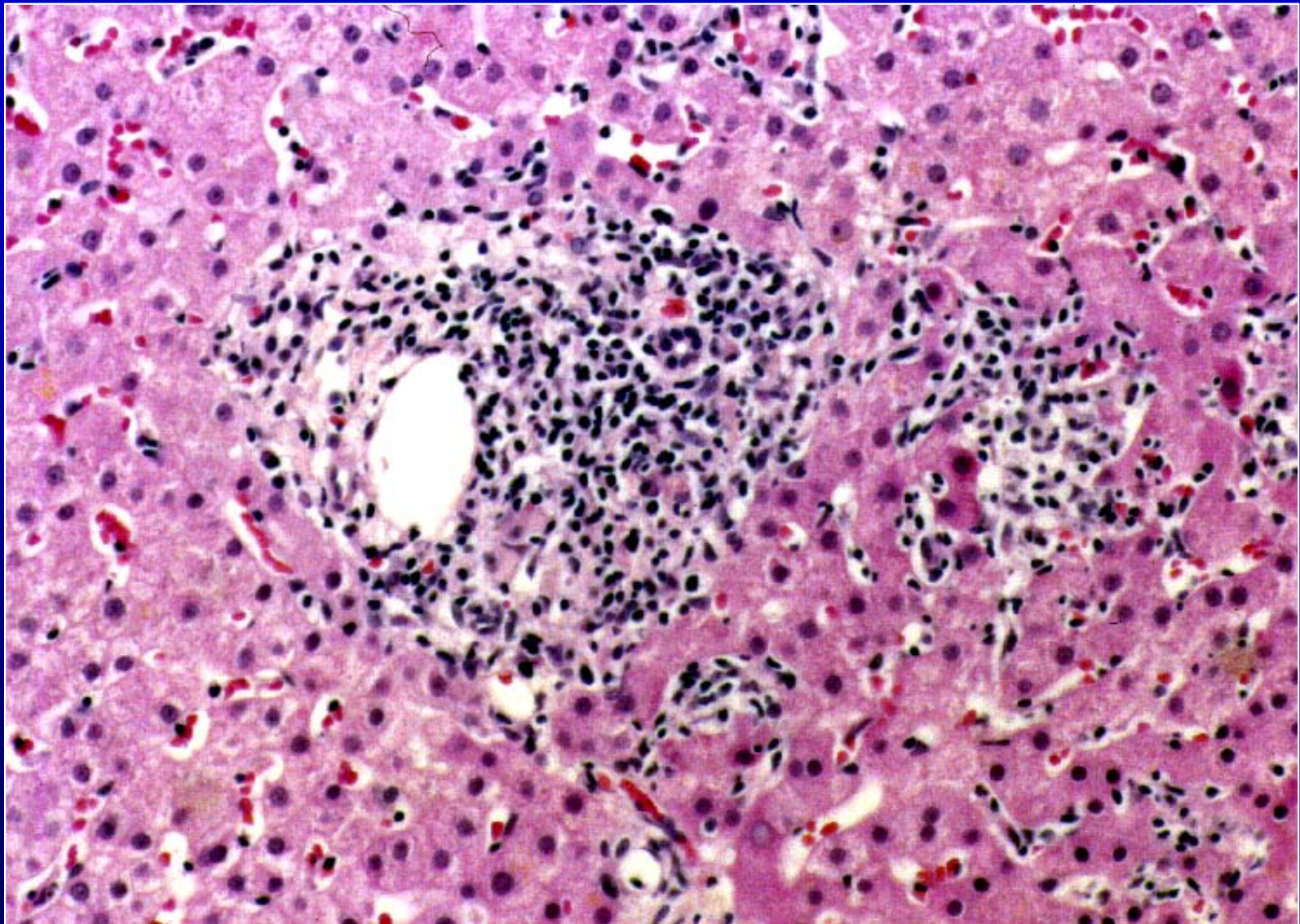
# Acute viral hepatitis



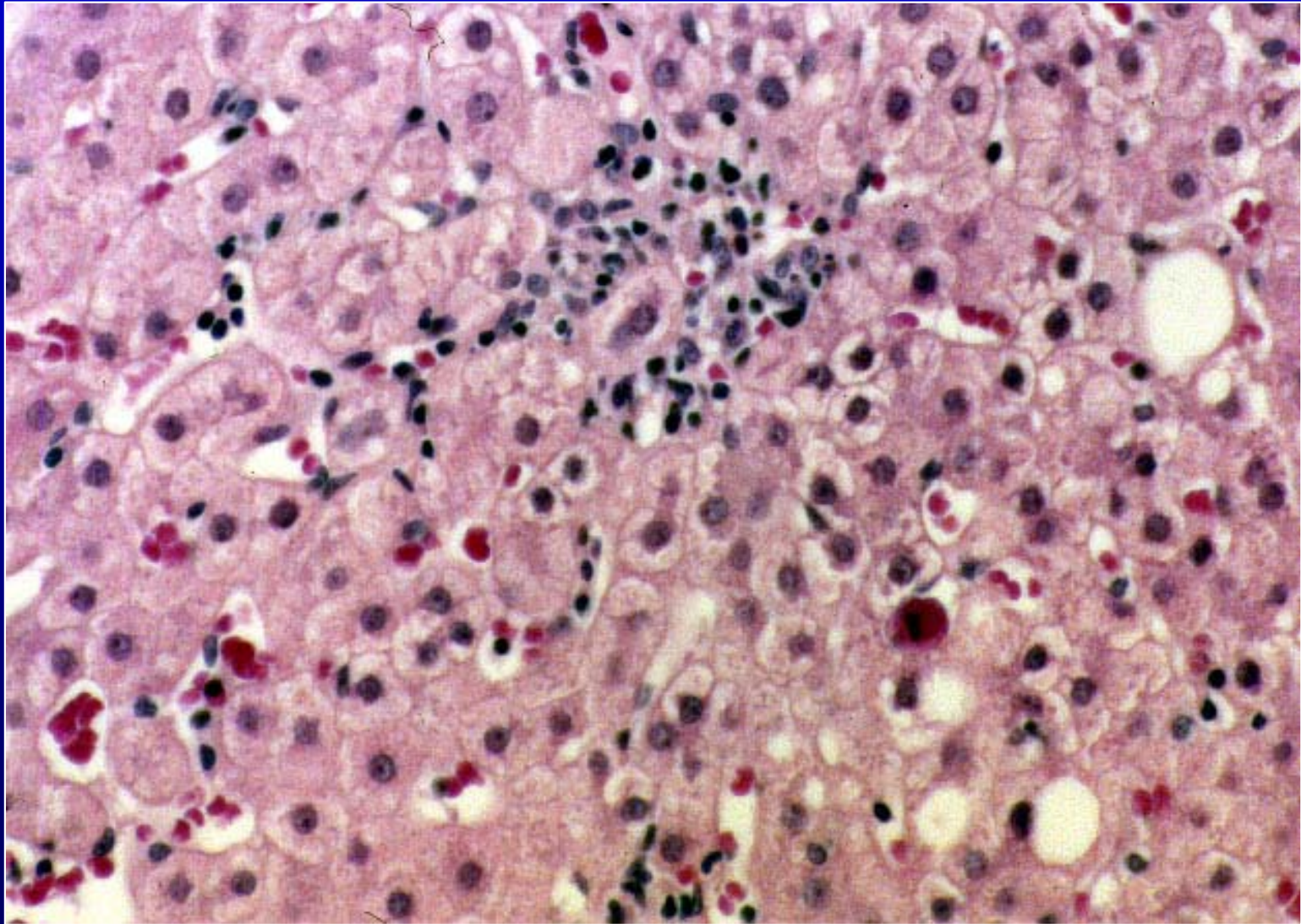
# Fulminant viral hepatitis



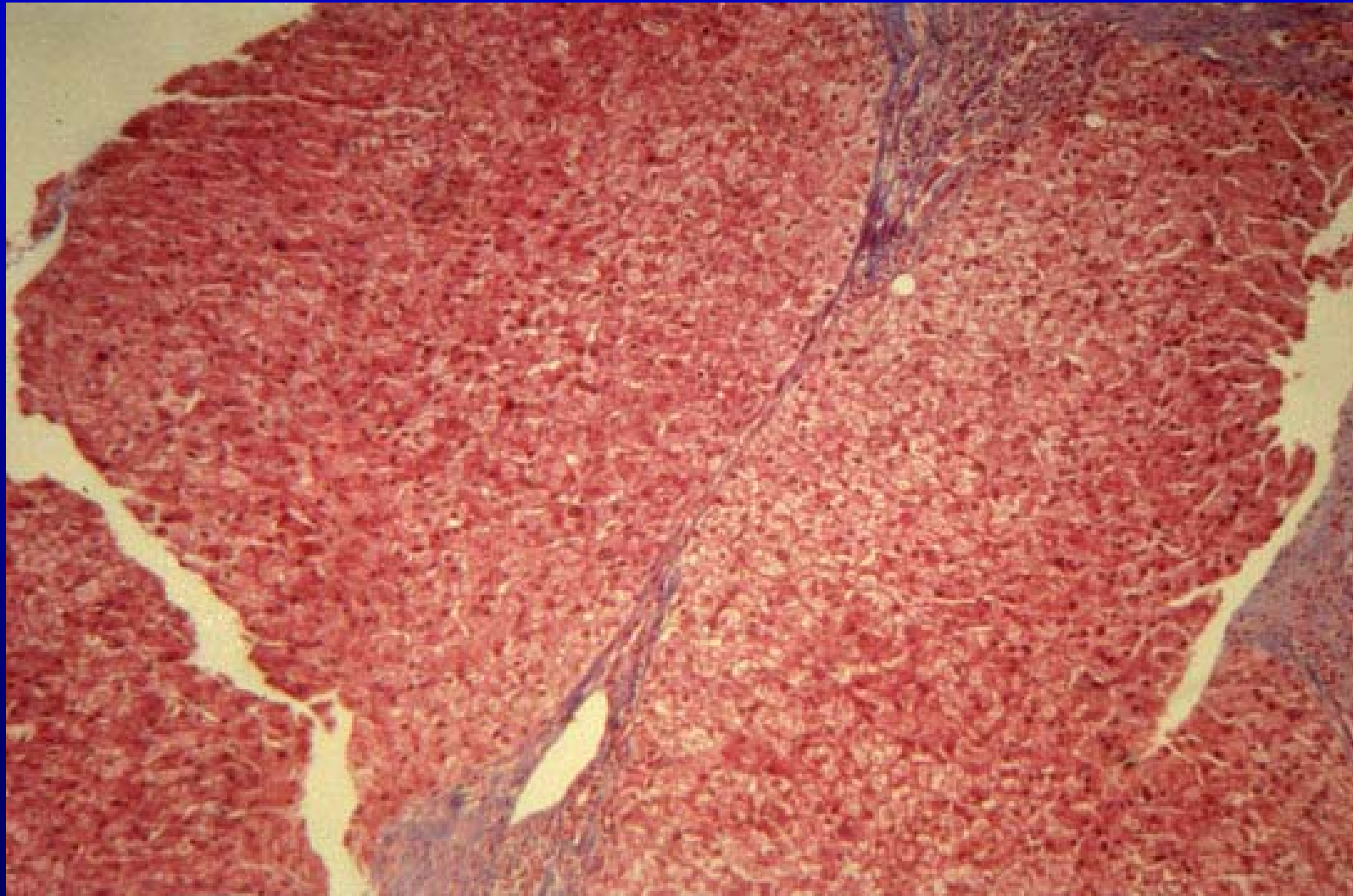
# Chronic hepatitis C



# Lobular activity



# Portal-portal bridging



# Early cirrhosis

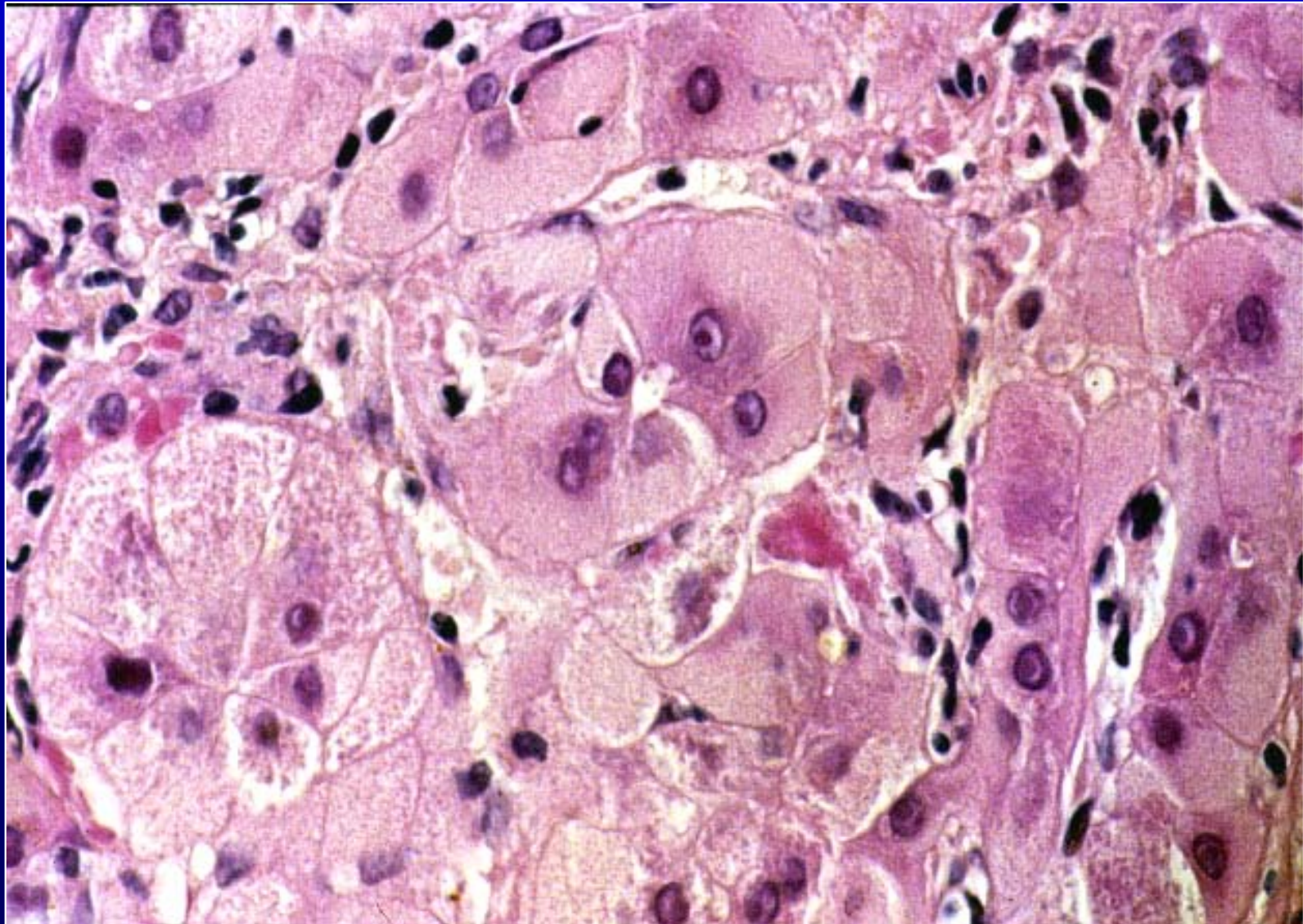




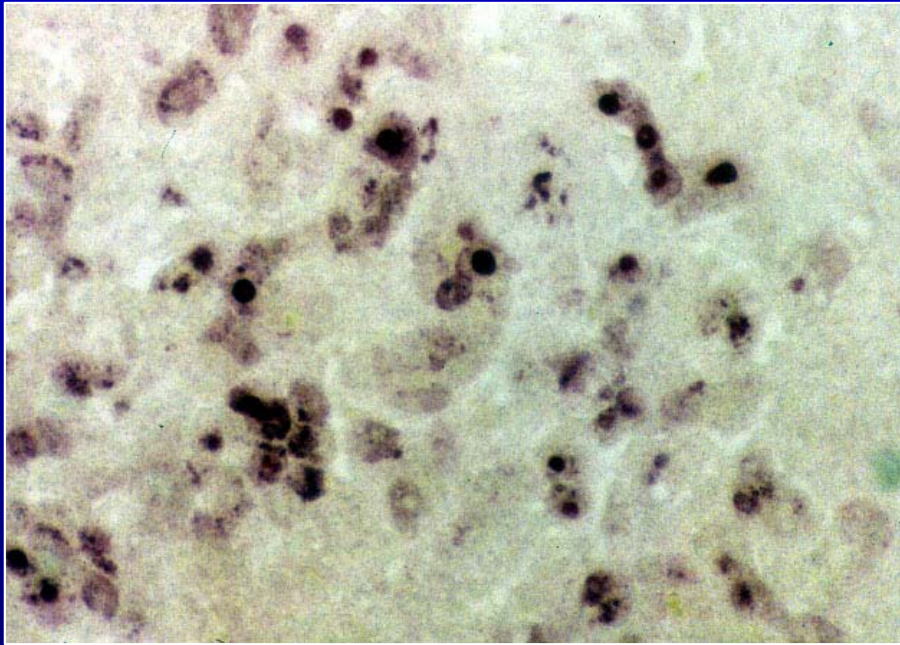
# Chronic Hepatitis- Etiologies

- Viral
  - Hepatitis B,C
- Autoimmune
  - Autoimmune hepatitis
  - Primary biliary cirrhosis
- Drug reaction
- Others (Wilson's disease, lymphoma)

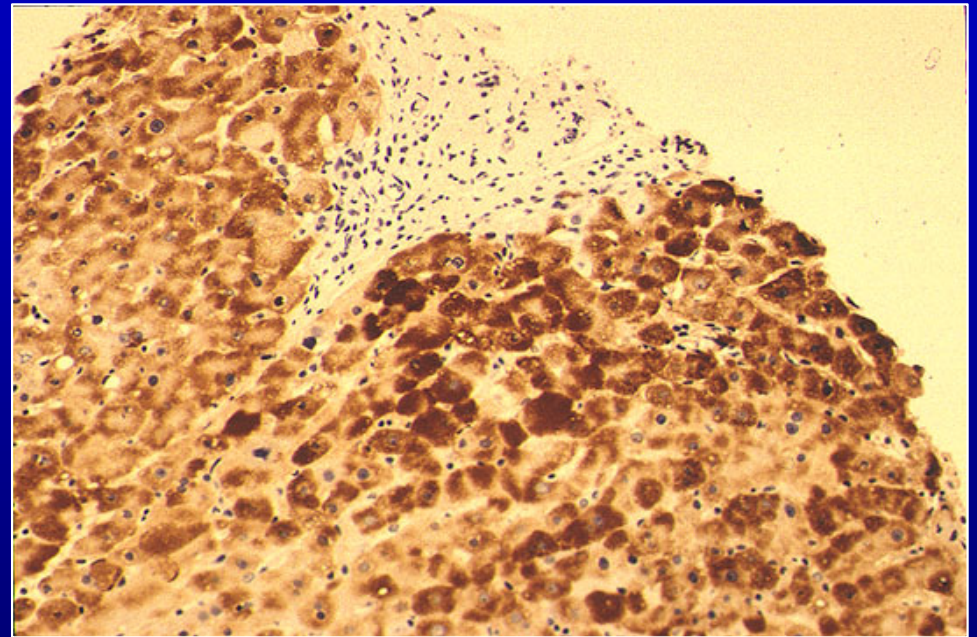
# Chronic Hepatitis B



# Hepatitis B virus immunostains



**HBV core Ag**

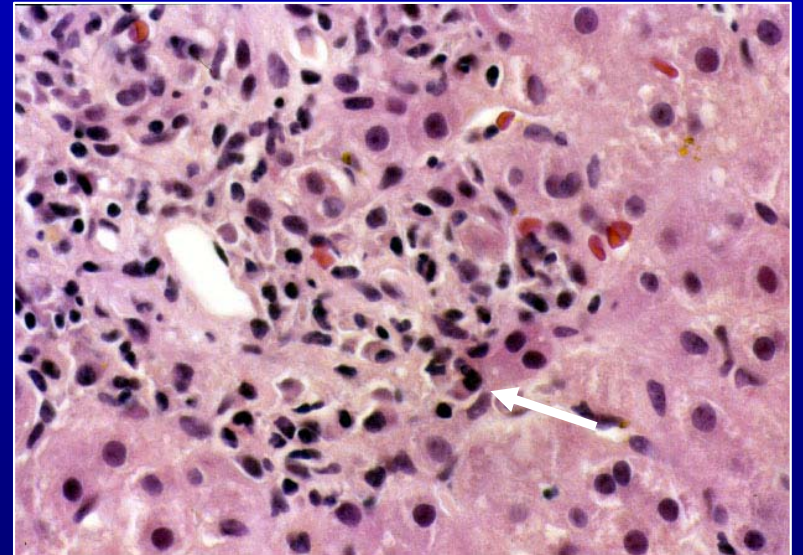
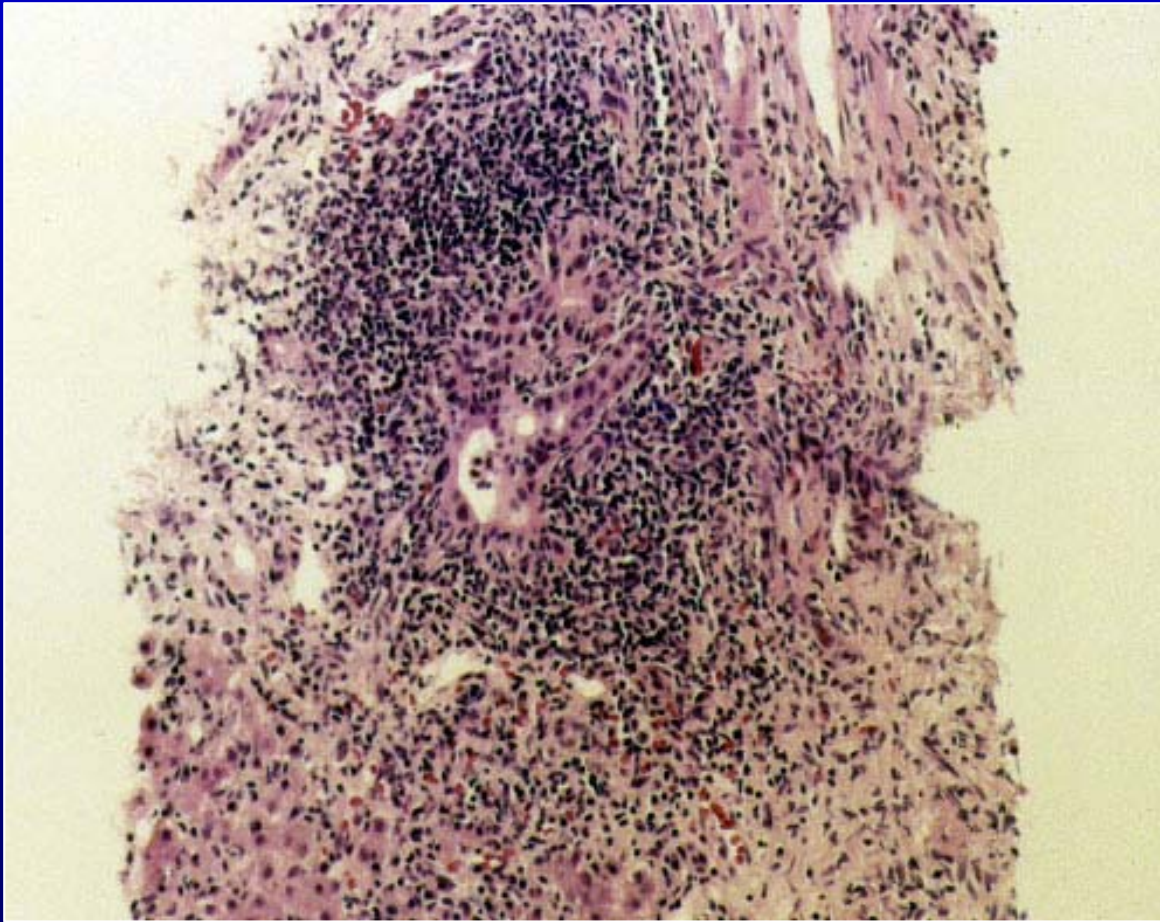


**HBV surface Ag**

# Autoimmune hepatitis

- **Clinical:** F>M, young-midage, abrupt or insidious onset, relapsing course; liver only or a/w systemic autoimmune phenomena
- **Labs:** ↑transaminases; +ANA (type I), +α-LKM (type II), +α-SLA (type III)
- **Histology:**
  - chronic hepatitis with marked piecemeal necrosis, lobular involvement
  - numerous plasma cells

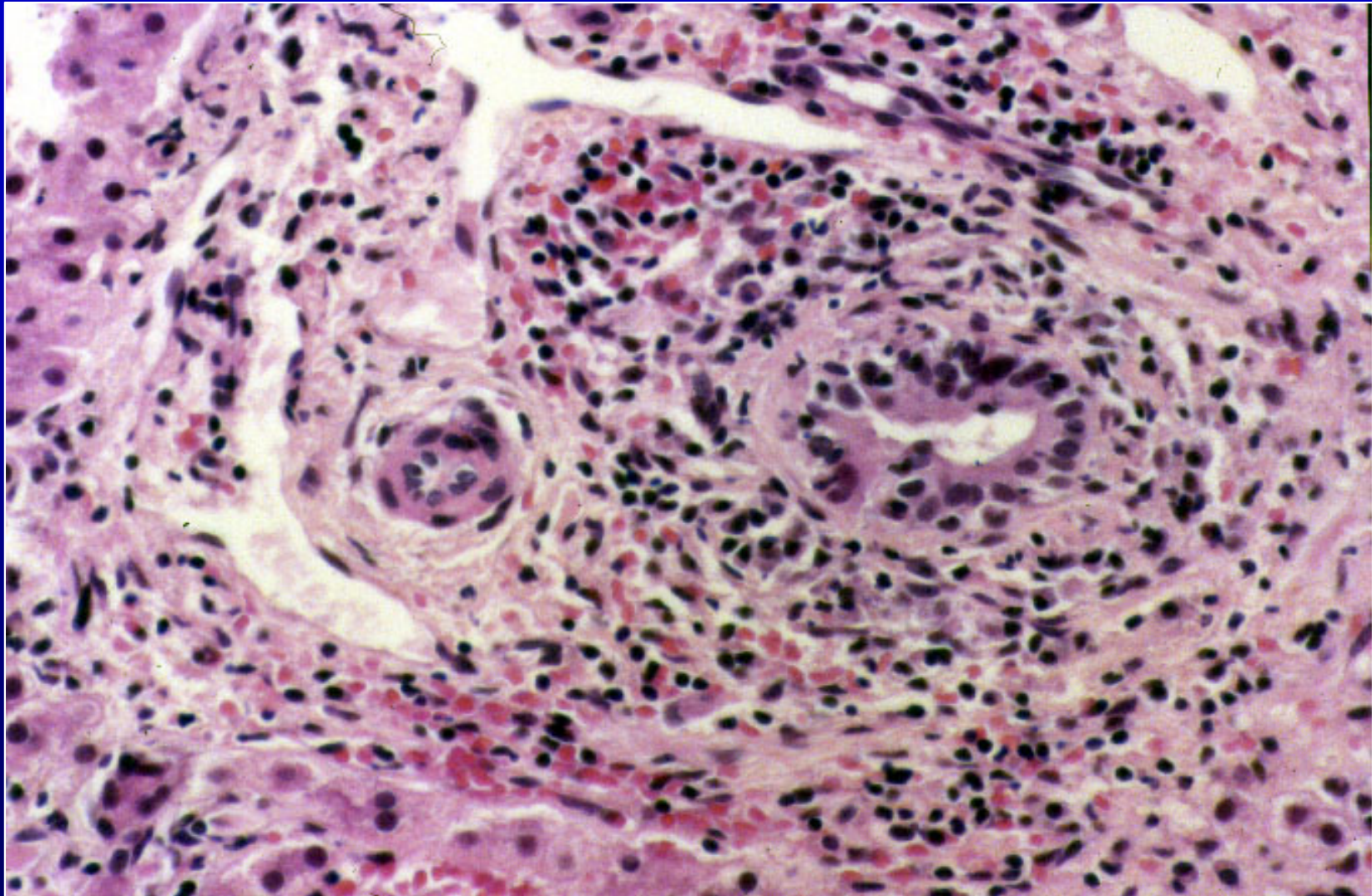
# Autoimmune hepatitis



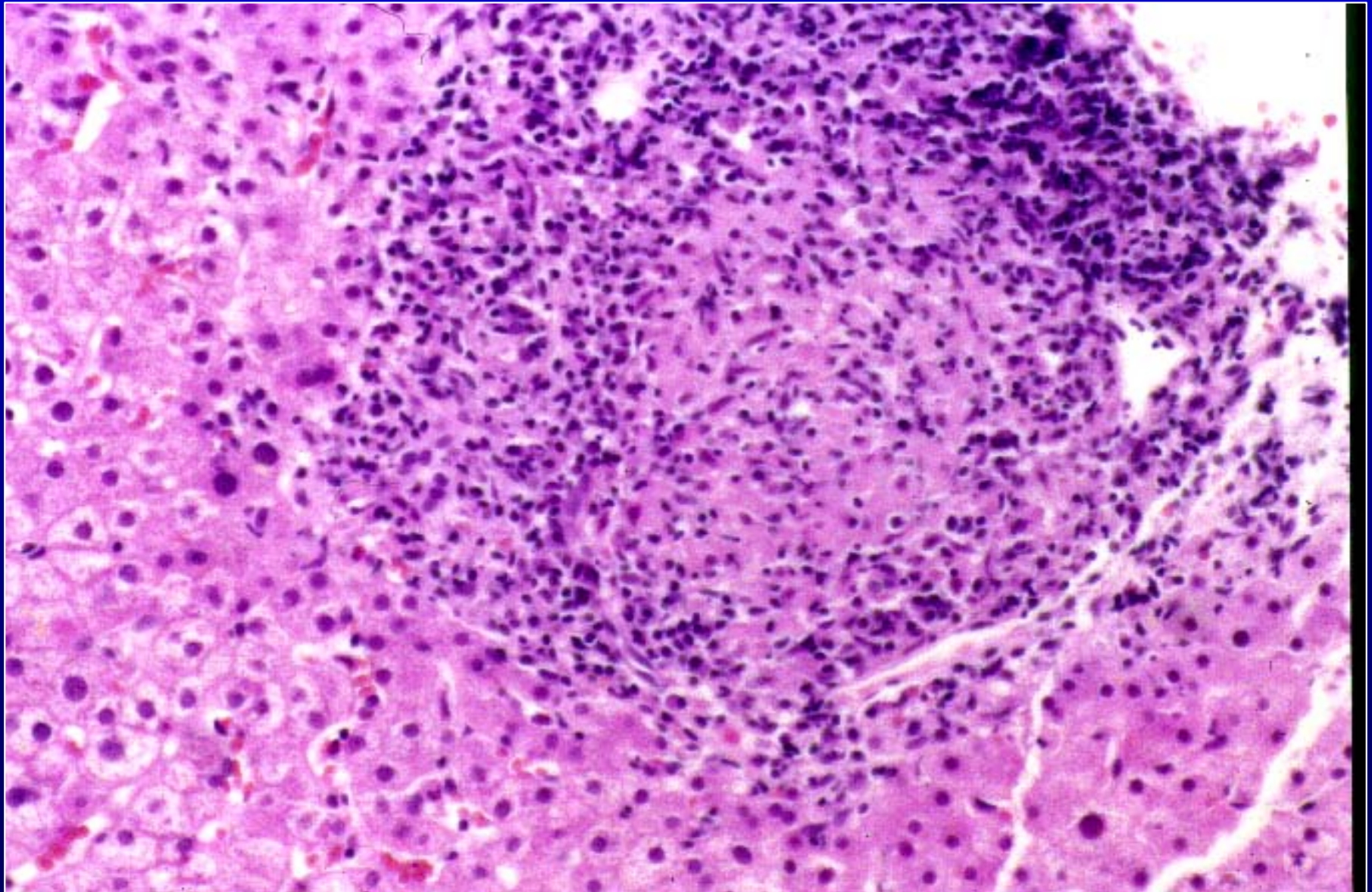
# Primary Biliary Cirrhosis

- **Clinical:** middle age, F>>M; insidious onset
  - a/w other autoimmune syndromes
- **Labs:** inc. AP, +AMA
- **Histologic stages:**
  - **I.** Florid duct lesion: BD damage, granulomas
  - **II.** Ductular proliferation, periportal hepatitis
  - **III.** Scarring and fibrosis
  - **IV.** Cirrhosis

# Primary Biliary Cirrhosis



# Primary Biliary Cirrhosis





# Chronic Hepatitis -Differential Diagnosis

	HCV	AIH	PBC
Portal Inflamm.	++	+	++
Piecemeal Necrosis	++	+++	++
Lobular Inflamm	+	+++	+/-
Plasma Cells	+	++	+/-
BD Damage/Loss	+	-/+	+++
BD Proliferation	+	-	+++
Granulomas	-	-	++

# Cholestasis

**Definition:** Accumulation of bile in hepatic tissue

**Etiologies:**

- Bile duct obstruction
- Drug reaction
- Sepsis
- Acute viral hepatitis
- Graft-versus-host disease
- Other (cholestatic syndromes):
  - Cholestasis of pregnancy, benign recurrent cholestasis

# Cholestasis-pathology

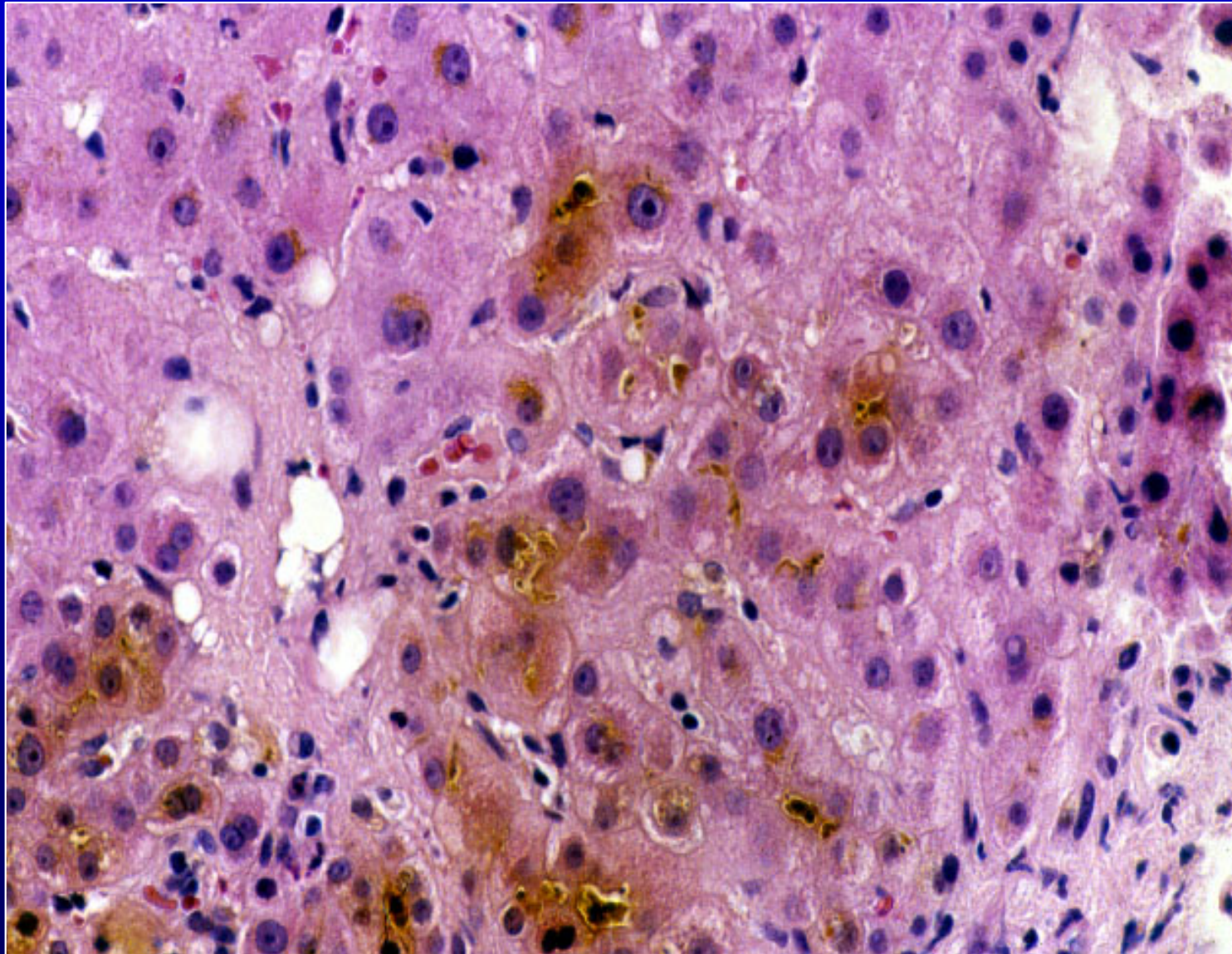
## Acute-Subacute

- Bile accumulation
  - canalicular, centrilobular
  - (late) bile lakes
- Hepatocyte “feathery” degeneration
- Portal tract inflammation (PMNs)
- Bile duct proliferation

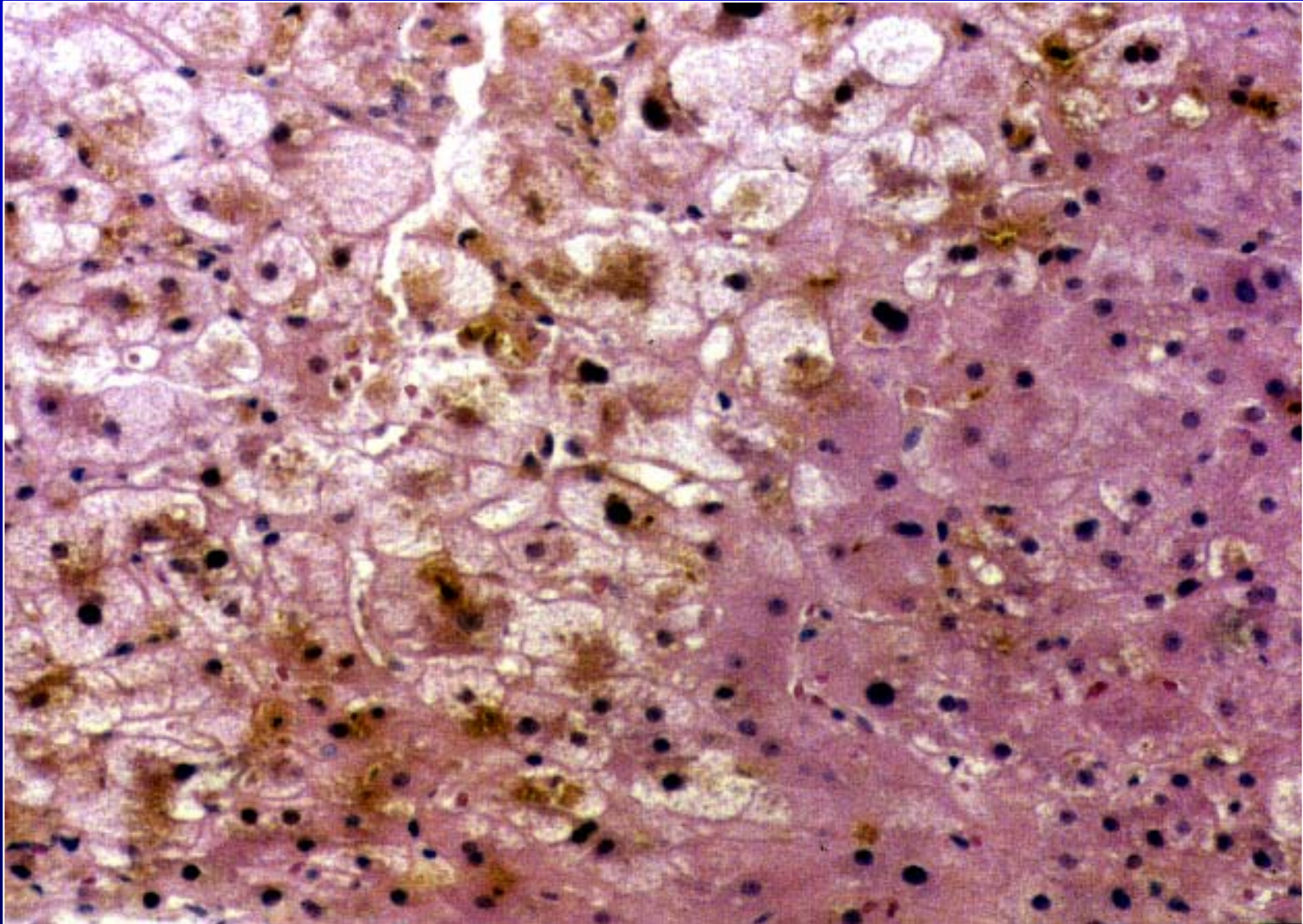
## Chronic

- Fibrosis

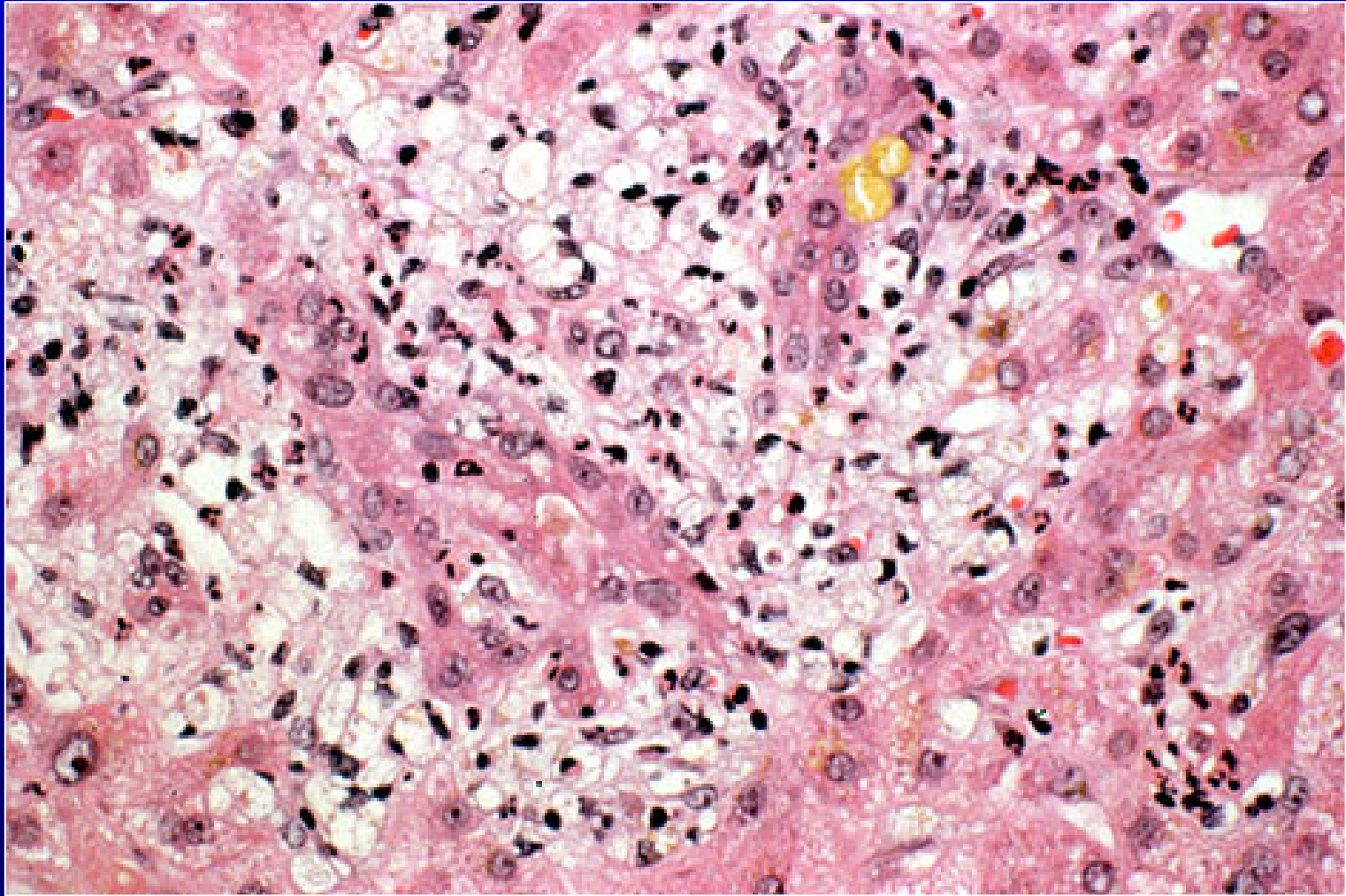
# Canalicular cholestasis



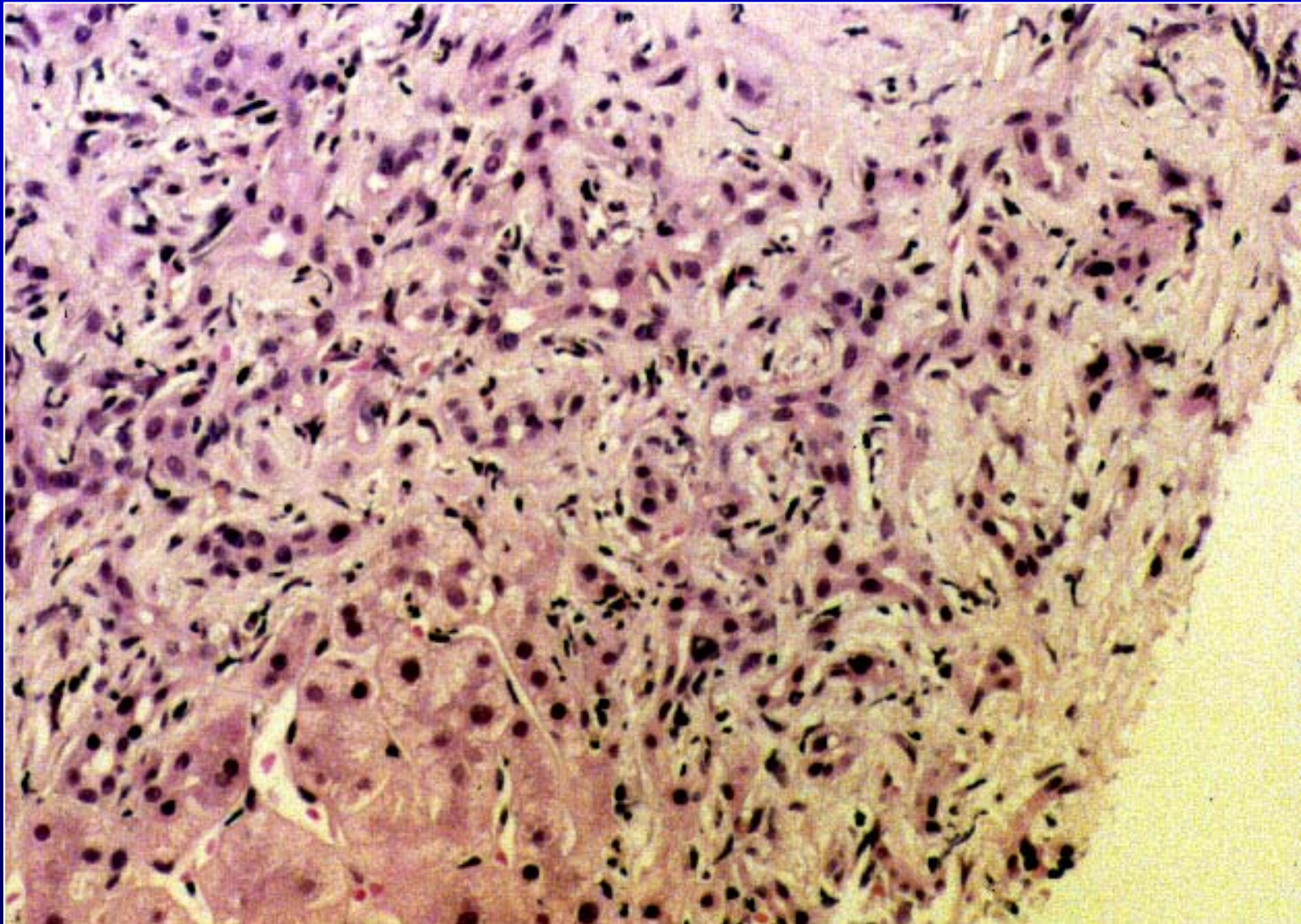
# Feathery degeneration



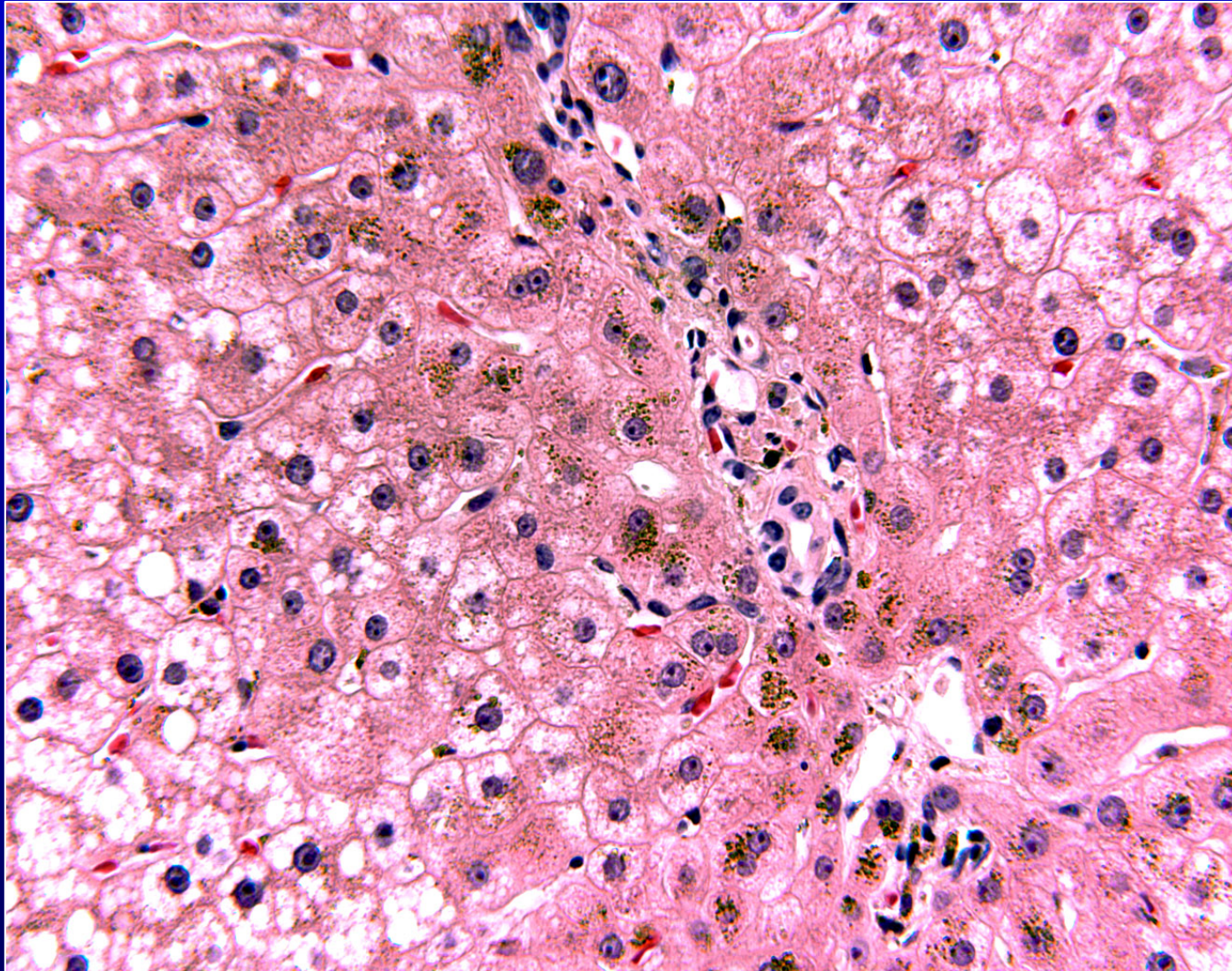
# Bile duct obstruction



# Bile ductular proliferation

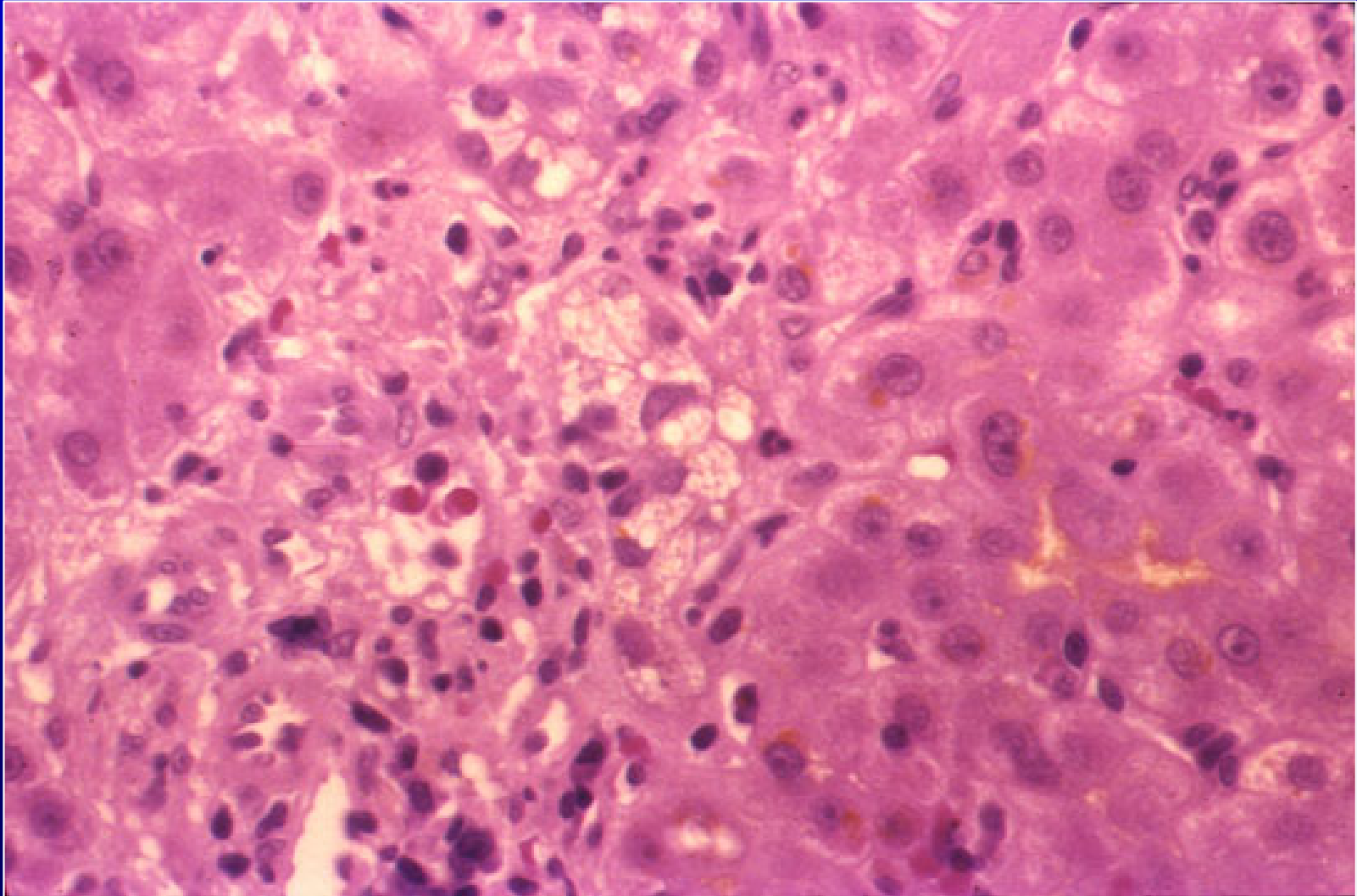


# GVHD

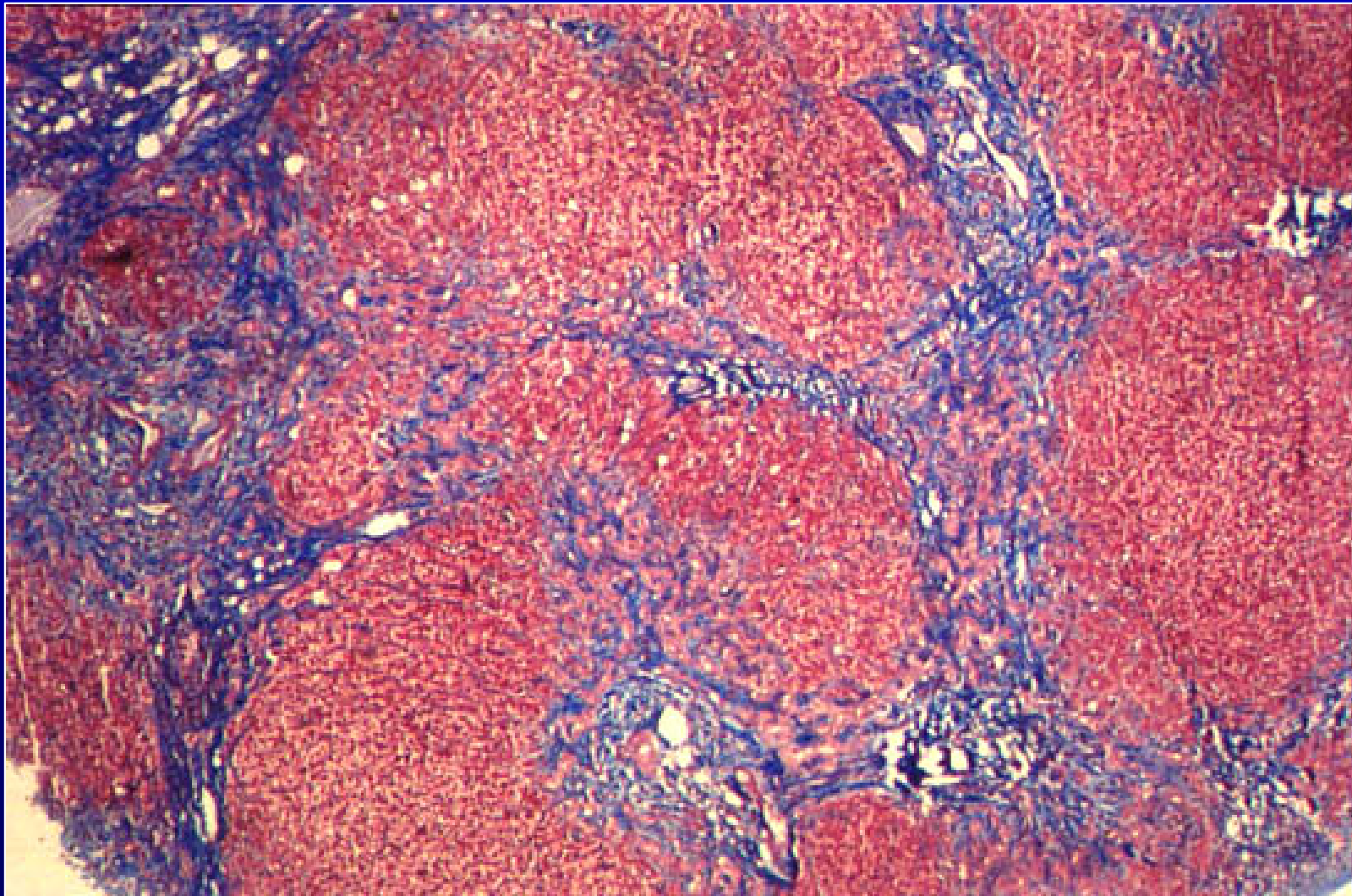




# Chronic cholestasis



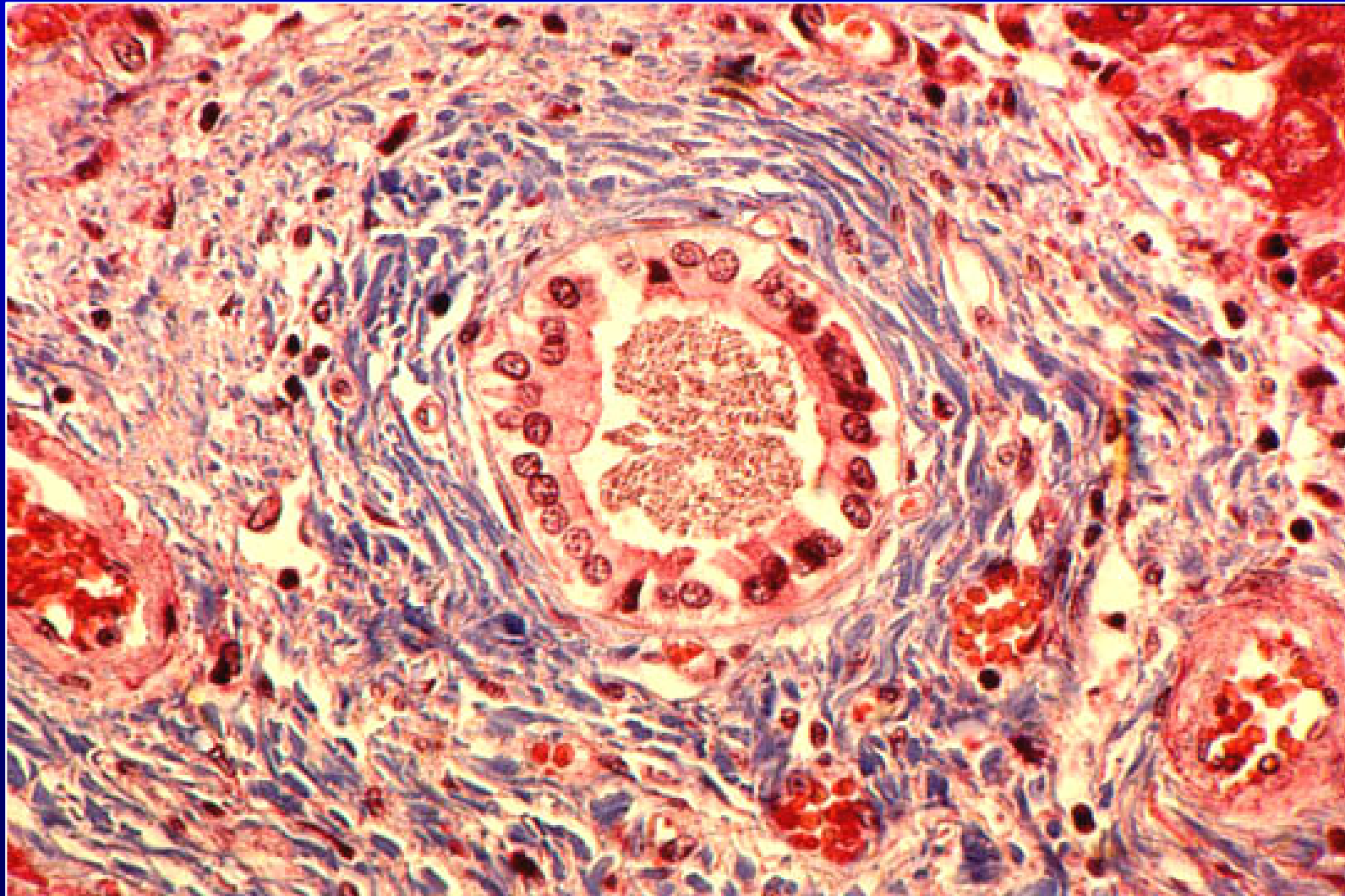
# Portal-portal bridging



# Primary Sclerosing Cholangitis

- **Clinical:** adults, M≈F, a/w ulcerative colitis  
jaundice, pruritus, RUQ pain
- **Radiology:** Strictures (“beading”) of bile ducts
- **Histology:**
  - Periductular concentric fibrosis
  - Bile duct inflammation, proliferation, and loss
  - Parenchyma: cholestasis
  - Progression: fibrosis, cirrhosis

# Primary sclerosing cholangitis



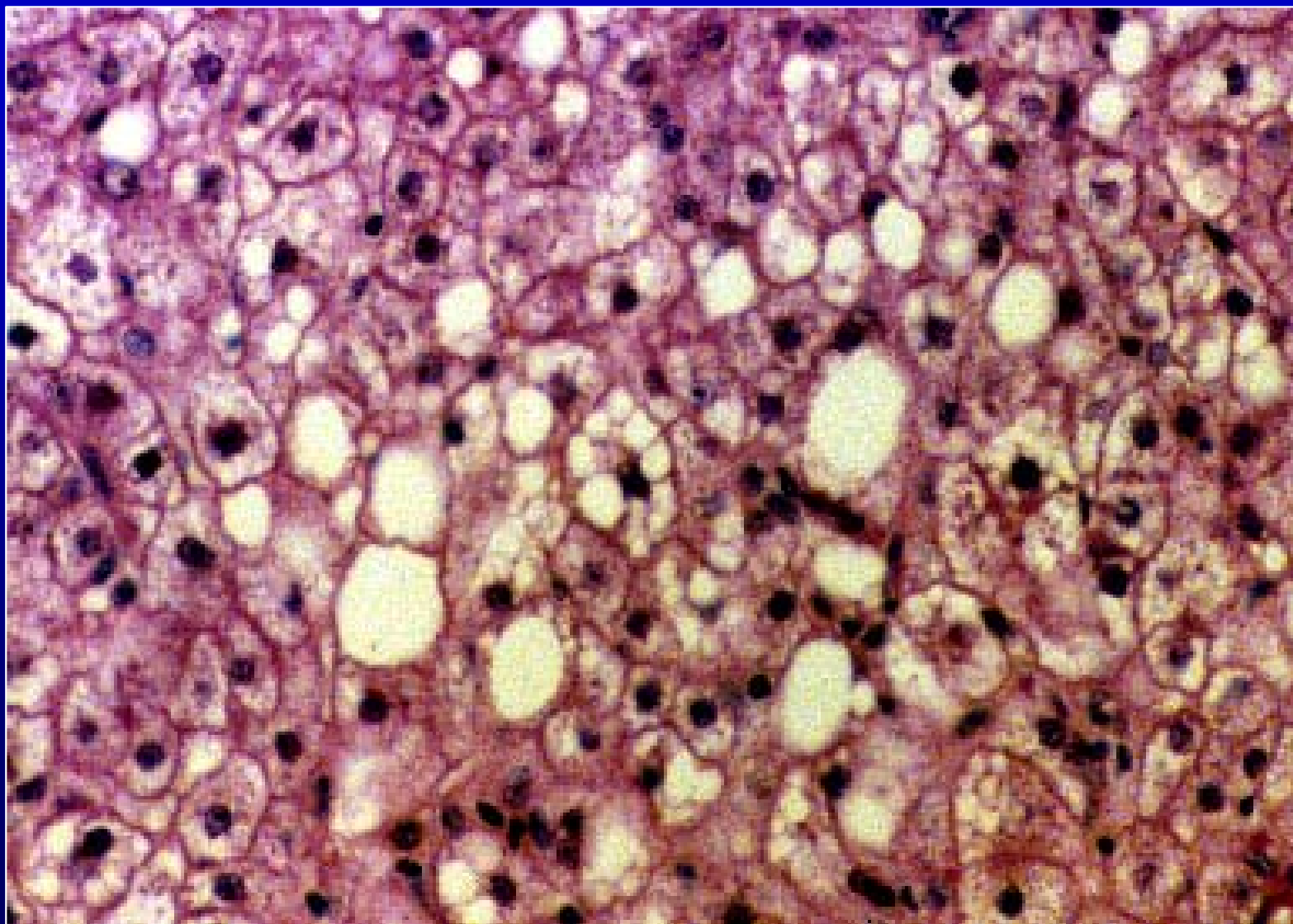
# Drug-induced Liver Disease

Microsteatosis	Tetracycline, salicylates
Macrosteatosis	EtOH, methotrexate
Cholestasis	Cyclosporine, OCS
Necrosis	Acetaminophen
Hepatitis	Isoniazid, phenytoin
Granulomas	Allopurinol, sulfonamides
Fibrosis/cirrhosis	EtOH, methotrexate, amiodarone
Venous occlusion	Cytotoxic chemotherapy

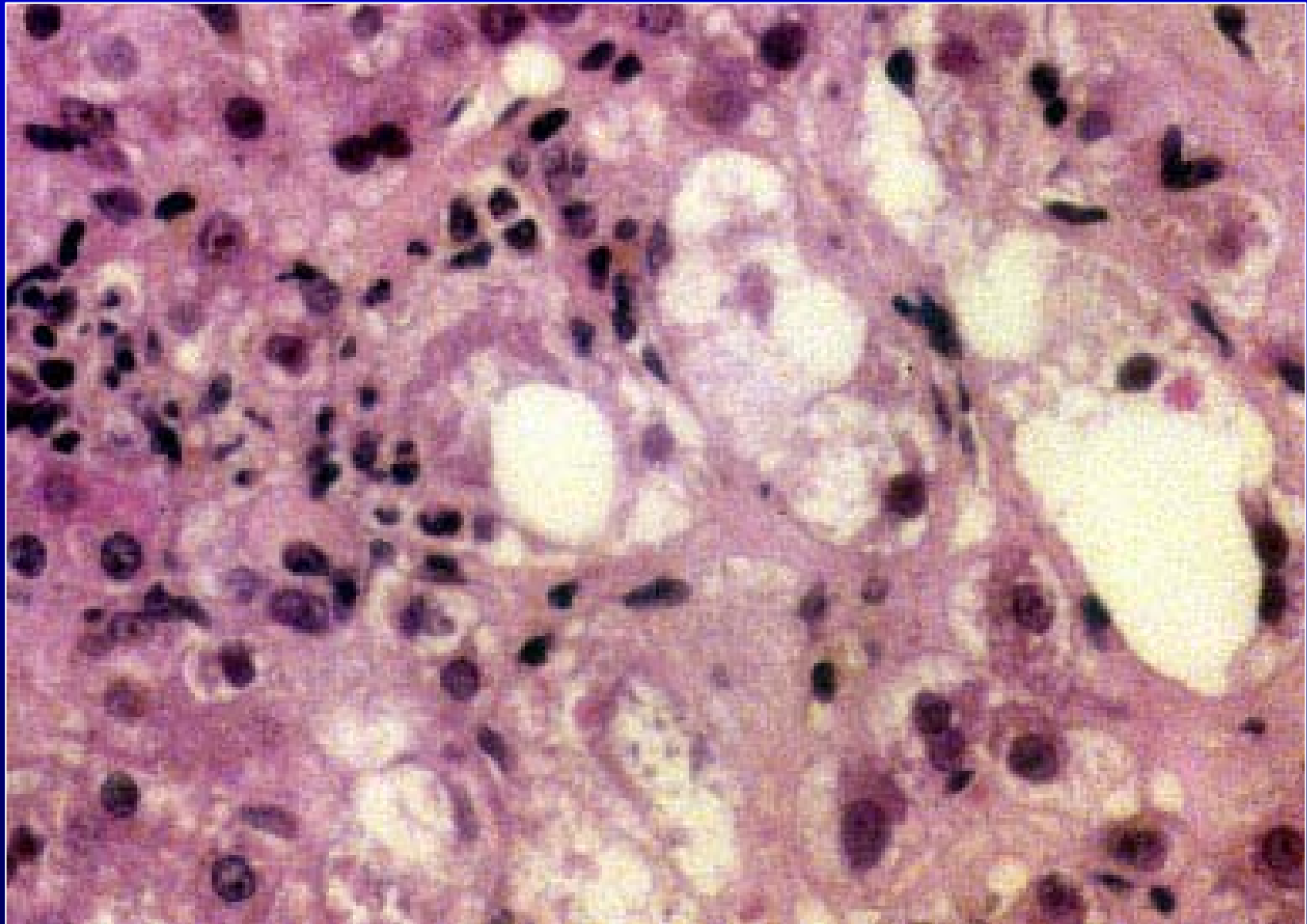
# Steatosis- Etiologies

- Microvesicular
  - Reyes Syndrome
  - Drug reactions (e.g. tetracycline)
  - Fatty liver of pregnancy
- Macrovesicular
  - Alcohol
  - Drug reaction (e.g. steroids)
  - Others (obesity, diabetes, malnutrition)

# Steatosis

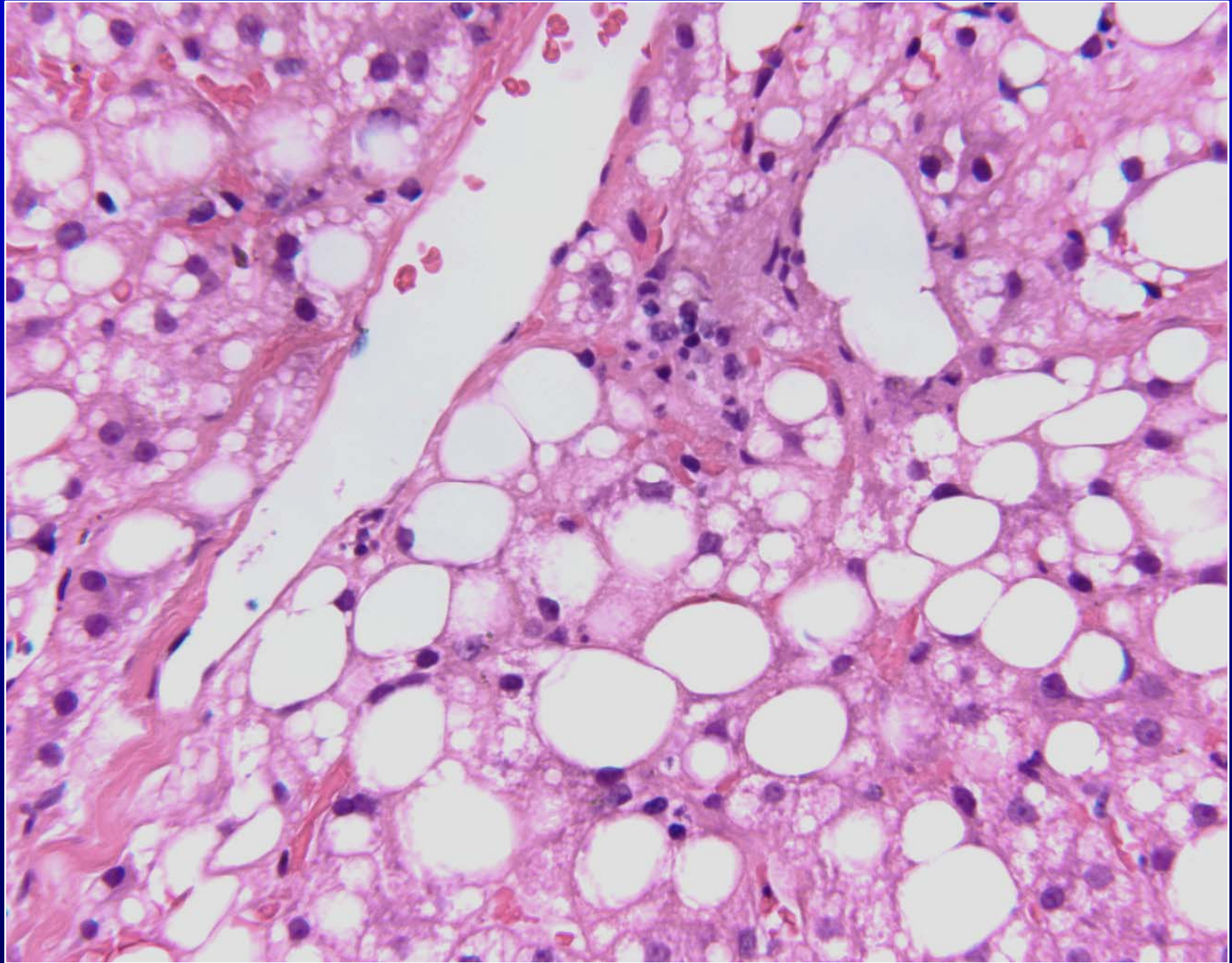


# Alcoholic hepatitis

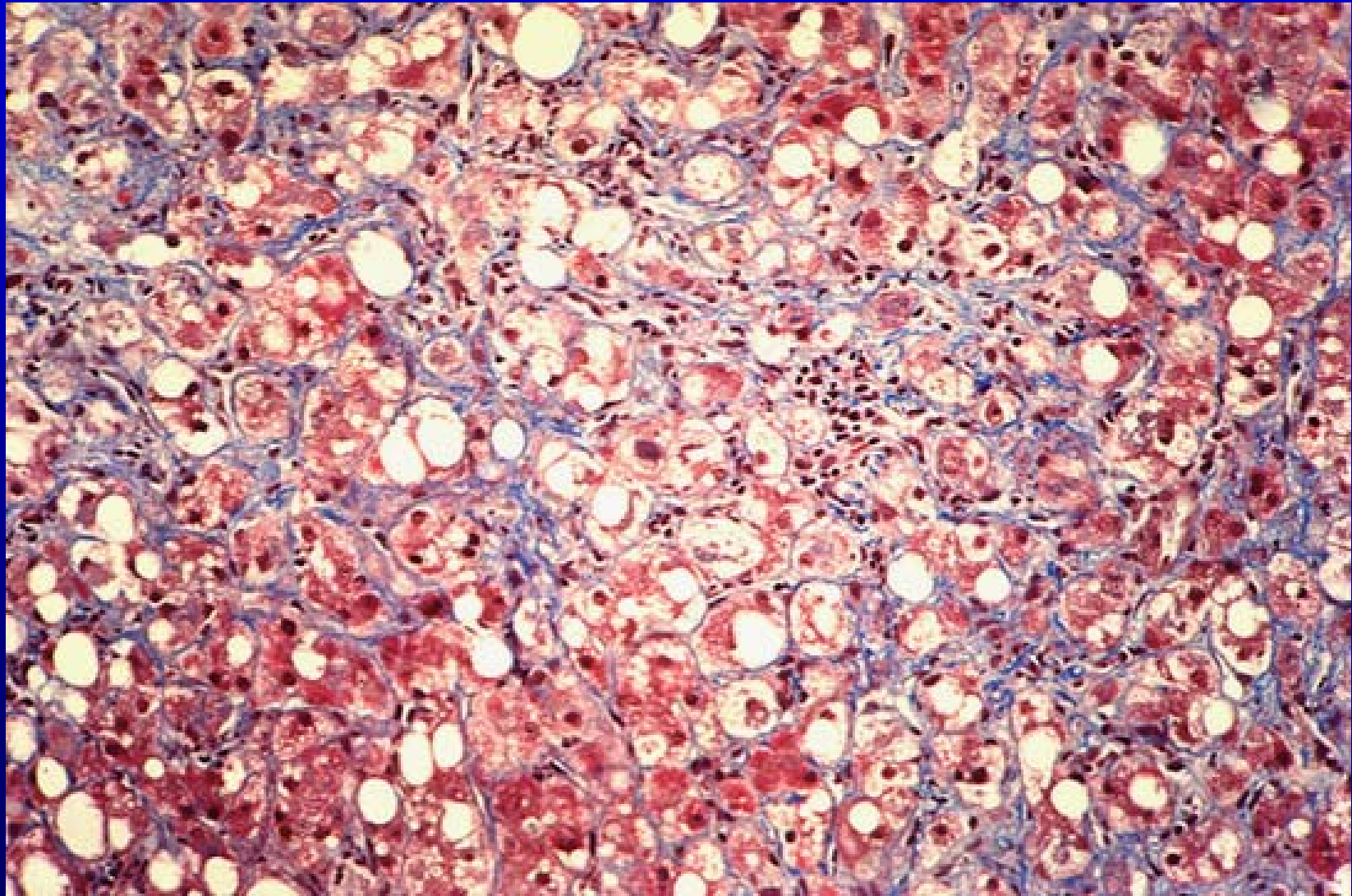




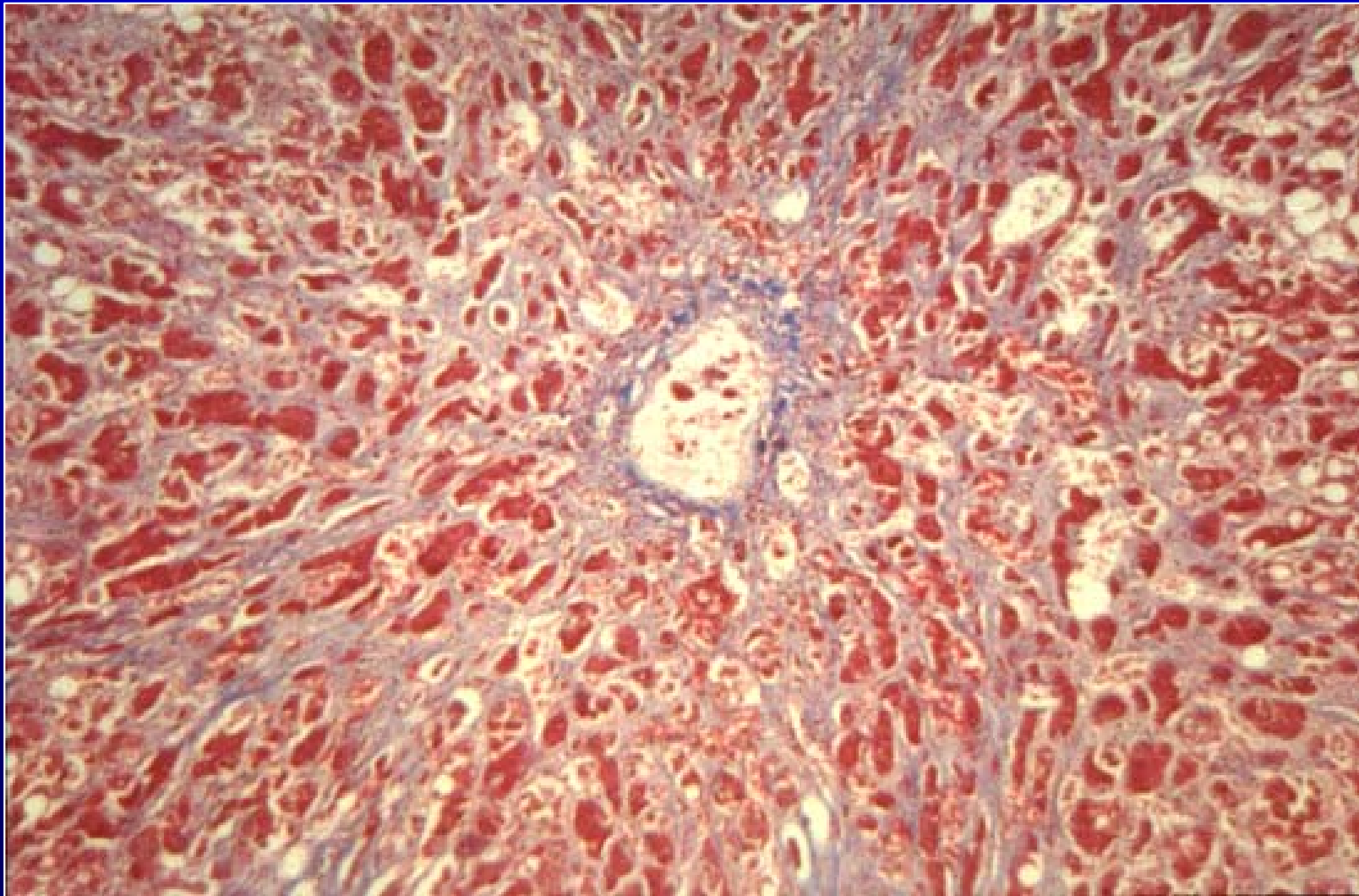
# NASH



# Sinusoidal fibrosis



# Pericentral/sinusoidal fibrosis



# Cirrhosis-etiological

- Alcohol (60-70%)
- Chronic viral hepatitis (10-20%)
- Biliary (5-10%)
  - Primary biliary cirrhosis
  - Secondary (i.e.chronic biliary obstruction)
- Metabolic (5%)
  - Hemochromatosis, Wilson's disease
  - $\alpha$ 1-antitrypsin deficiency
- Cryptogenic (10-15%)

# Cirrhosis

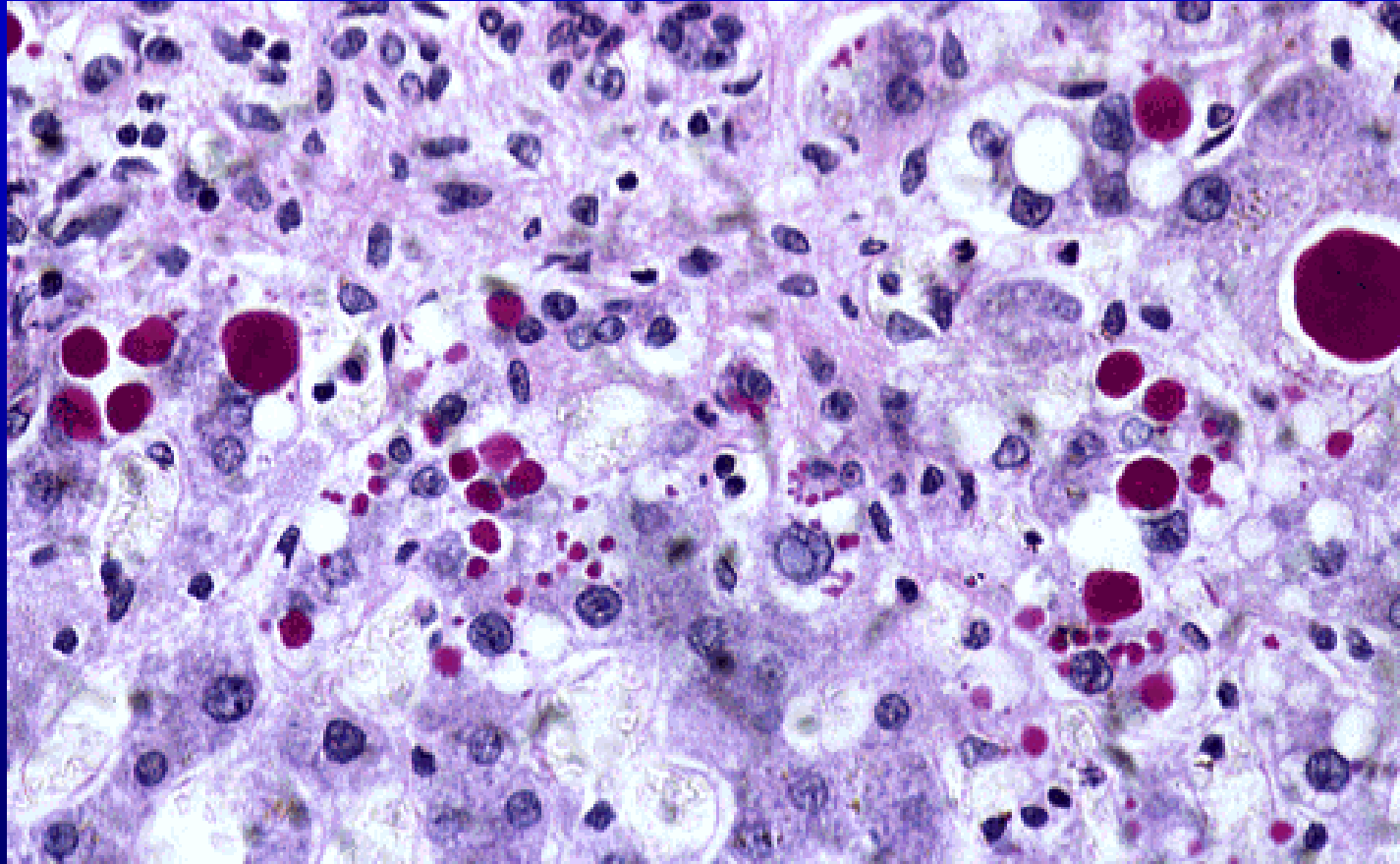


# Cirrhosis- assessment of cause

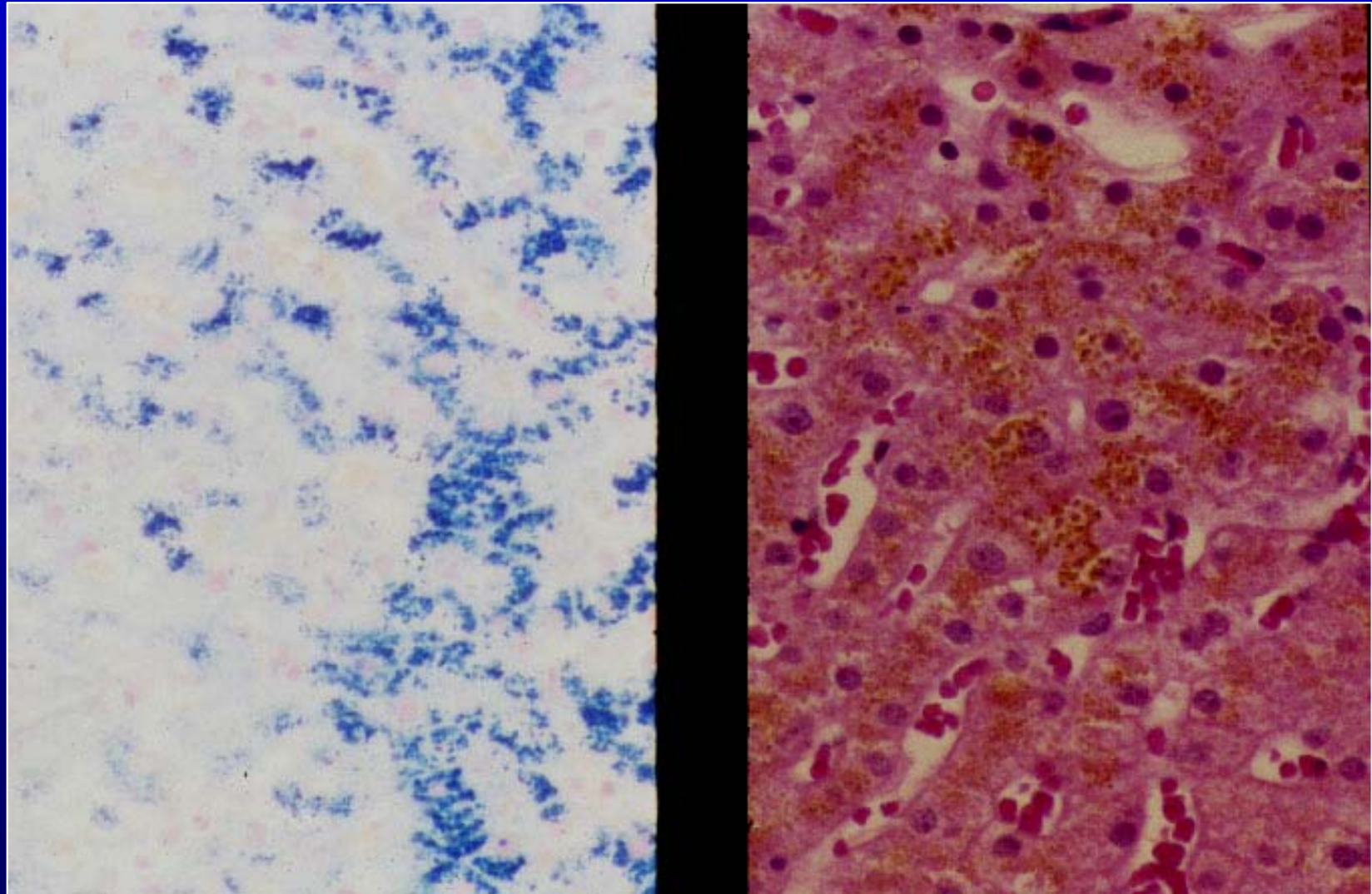
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- Pattern of nodules and fibrosis
- Bile ducts
- Blood vessels
- Steatohepatitis?
- Pattern of hepatitis
- Abnormal deposits

# $\alpha$ 1-antitrypsin deficiency

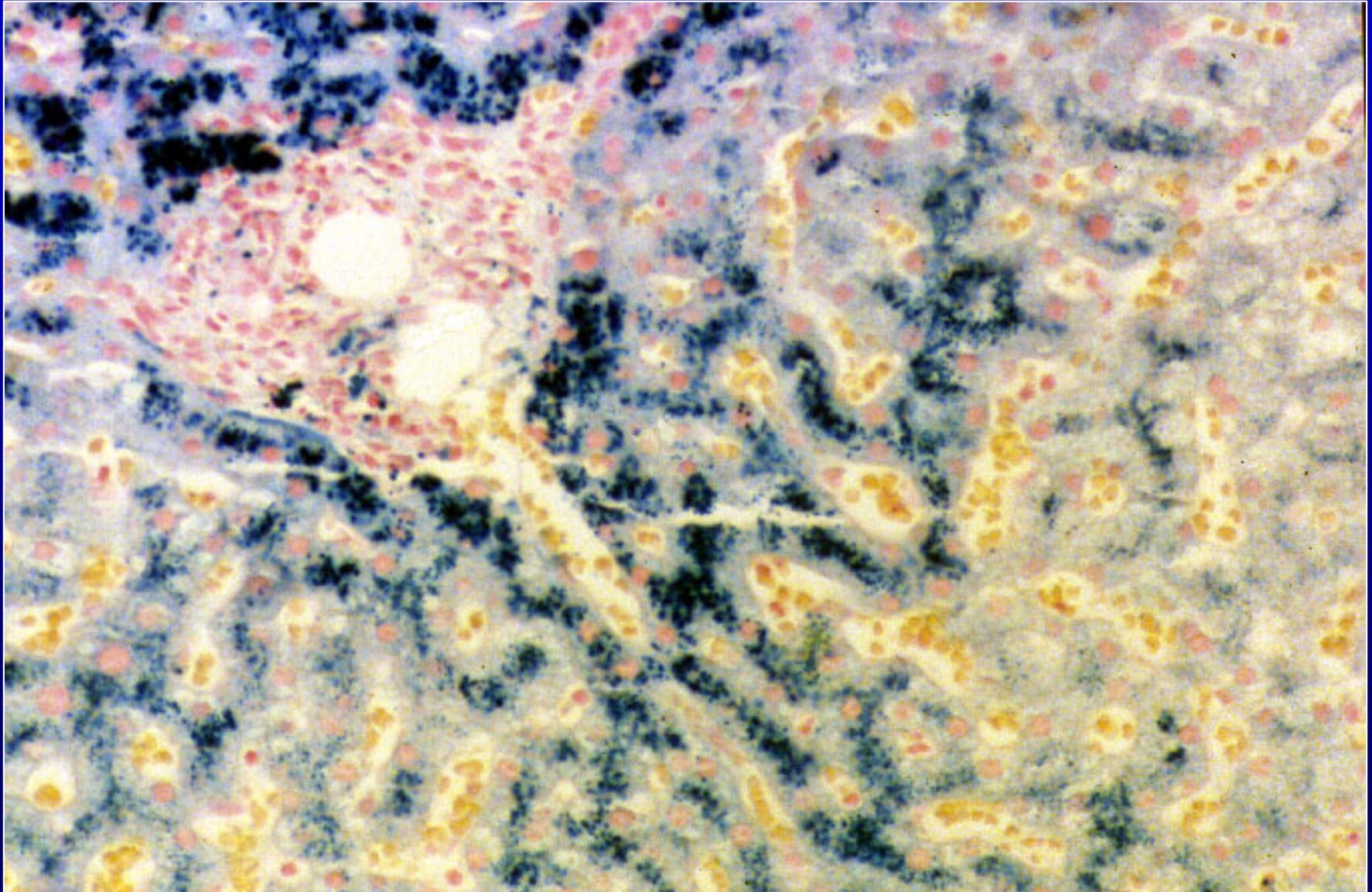


# Hemochromatosis

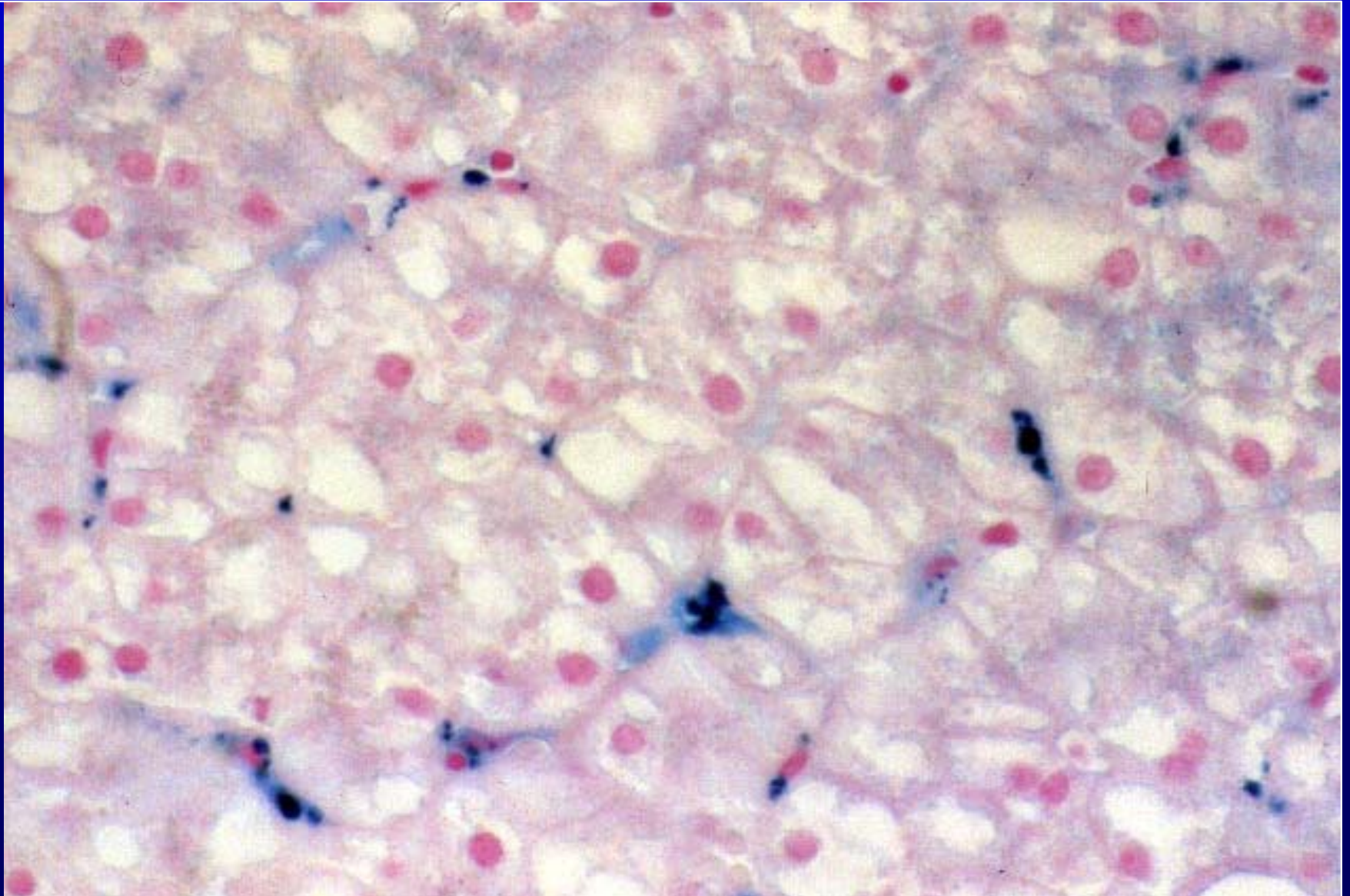




# Hemochromatosis



# secondary iron overload

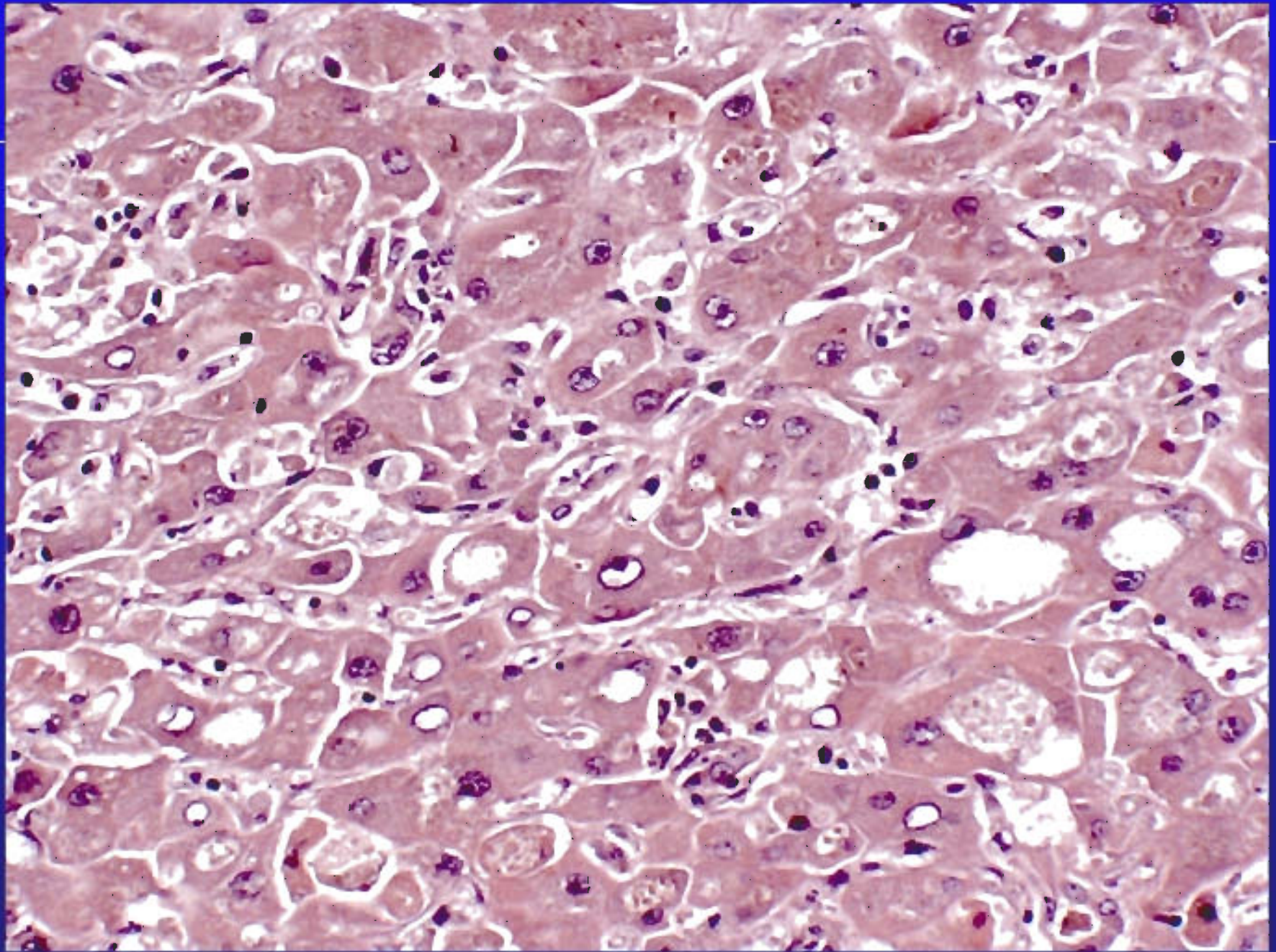


# Wilson's disease

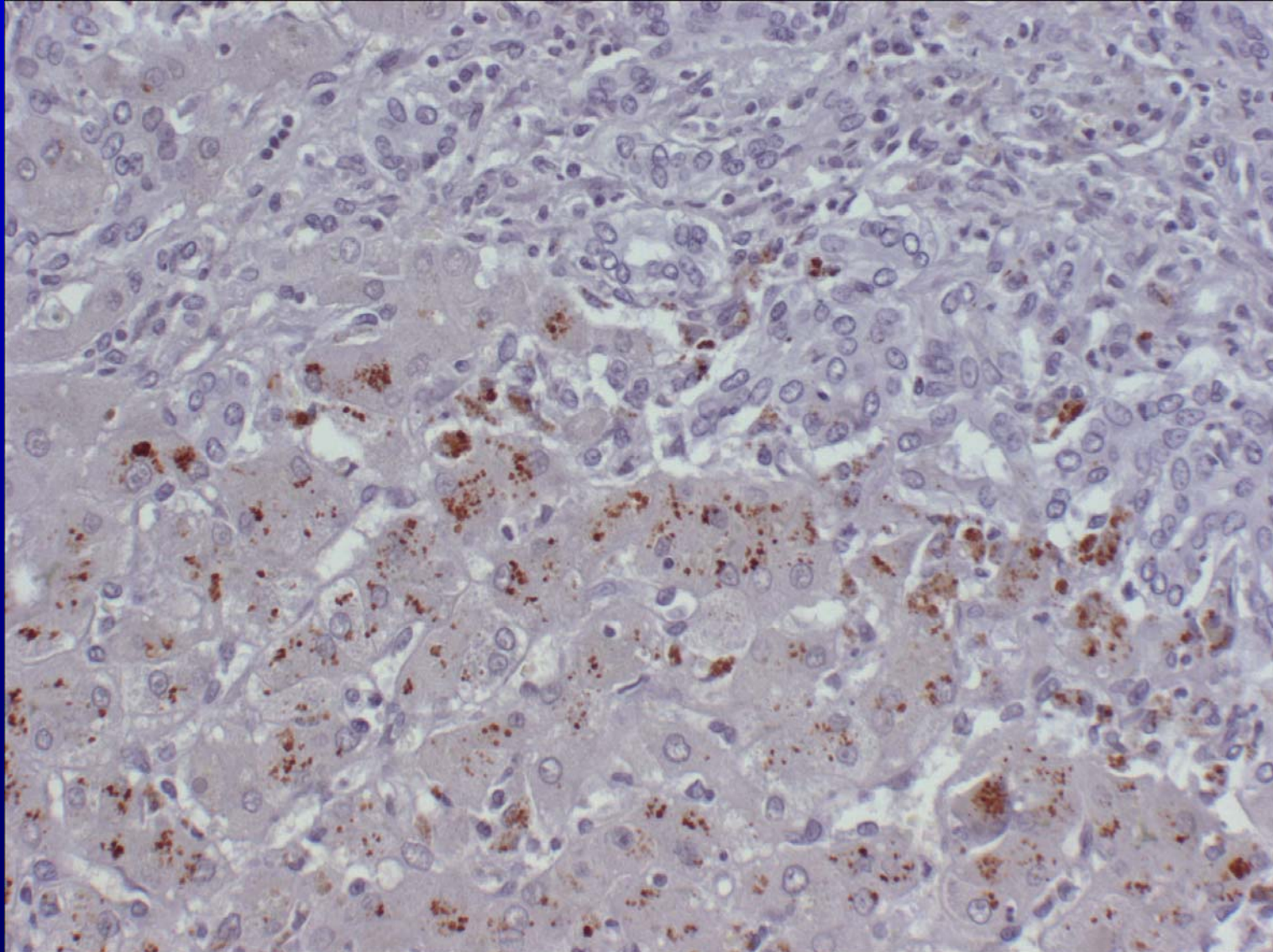
- Autosomal recessive disorder of copper overload
- Incidence 1:30,000
- Age of onset: 3-40 years
- Molecular defect:
  - ATP7B gene, 13q12
  - membrane ATPase with copper-binding domains
  - missense mutations in ATP-binding domain

# Wilson's disease- hepatic pathology

- Early (precirrhotic):
  - chronic hepatitis, steatosis
  - ballooning, Mallory bodies , apoptotic bodies
  - glycogenated nuclei
  - Cu stain may be negative
- Fulminant hepatic failure
- Late (cirrhotic)



# Copper stain



# Hepatocellular Neoplasms and Masses

## With cirrhosis

- **Macroregenerative Nodule**
- **Borderline (dysplastic) Nodule**
- **Hepatocellular Carcinoma**

## Without cirrhosis

- **Hepatic adenoma**
- **Focal nodular hyperplasia**
- **Fibrolamellar HCC**
- **HCC**
- **Nodular regenerative hyperplasia**

# Hepatic malignancies

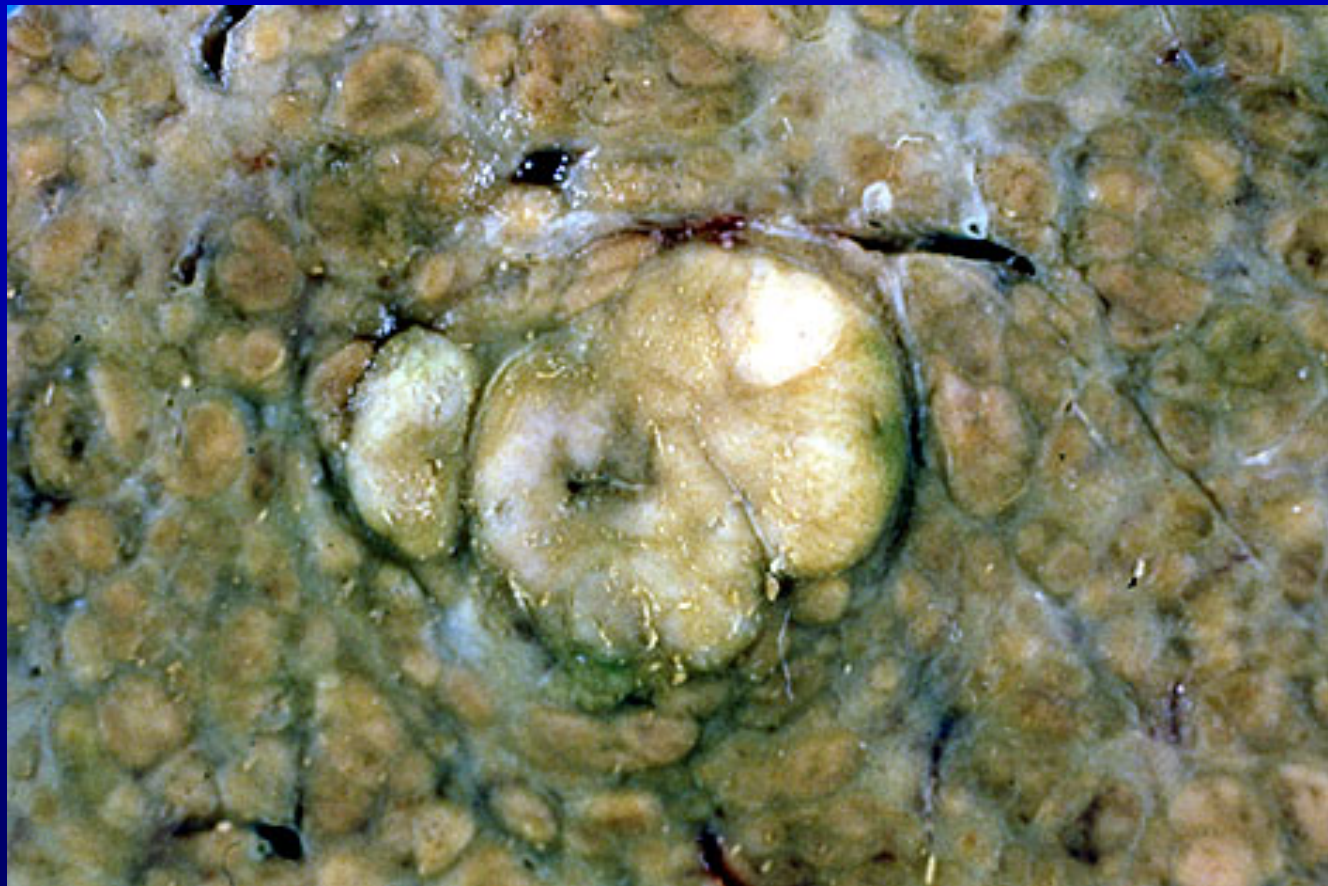
- Overall, metastases most common

## Primary Hepatic malignancies

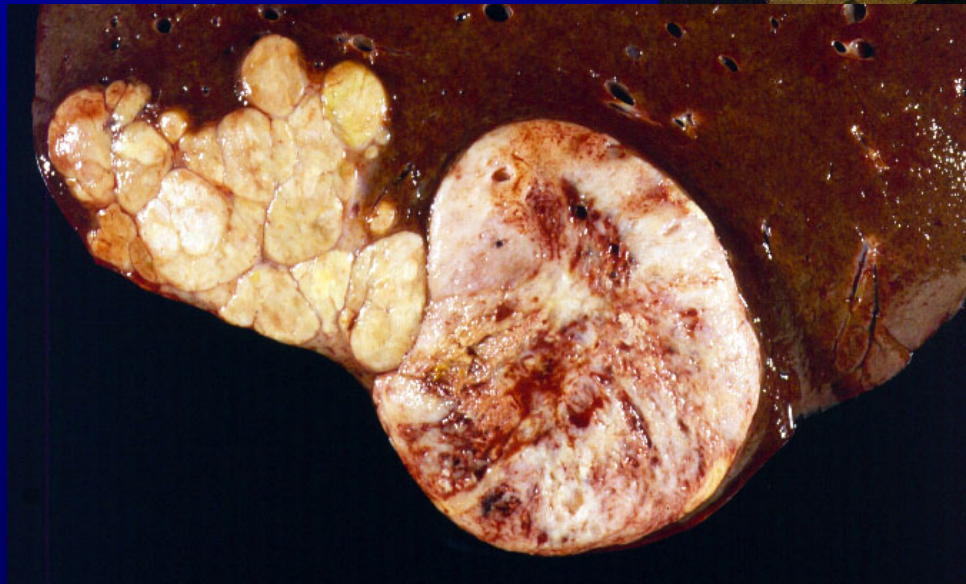
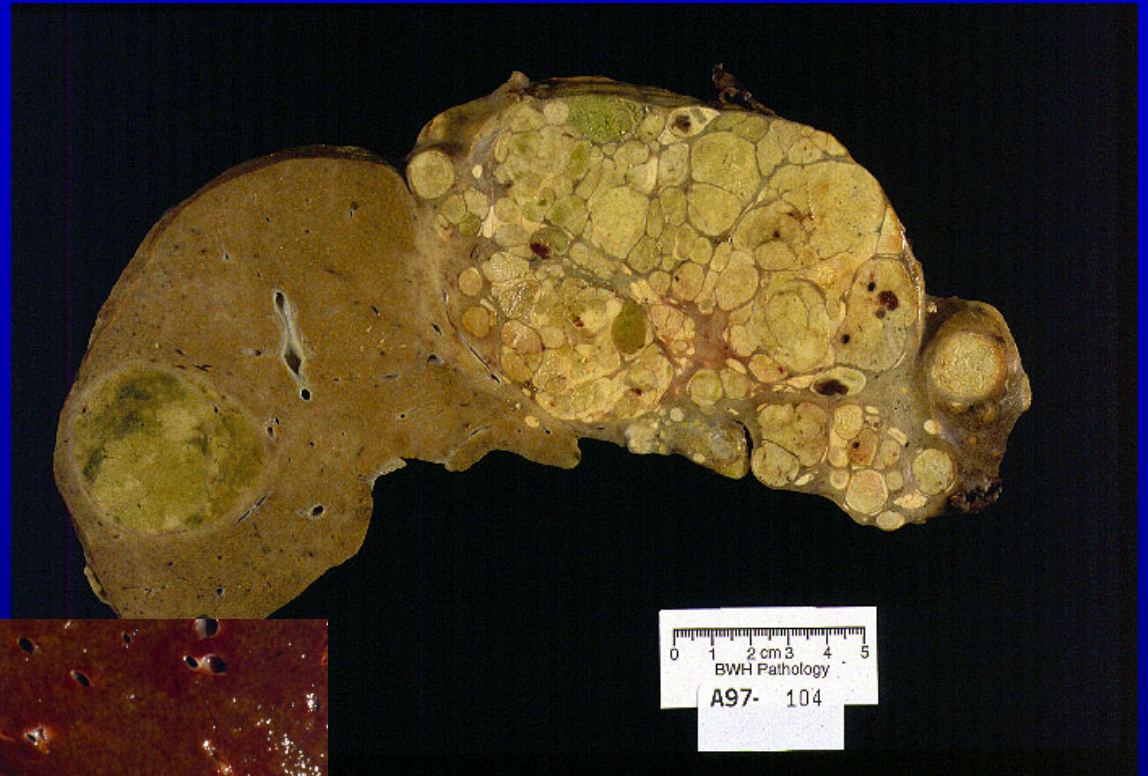
- Hepatocellular CA 65-70%
- Intrahepatic cholangioCA 20%
- HCC-cholangioCA 2%
- Sarcomas, lymphoma, other 2-3%



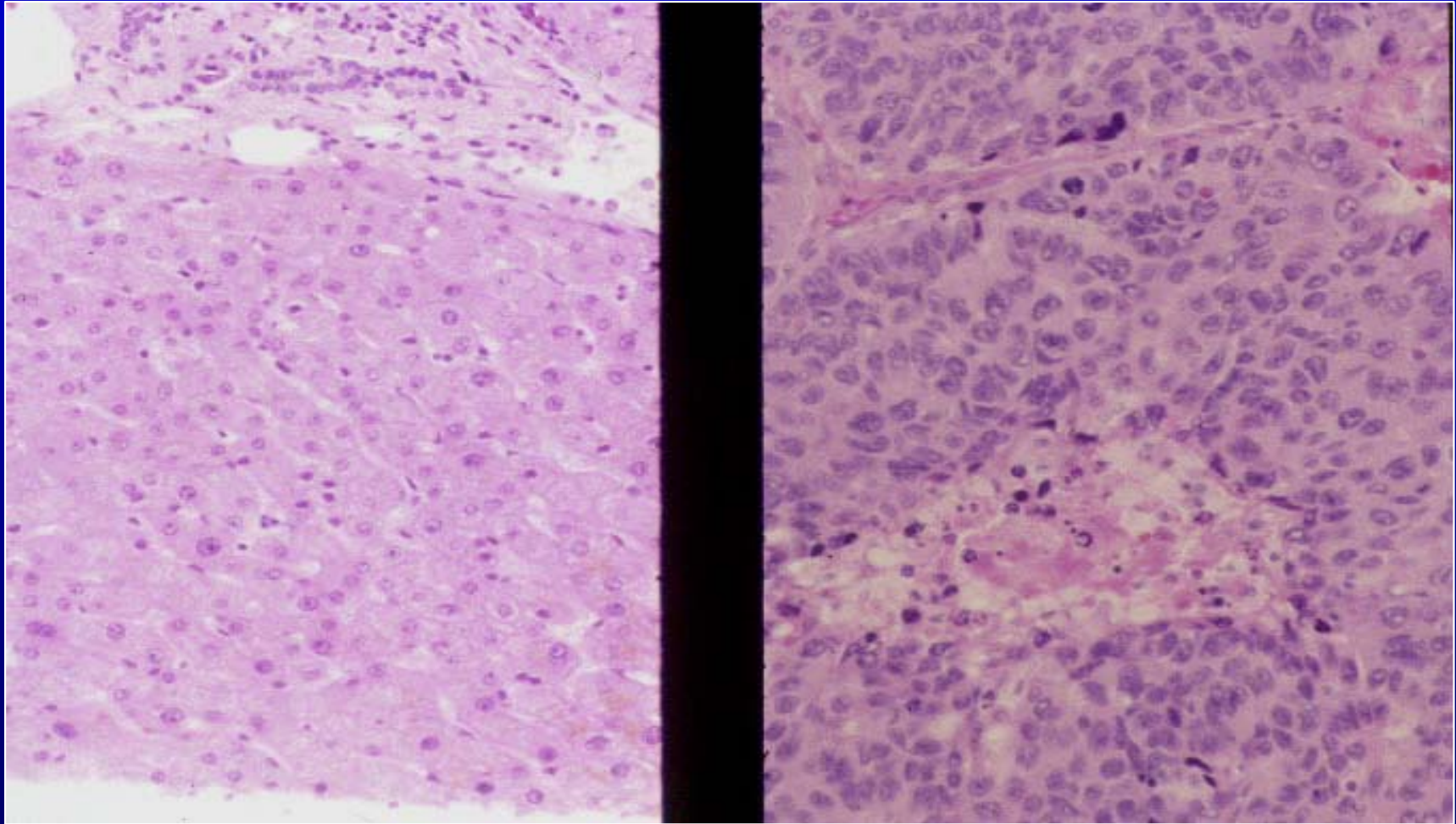
# HCC-Gross



# HCC- gross



# Non-neoplastic vs neoplastic hepatocytes



**Normal**

**HCC**

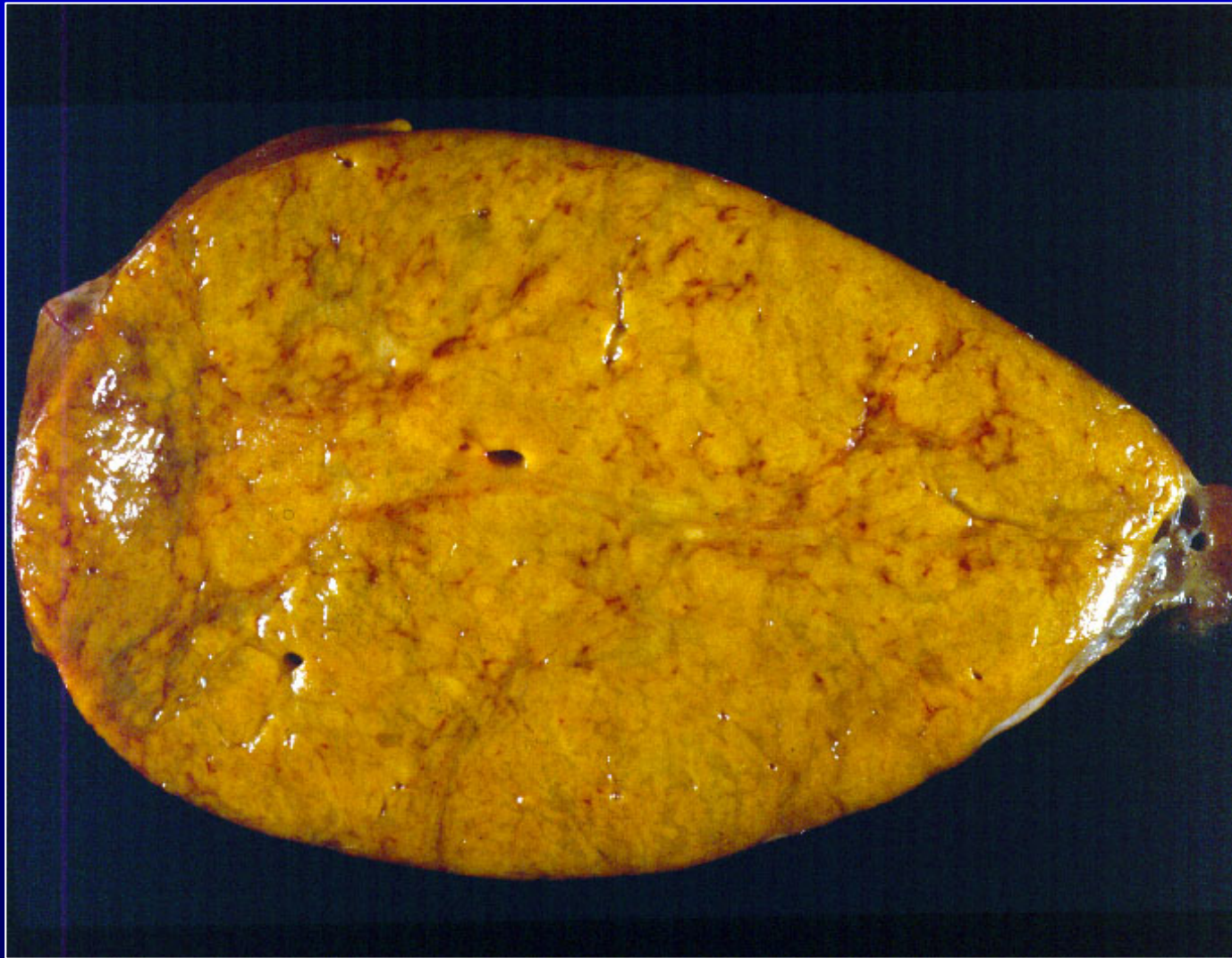
# HCCa vs regenerative nodule

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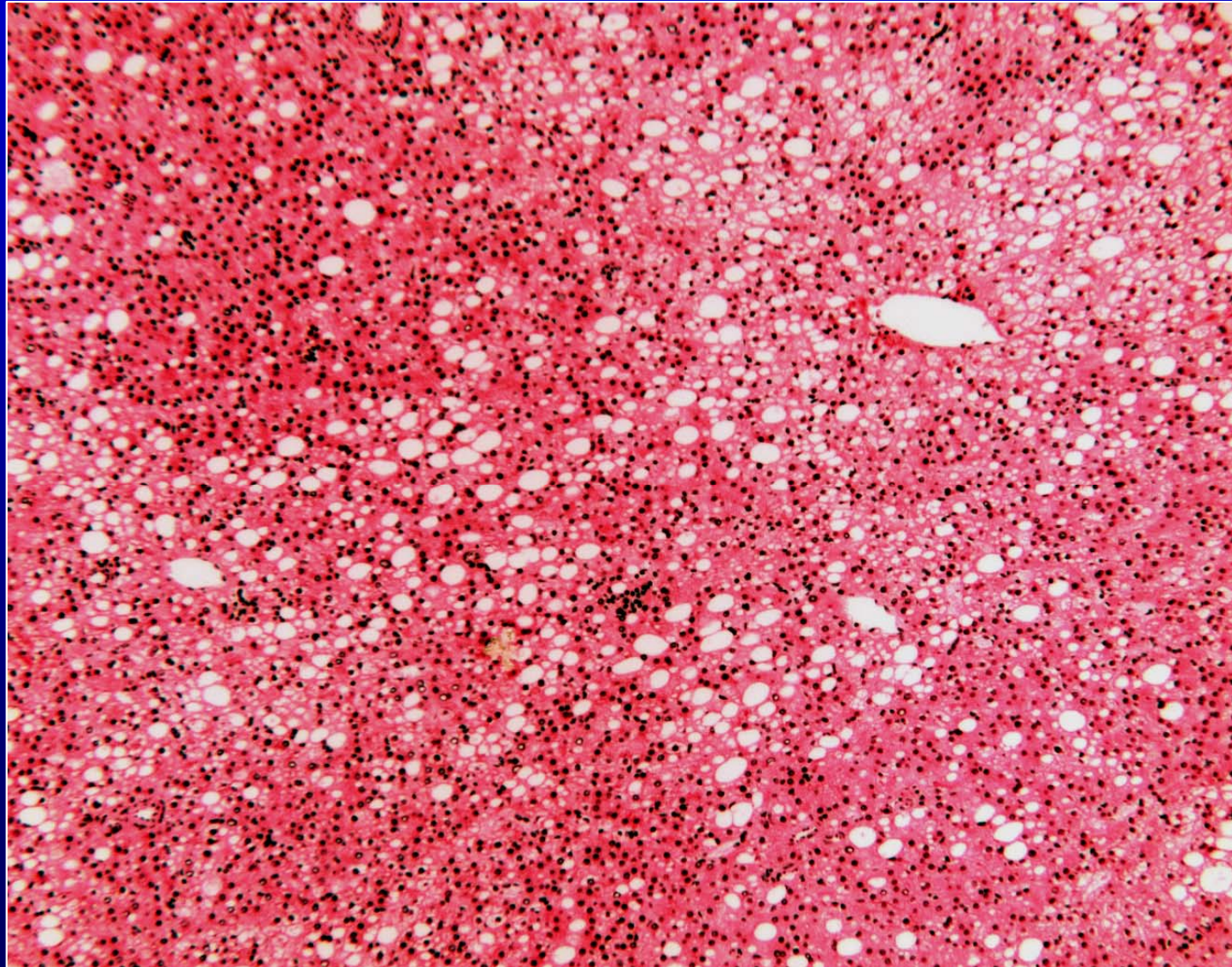
<b>Feature</b>	<b>HCC</b>	<b>Regen nodule</b>
<b>Plates &gt; 2 cells thick</b>	++	-
<b>Small cell change</b>	++	-/+
<b>Portal tracts</b>	-	+
<b>Infiltrative edge</b>	+/-	-

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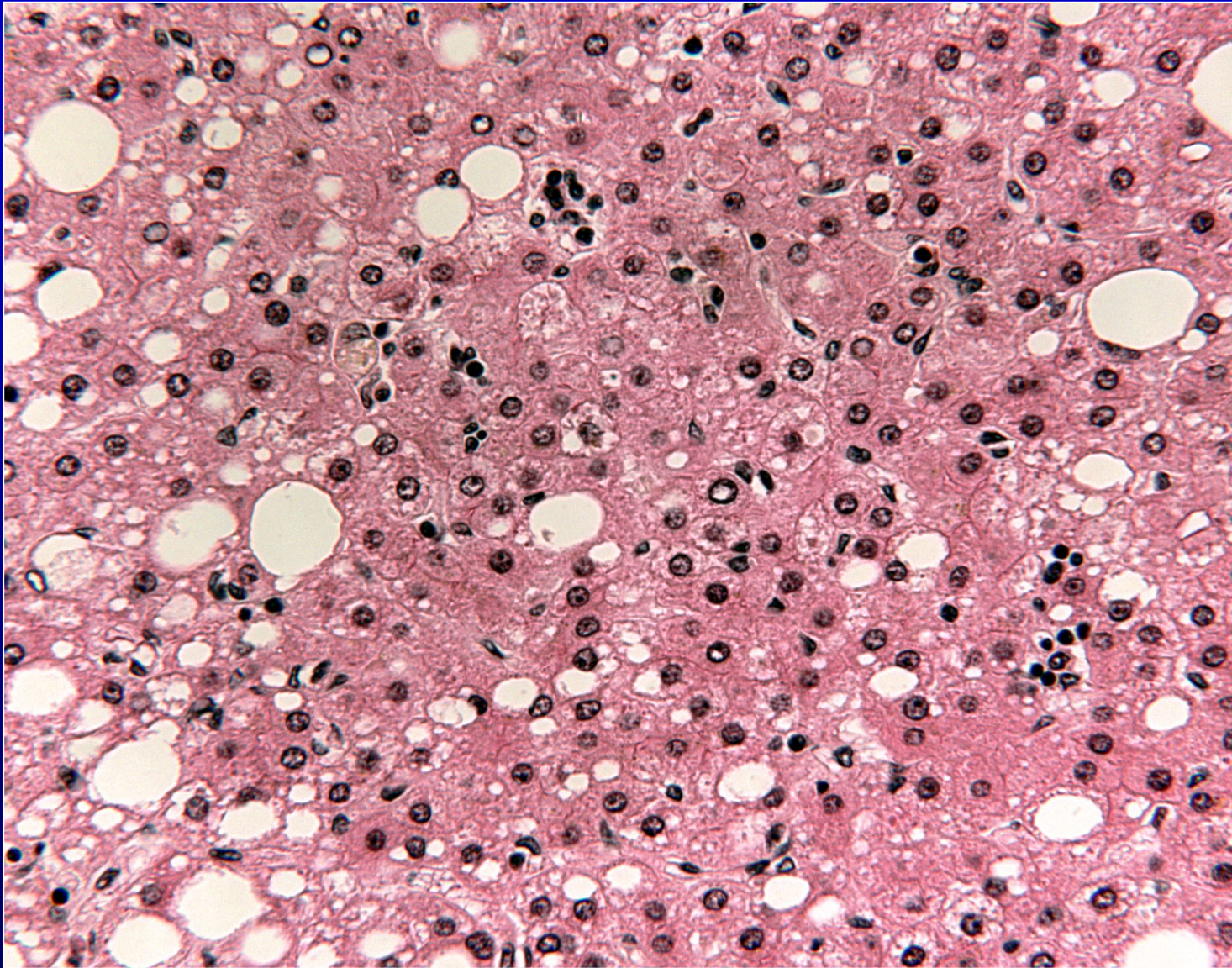
# Hepatic adenoma-gross



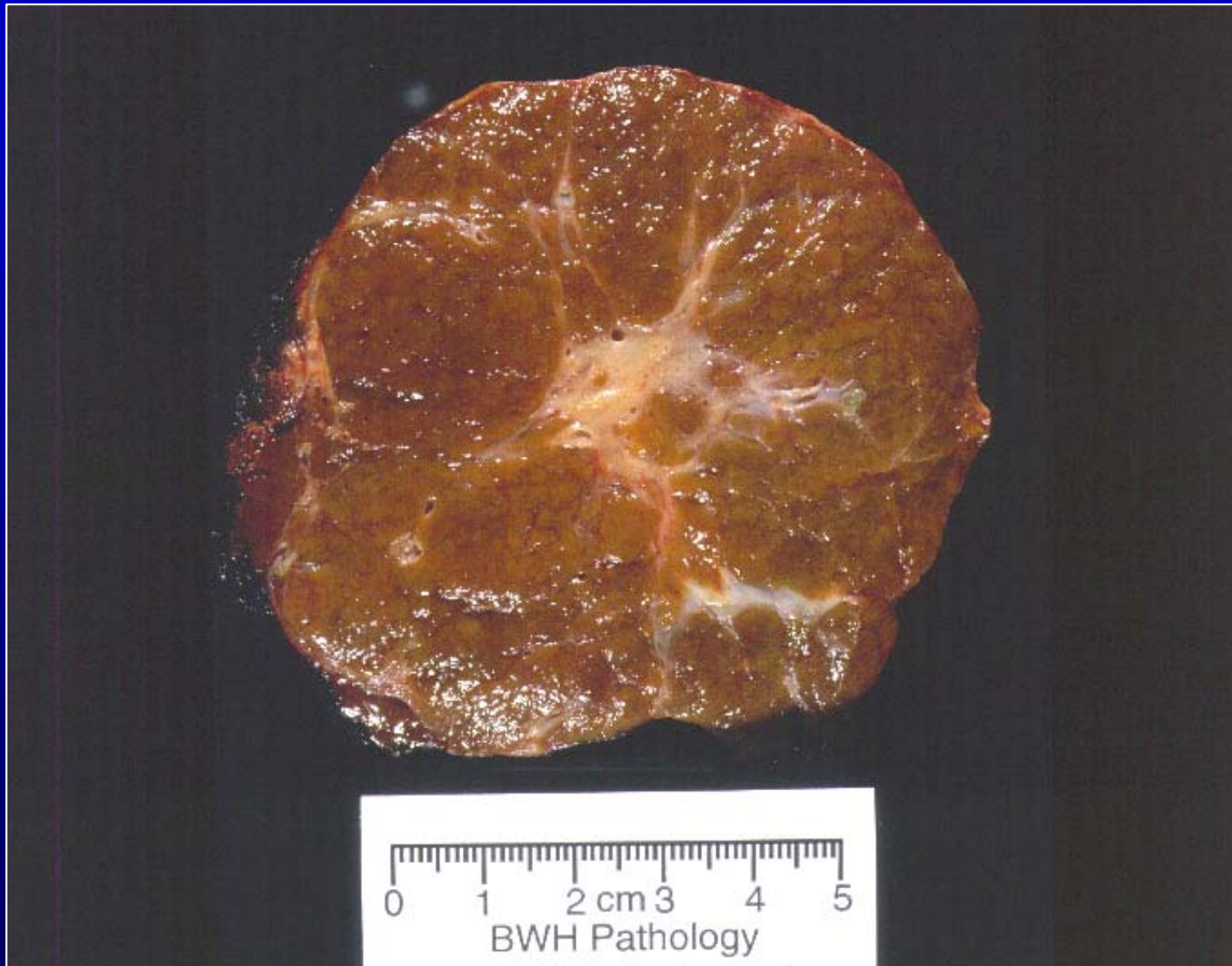
# Hepatic adenoma



# Hepatic adenoma

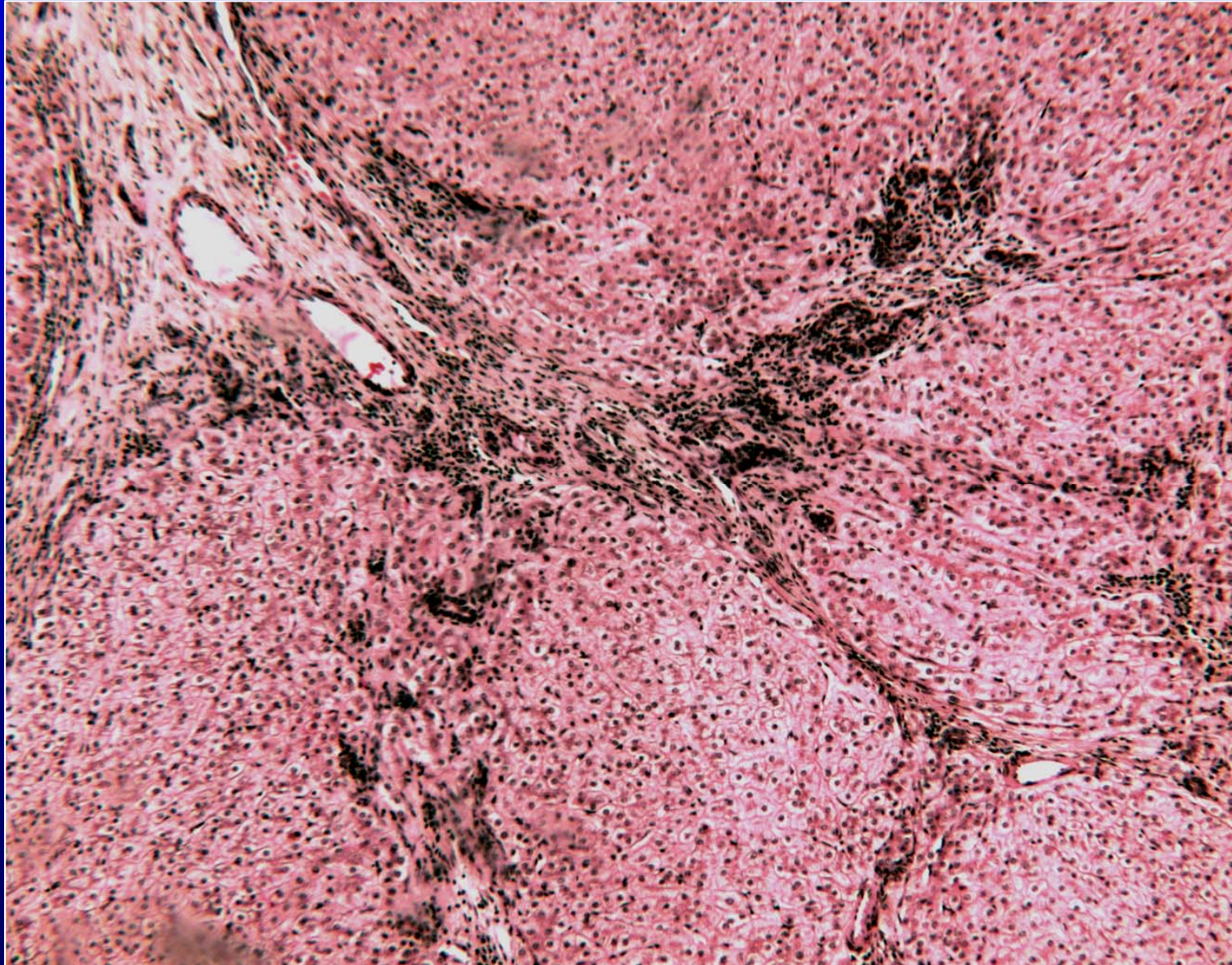


# Focal nodular hyperplasia- gross

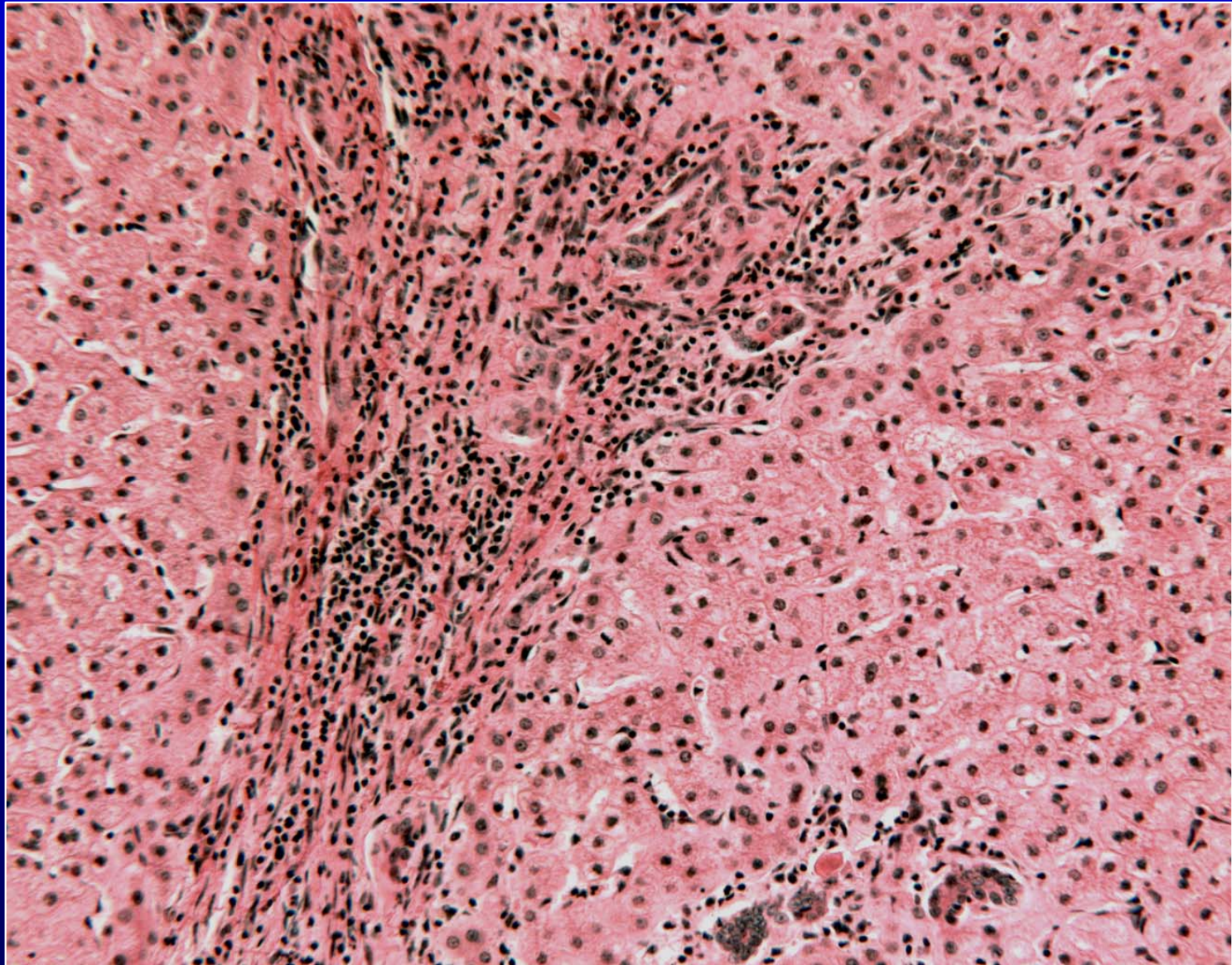




# Focal nodular hyperplasia



# Focal nodular hyperplasia



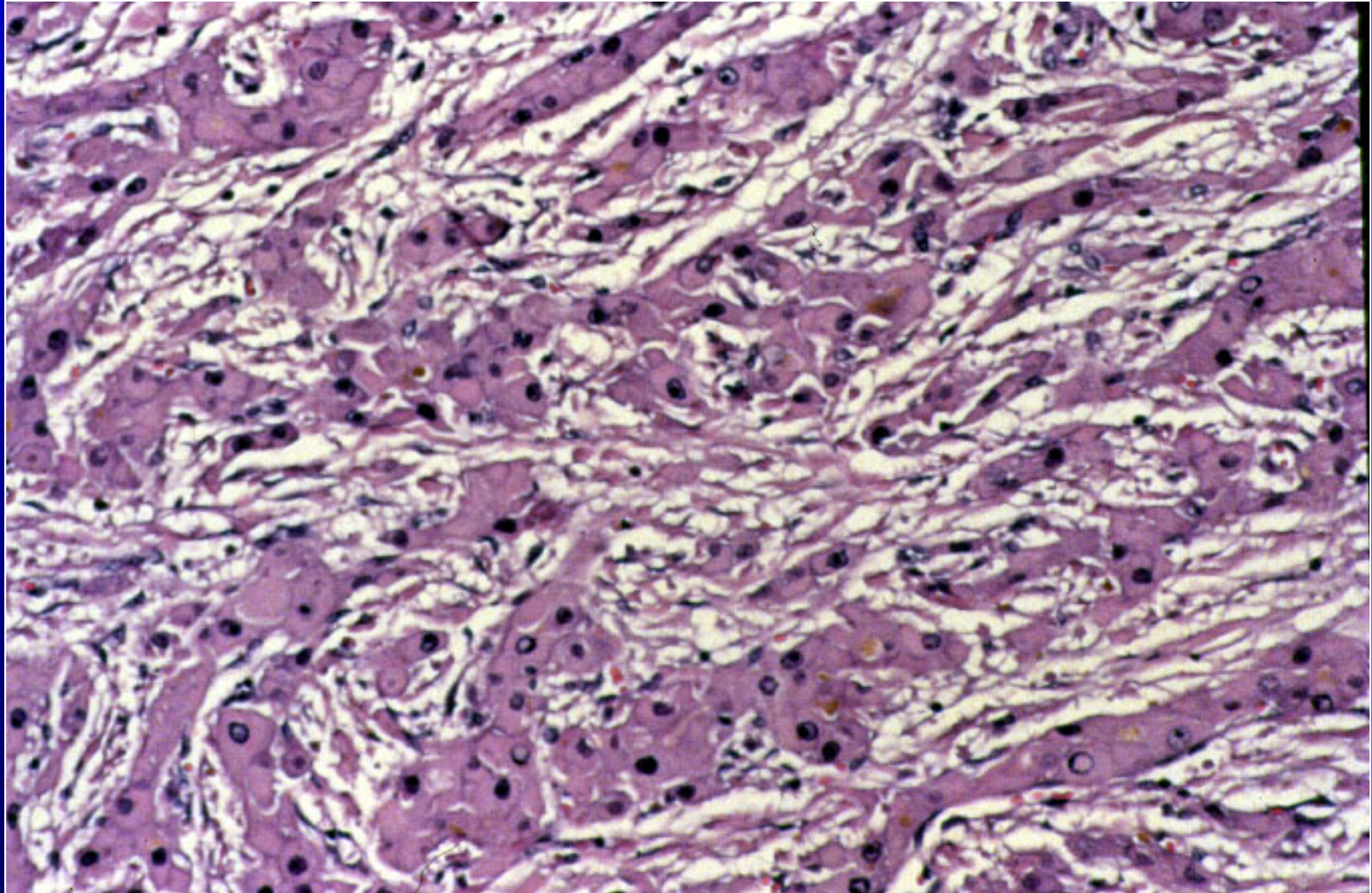
# Fibrolamellar HCC

- young adults, M=F
- Low association with cirrhosis (<10%), HBV, HCV
- **Gross:** Firm circumscribed mass, central fibrous septa
- **Micro:** Nests, cords of eosinophilic tumor cells  
Lamellar bands of collagen surrounding tumor cells
- **Prognosis:** slow growing, resected 5 year survival 40-50%
- **Ddx:** FNH, HCC, metastatic CA

# Fibrolamellar HCC- gross



# Fibrolamellar HCC



# Cholangiocarcinoma

