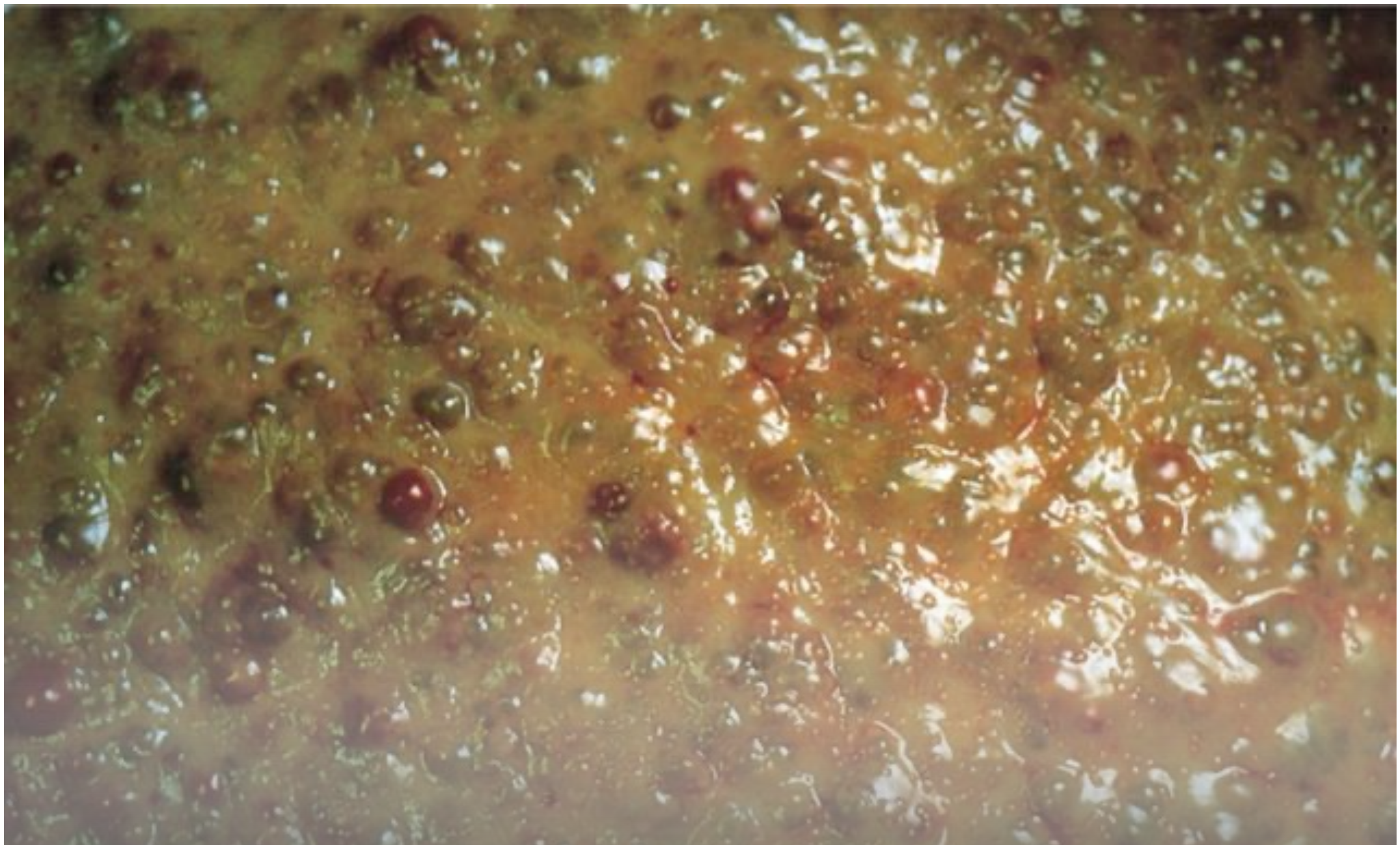




Liver, Gallbladder, and Pancreas Pathology

Kristine Krafts, M.D.

GI Pathology Outline

- Esophagus
- Stomach
- Intestine
- Liver
 - Hepatitis
 - Alcoholic liver disease
 - Hemochromatosis
 - Wilson disease
 - Carcinoma

Liver Learning Objectives

- For hepatitis A, B, and C, compare and contrast the transmission, and risk of developing chronic hepatitis and carcinoma
- Explain normal bilirubin metabolism (How is it made? What happens to it in the liver? How is it excreted?)
- What's the difference between conjugated and unconjugated bilirubin?
- Explain why conjugated bilirubin could appear in excess in the blood, and list two specific causes.
- Same thing for unconjugated hyperbilirubinemia – why would it happen? List 3 causes.

Liver Learning Objectives

- What's the difference between hepatocyte integrity and hepatocyte function? What lab tests could you use to distinguish between the two?
- What substances increase in the blood when the biliary tree is damaged or not working?
- Describe what a liver with cirrhosis looks like. What causes cirrhosis? What are the potential consequences?
- How would you define portal hypertension in your own words? What's the usual cause? What are four clinical consequences?

Liver Learning Objectives

- List typical causes and symptoms of liver failure.
- What oral manifestations could you see in someone with a damaged liver?
- What are two liver conditions caused by excessive alcohol use that are typically reversible with abstinence?
- What typically happens to the liver if a person continues to use alcohol excessively and chronically?
- What are some causes of death in end-stage alcoholism?

Liver Learning Objectives

- Describe the inheritance pattern of hereditary hemochromatosis. What does the mutation in the hemochromatosis gene cause? What are some symptoms and treatments of this disease?
- Same questions for Wilson disease!
- What are the causes, symptoms, and general mortality (not numbers) of liver carcinoma?

Gallbladder Learning Objectives

- What's the difference between cholelithiasis and cholecystitis?
- List risk factors for cholesterol stones and pigment stones.
- List the possible presentations of cholelithiasis.

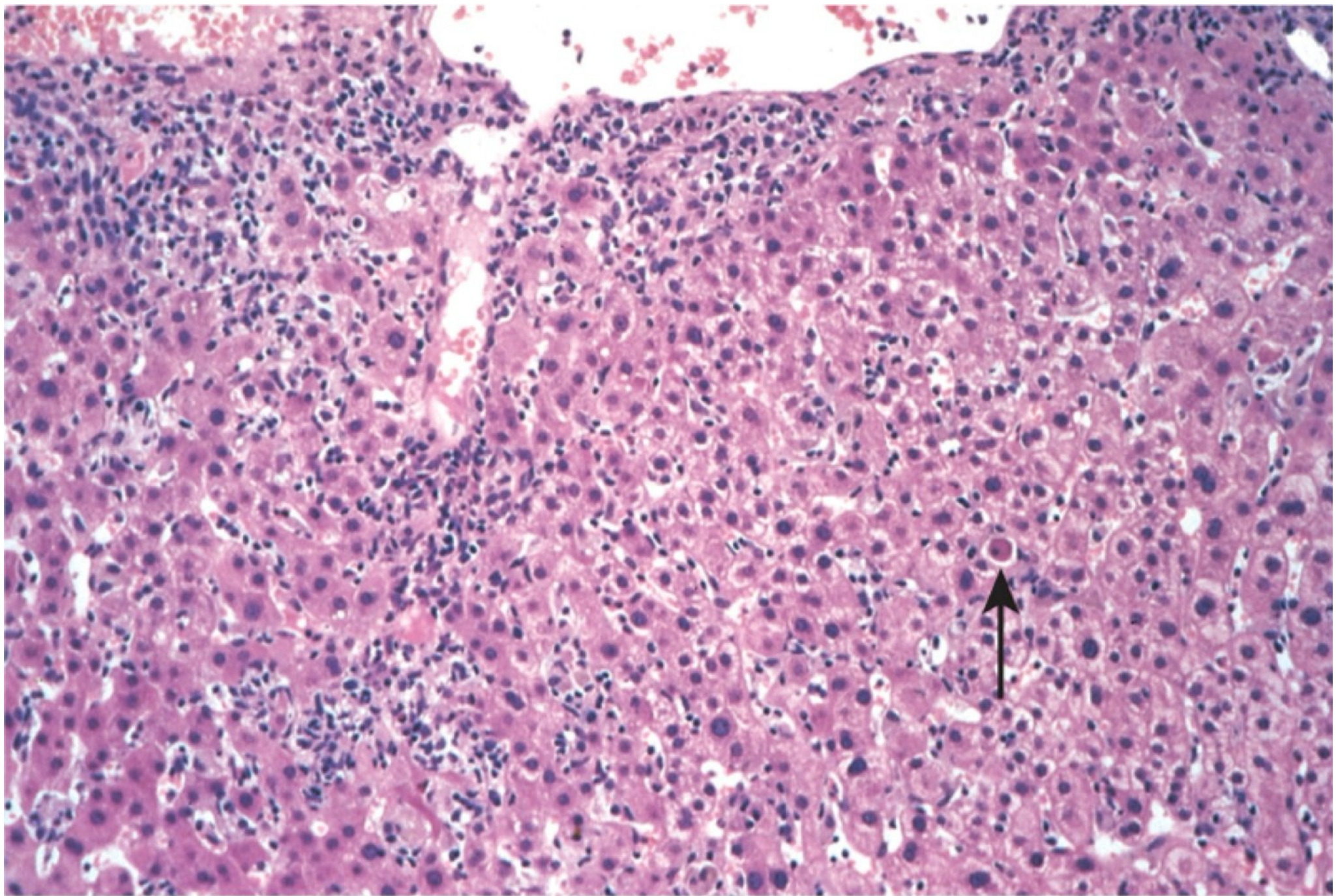
Pancreas Learning Objectives

- Define acute pancreatitis, list how it presents and what causes it, and list two substances that increase in the blood. What's the general prognosis?
- Define chronic pancreatitis, identify the most common cause, and describe its symptoms and prognosis.
- What's the biggest risk factor for pancreatic carcinoma? Why is the mortality so high?

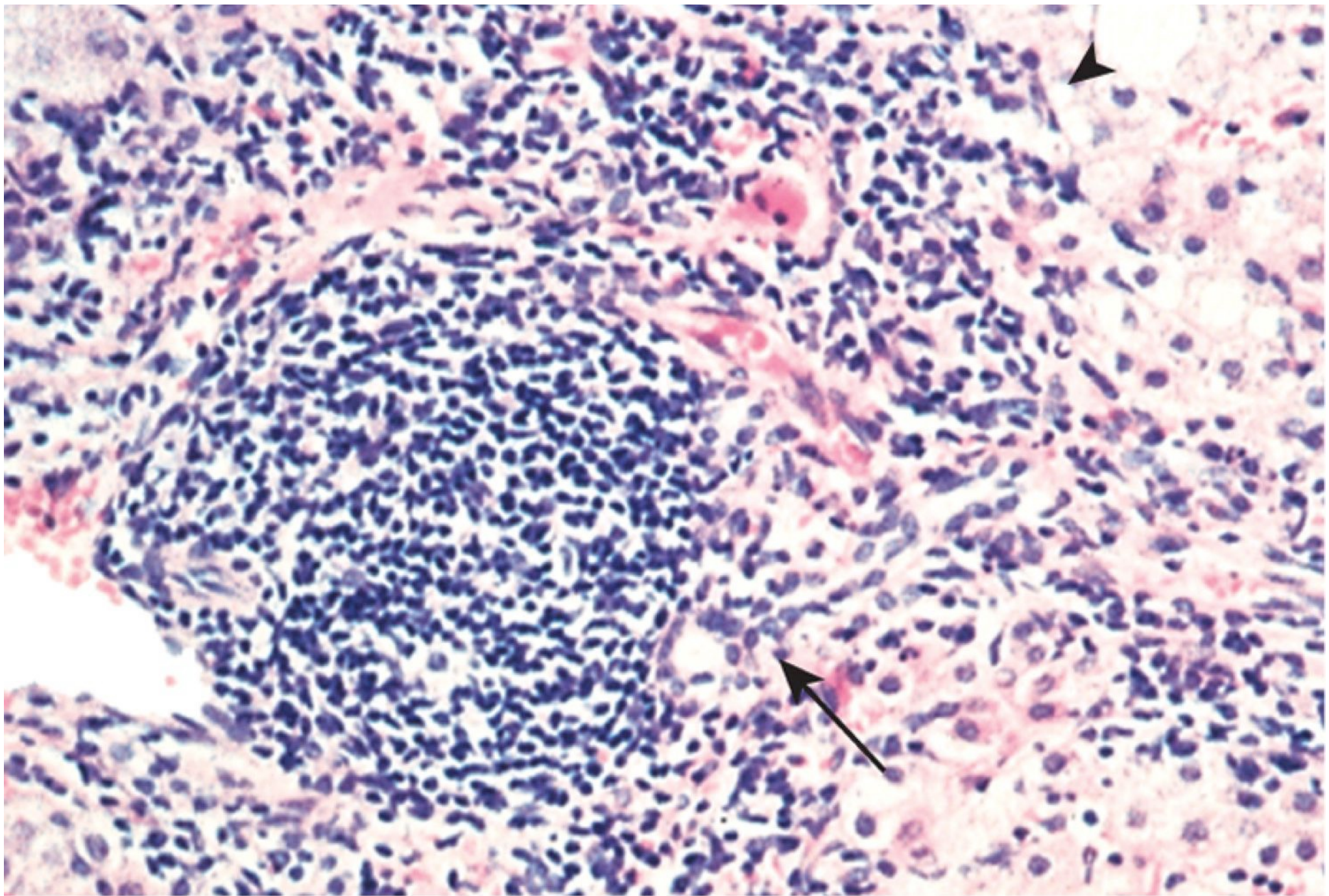
Viral Hepatitis

- Caused by Hepatitis A, B, or C viruses
- Some cases asymptomatic
- Some cases symptomatic:
 - Acute (jaundice)
 - Chronic (may lead to cirrhosis and liver failure)
 - Fulminant (liver failure)

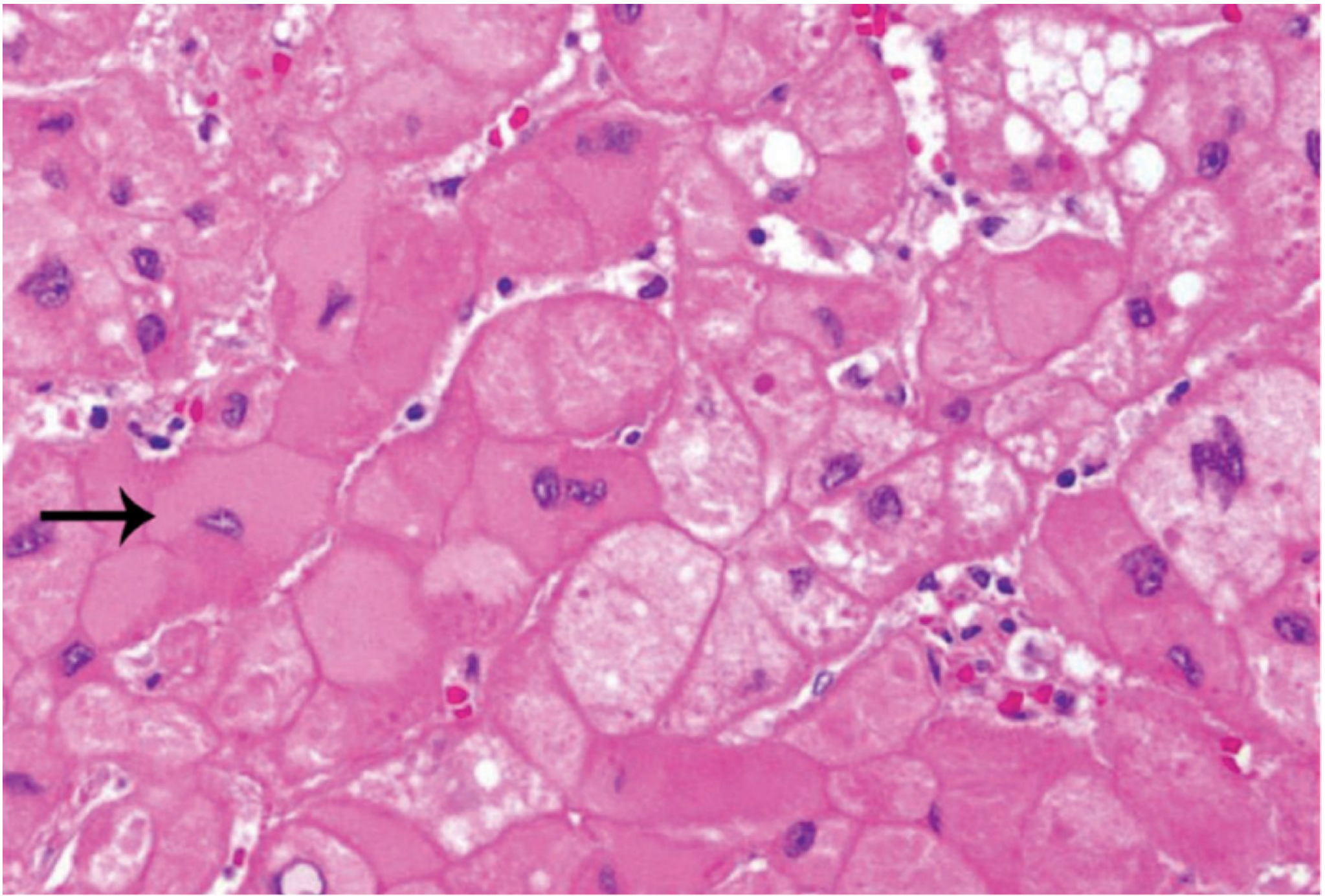
	Hepatitis A	Hepatitis B	Hepatitis C
Transmission	Fecal-oral	Body fluids Needles	Body fluids Needles
Chronic Hepatitis	None	5%	>85%
Carcinoma	No	Yes	Yes
Other stuff	50% of people > 50 are +	Vaccine effective	New drugs are promising
Bottom line	Benign, self- limited disease	Most recover; small % die	Nasty! Almost 10% die



Acute viral hepatitis

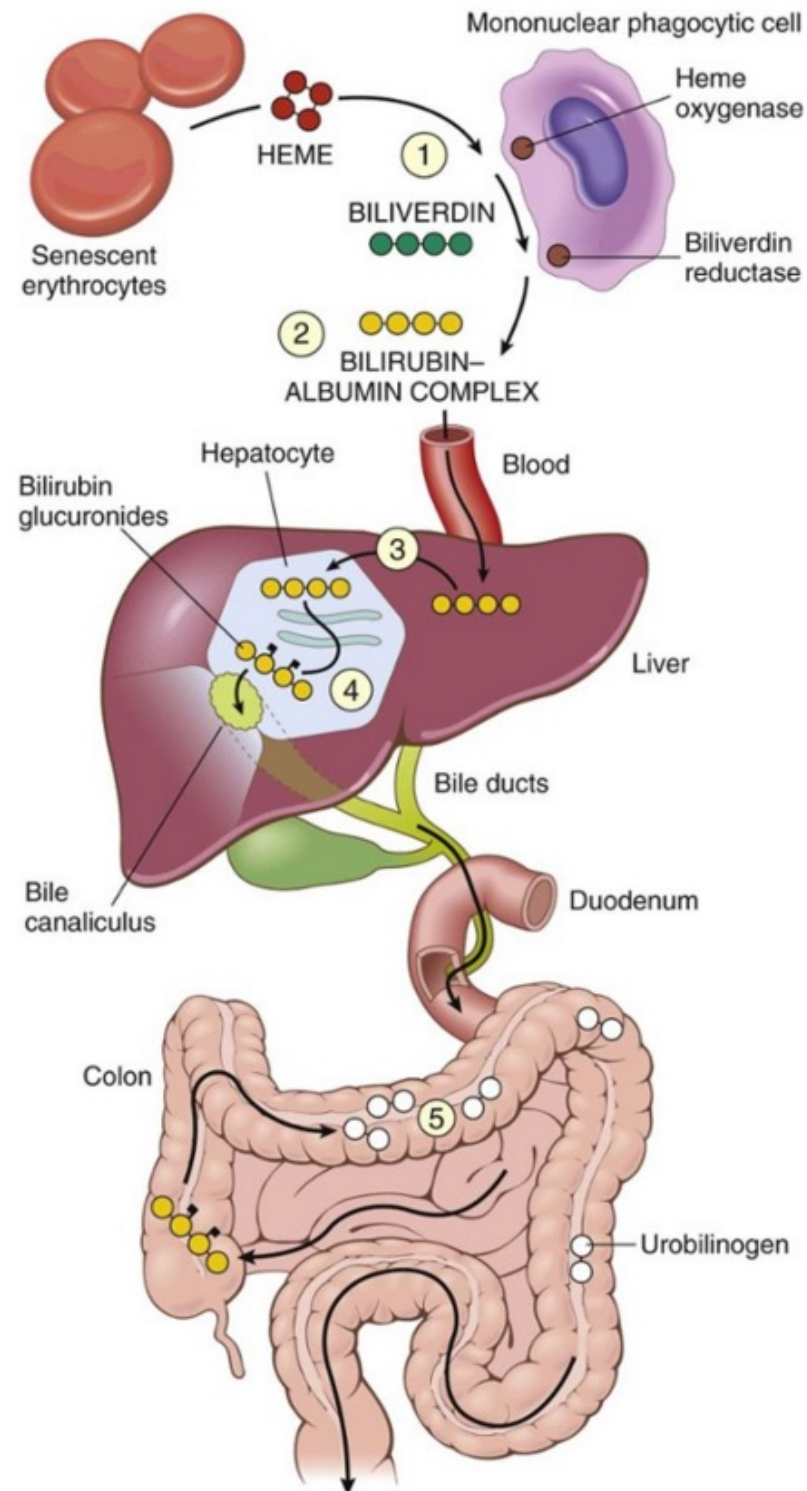


Chronic viral hepatitis



Chronic viral hepatitis: ground-glass hepatocytes

Bilirubin metabolism and elimination



Jaundice

- Yellow discoloration of the skin due to hyperbilirubinemia (excess bilirubin in the blood)
- The amount of bilirubin in the blood depends on the rate of:
 - bilirubin production (from breakdown of red cells)
 - bilirubin uptake by the liver
 - bilirubin conjugation by the liver
 - bilirubin excretion into bile ducts

Hyperbilirubinemia

- Conjugated bilirubin = water-soluble (excreted in urine)
- Unconjugated bilirubin = insoluble (toxic to tissues!)
- Causes of **conjugated** hyperbilirubinemia:
 - blockage in bile flow (e.g., tumor near bile duct)
 - congenital disorders affecting bile excretion
- Causes of **unconjugated** hyperbilirubinemia:
 - excess bilirubin production (e.g., massive hemolysis)
 - impaired bilirubin uptake by liver
 - Impaired bilirubin conjugation



Icterus (only eyes are yellow; may precede jaundice)



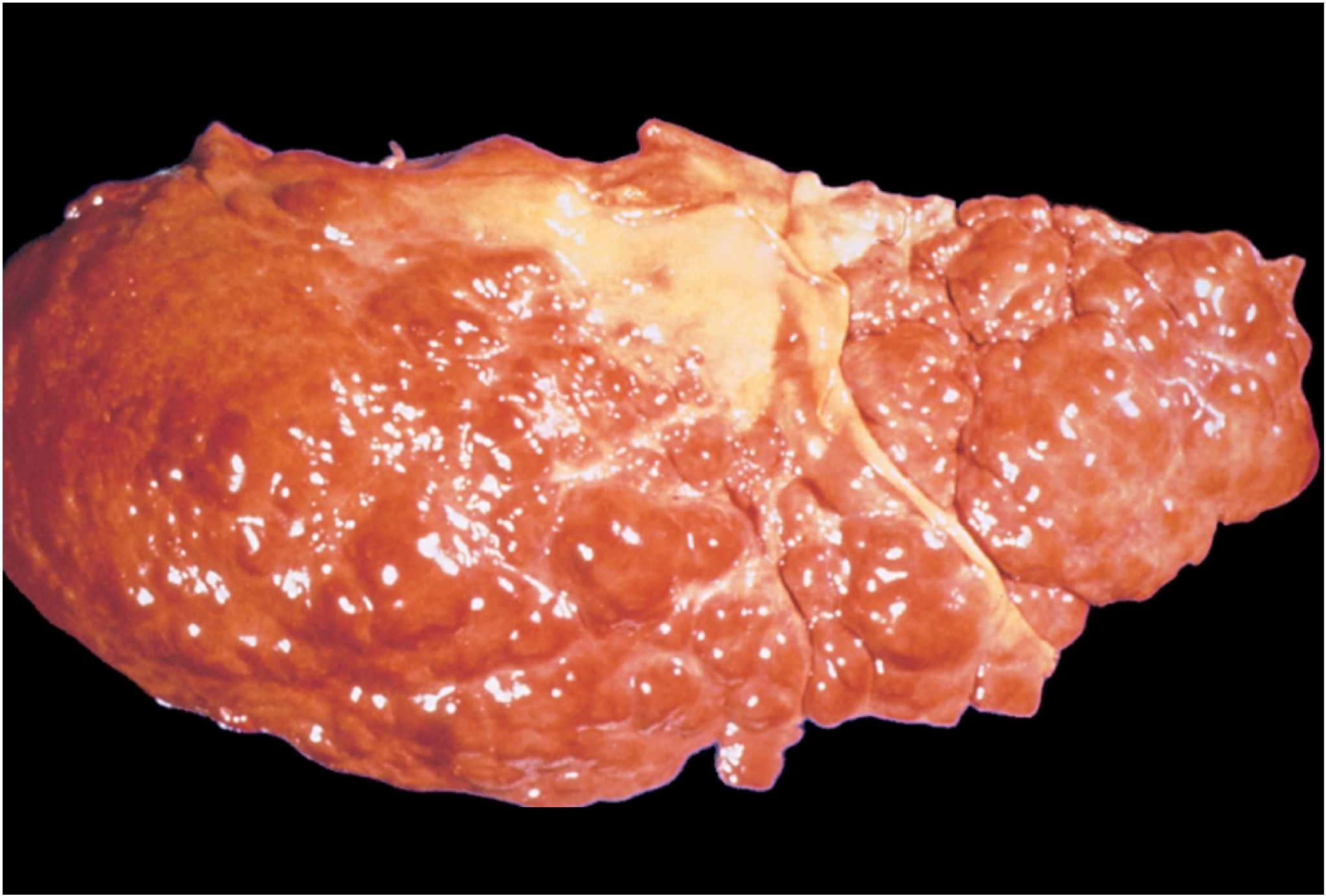
Jaundice (yellow skin, eyes, mucous membranes)

Laboratory Tests

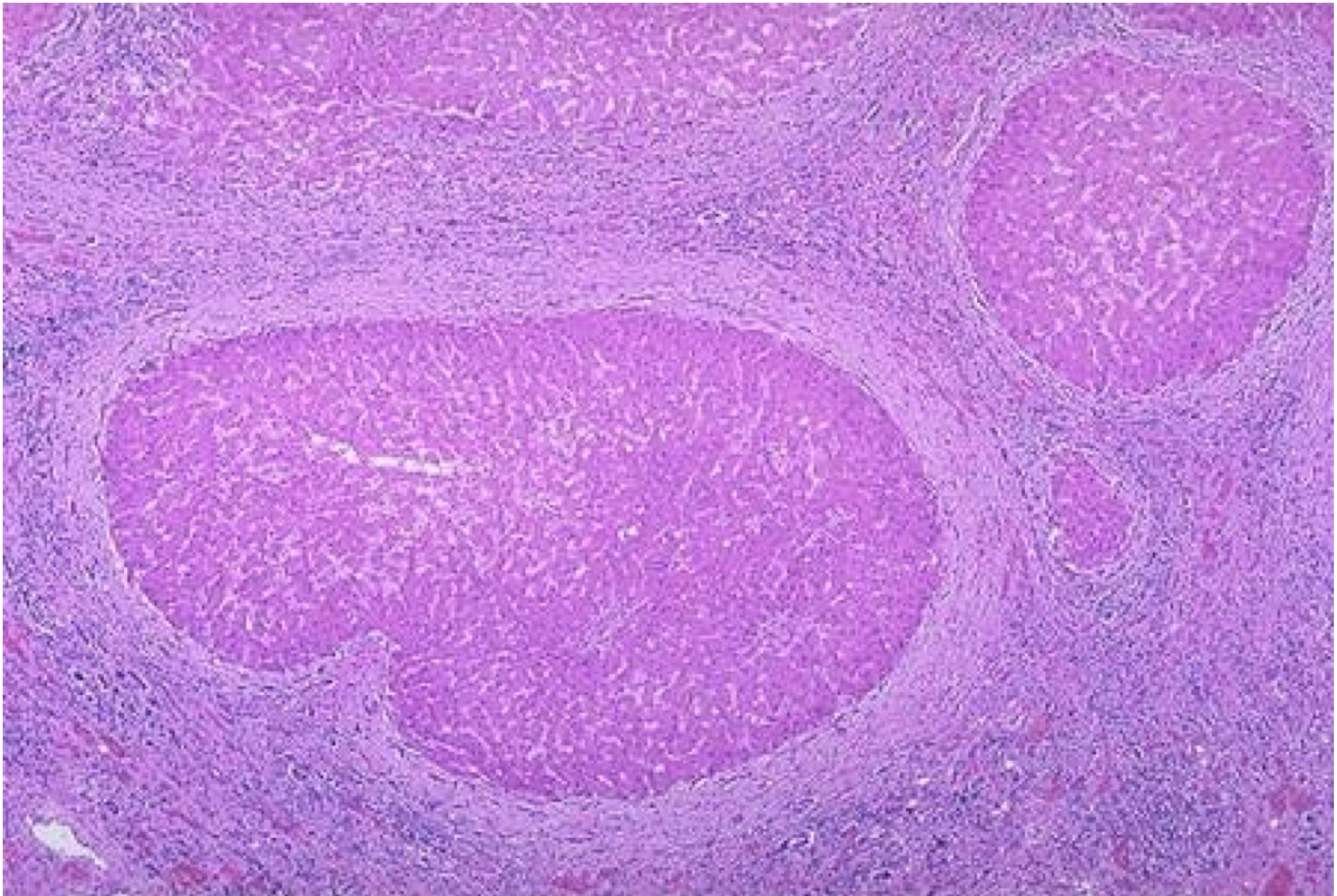
Hepatocyte integrity	Serum aspartate aminotransferase (AST)
	Serum alanine aminotransferase (ALT)
Biliary function	Serum bilirubin (total and direct)
	Serum alkaline phosphatase
Hepatocyte function	Serum albumin
	Prothrombin time

Cirrhosis

- Fibrotic, nodular liver
- Causes: alcoholism, hepatitis
- Leads to portal hypertension and liver failure
- Increased risk of liver carcinoma



Cirrhosis

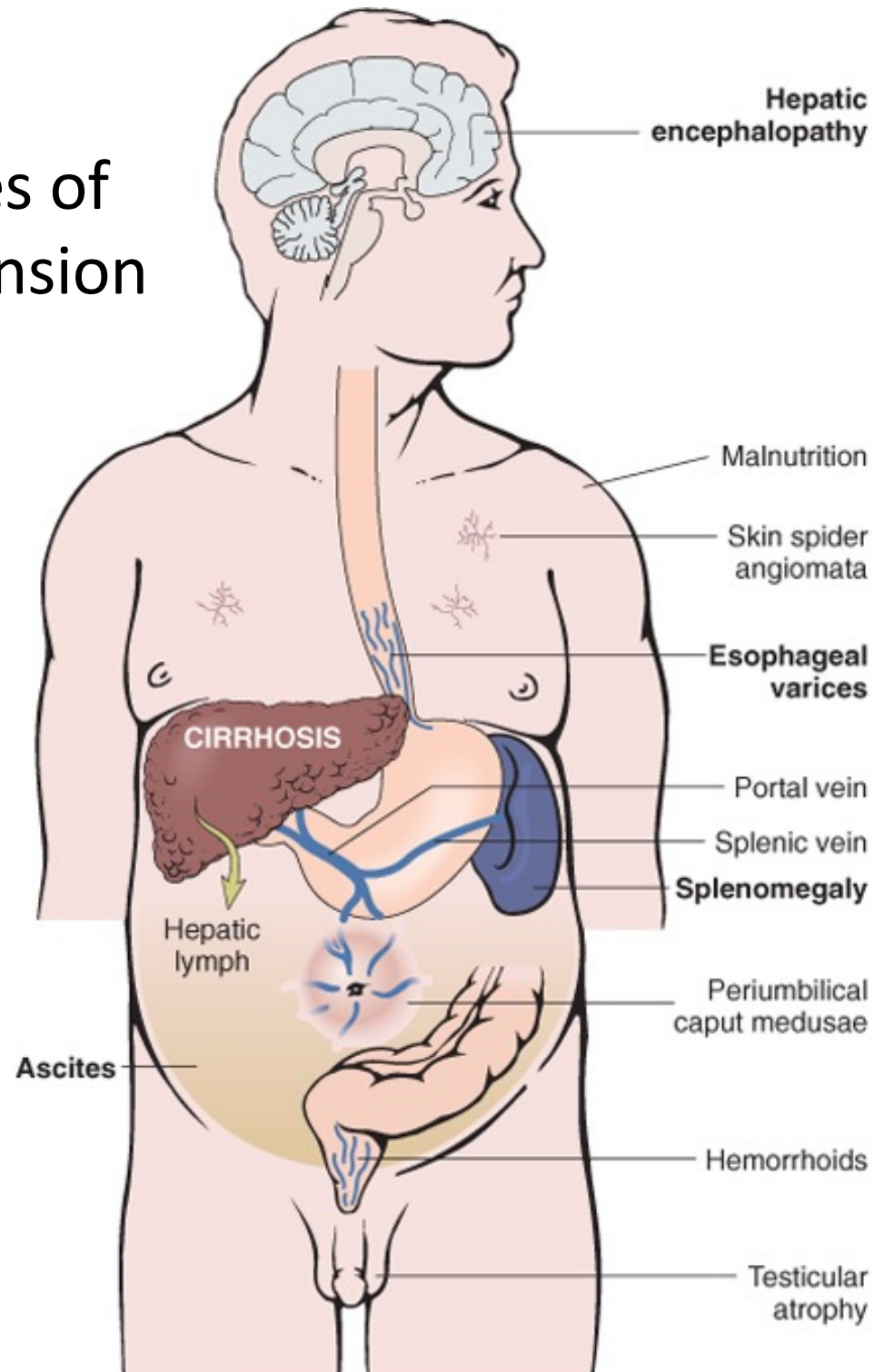


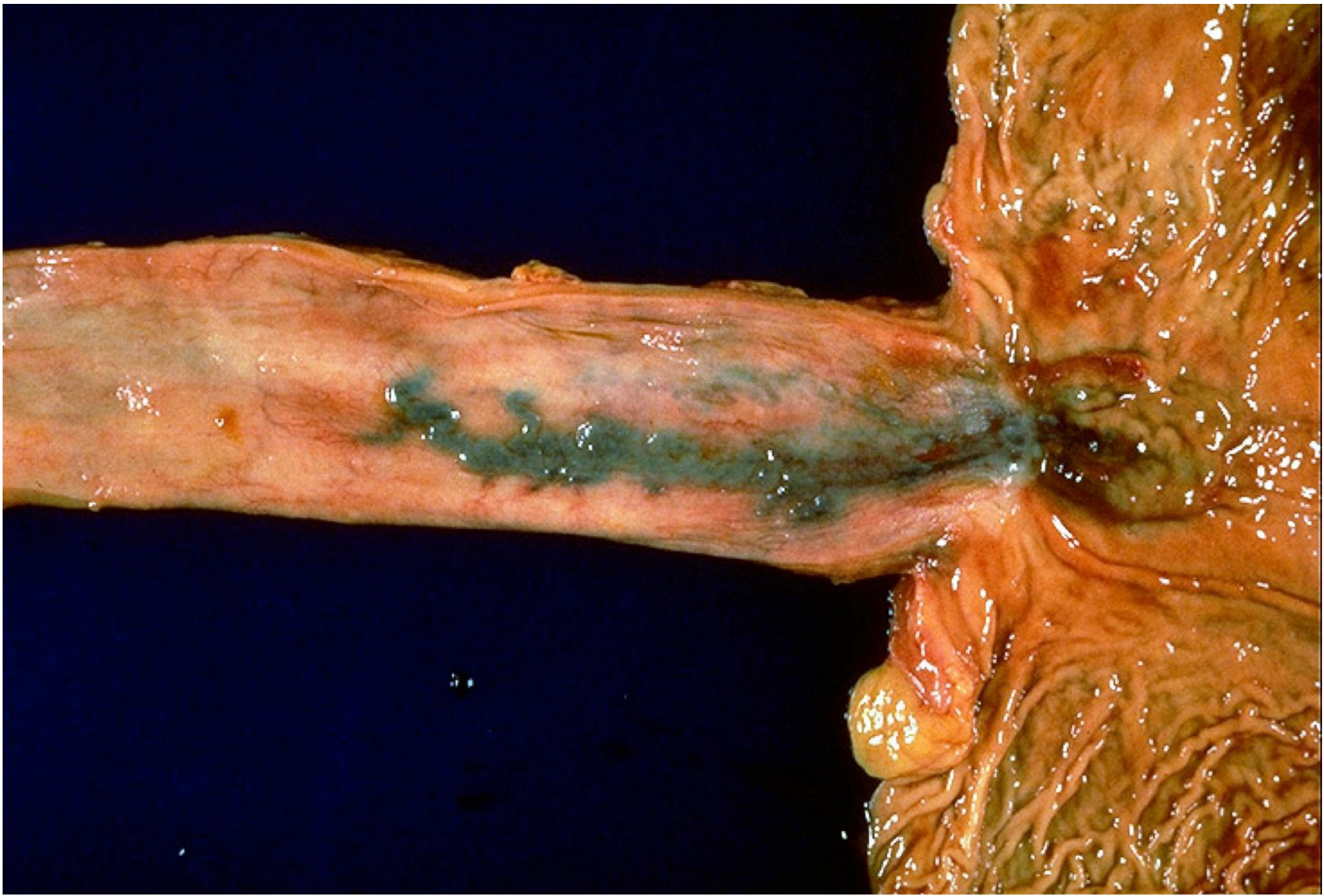
Cirrhosis

Portal Hypertension

- Impaired flow of blood through liver
- Blood backs up in portal system
- Most common cause: cirrhosis
- Four main clinical consequences
 - ascites (↑ fluid in peritoneal cavity)
 - esophageal varices (dilated esophageal veins)
 - congestive splenomegaly
 - hepatic encephalopathy

Consequences of portal hypertension





Esophageal varices



Caput medusae (dilated periumbilical veins)



Medusa

Liver Failure

- End point of severe liver disease
- Causes: fulminant hepatitis, cirrhosis, drug overdose
- Symptoms: jaundice, edema, bleeding, hyperammonemia
- Multiple organ-system failure
 - Hepatic encephalopathy
 - Hepatorenal syndrome

Oral Manifestations of Liver Injury

- Hematomas, gingival bleeding
- Jaundiced mucosa
- Glossitis (in alcoholic hepatitis)
- Reduced healing after surgery

Alcoholic Liver Disease

- 100,000 -200,000 deaths/year
- Effects on liver: steatosis, hepatitis, cirrhosis
- How much do you need to drink?
 - Short-term ingestion of 8 beers/day → reversible steatosis
 - Long-term ingestion of 5 beers/day → severe injury



More youth with irreversible liver disease now

Alcoholics Anonymous most effective path to alcohol abstinence

A Stanford researcher and two collaborators conducted an extensive review of Alcoholics Anonymous studies and found that the fellowship helps more people achieve sobriety than therapy does.

March 11, 2020 - By Mandy Erickson

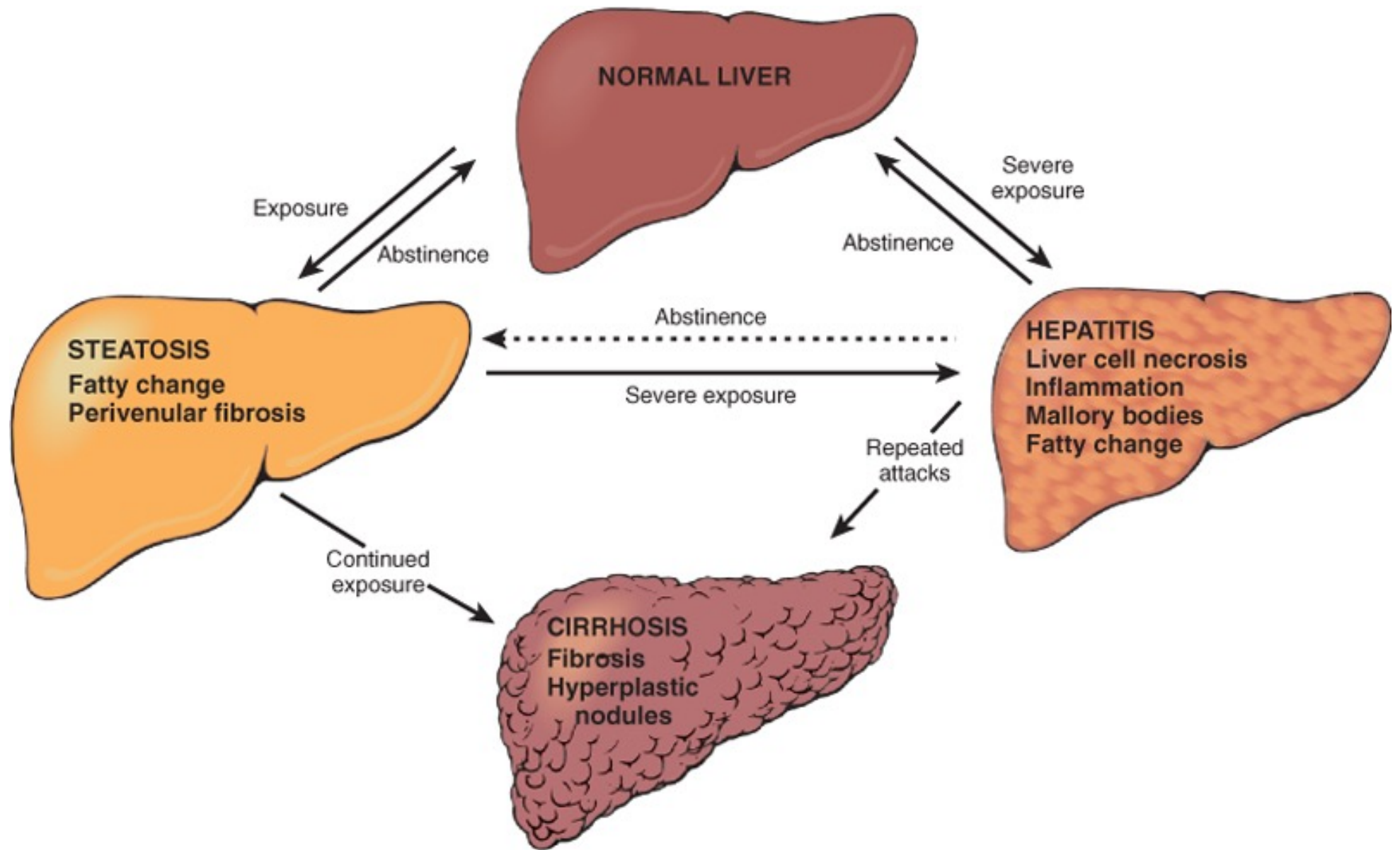
Alcoholics Anonymous, the worldwide fellowship of sobriety seekers, is the most effective path to abstinence, according to a comprehensive analysis conducted by a [Stanford School of Medicine](#) researcher and his collaborators.

After evaluating 35 studies — involving the work of 145 scientists and the outcomes of 10,080 participants — [Keith Humphreys](#), PhD, professor of psychiatry and behavioral sciences, and his fellow investigators determined that AA was nearly always found to be more effective than psychotherapy in achieving abstinence. In addition, most studies showed that AA participation lowered health care costs.

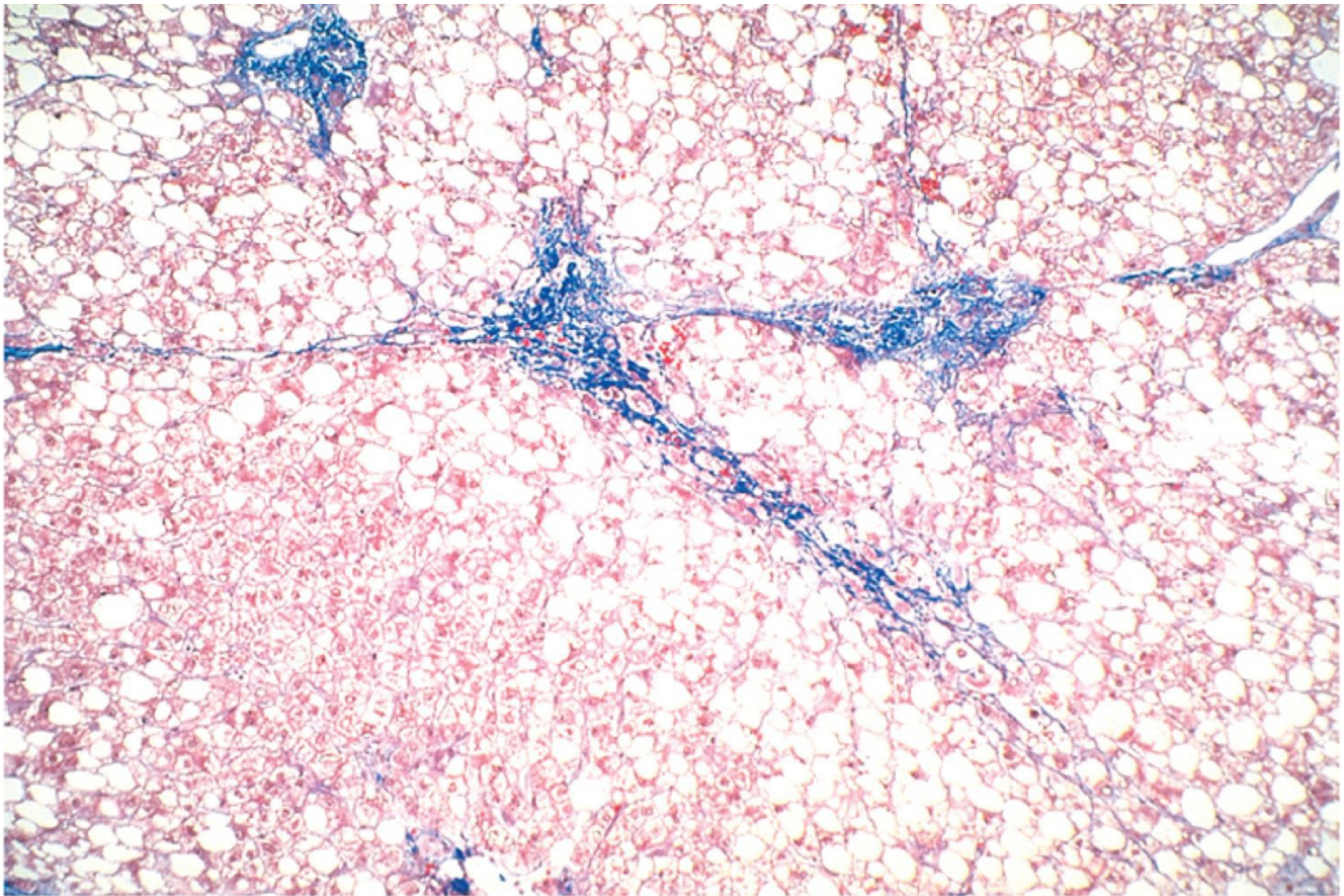
AA works because it's based on social interaction, Humphreys said, noting that members give one another emotional support as well as practical tips to refrain from drinking. "If you want to change your behavior, find some other people who are trying to make the same change," he said.



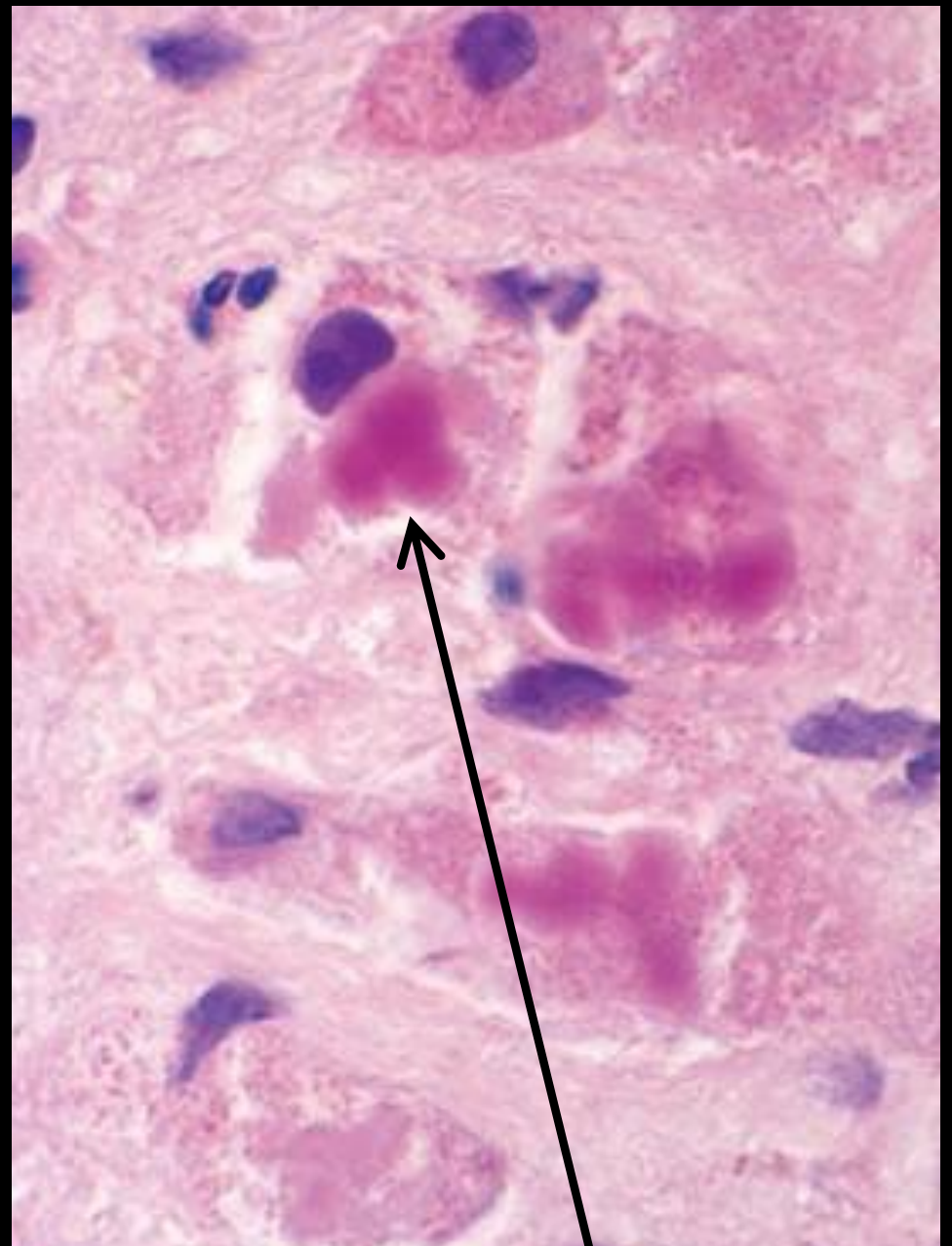
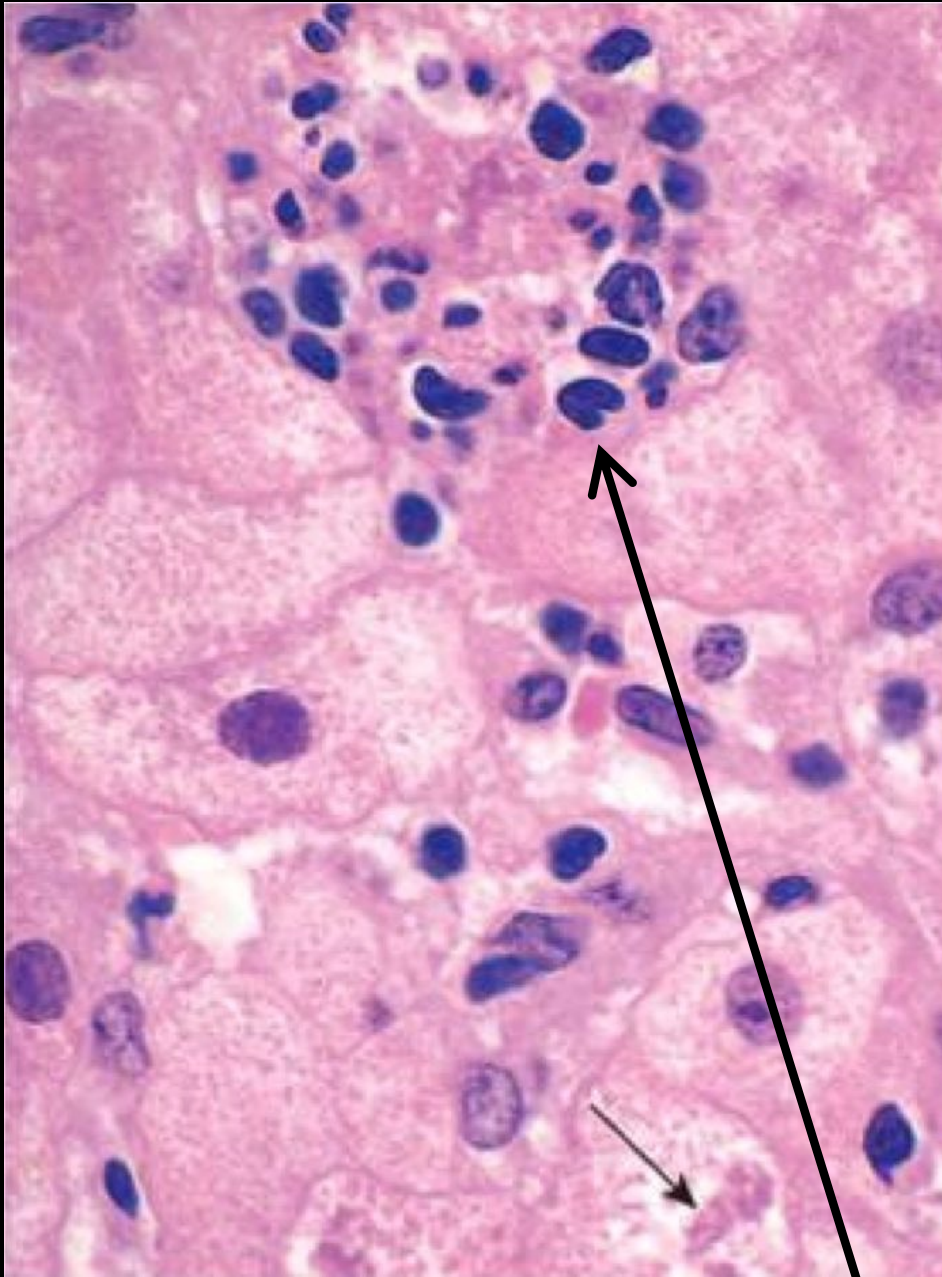
The Alcoholics Anonymous model — open to all and free — has spread around the globe, and AA now boasts over 2 million members in 180 nations and more than 118,000 groups.
Africa Studio



Alcoholic liver disease



Alcoholic steatosis



Alcoholic hepatitis: inflammation and Mallory bodies

Alcoholic Liver Disease

- Abstinence: 5ys is 90%
- Continued drinking: 5ys drops to 50-60%
- Causes of death in end-stage alcoholism:
 - Liver failure
 - Massive GI bleed
 - Infection
 - Hepatorenal syndrome
 - Hepatocellular carcinoma

Hereditary Hemochromatosis

- Autosomal recessive disease: ↑ body iron
- Cause: mutations in hemochromatosis gene (regulates iron absorption)
- Cirrhosis, skin discoloration, liver carcinoma
- Early detection and treatment (phlebotomy, iron chelators) = normal life expectancy



Grey-brown skin discoloration in hemochromatosis

Wilson Disease

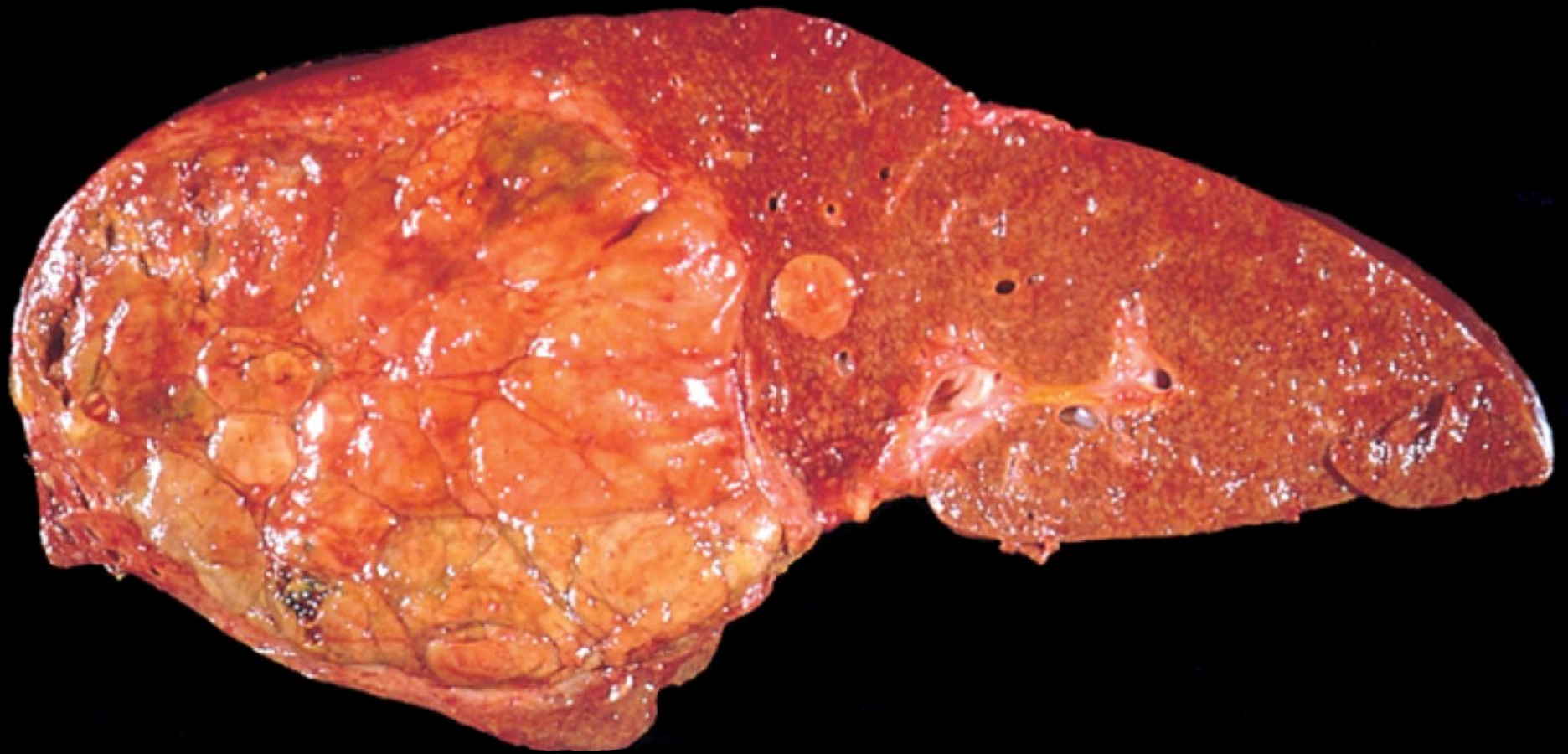
- Autosomal recessive disease: ↑ body copper
- Cause: mutation in gene regulating copper excretion
- Symptoms: acute and chronic liver disease, neuropsychiatric manifestations, Kayser-Fleisher rings in cornea
- Treatment: copper chelation therapy



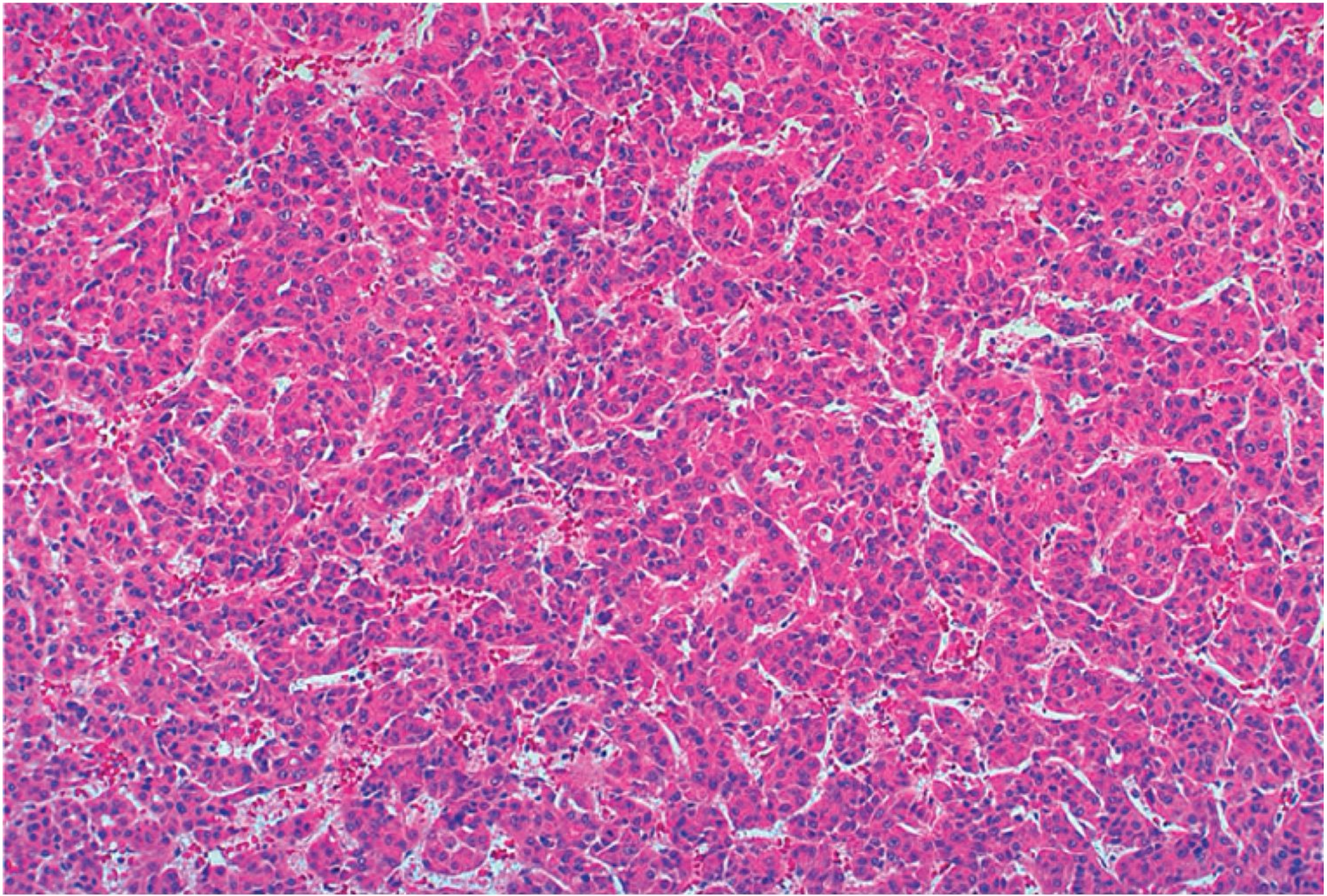
Kayser-Fleischer Rings

Hepatocellular Carcinoma

- Strongly associated with hepatitis B and C, chronic liver disease, and aflatoxins
- Rapid increase in liver size, worsening ascites, fever and pain
- ↑↑↑ alpha fetoprotein level
- Median survival 7 months (death from bleeding, liver failure, cachexia)



Hepatocellular carcinoma



Hepatocellular carcinoma

Metastatic Carcinoma

- Most common malignancy in the liver
- Usually multiple lesions
- Most common primaries: colon, lung, breast, pancreas, stomach.



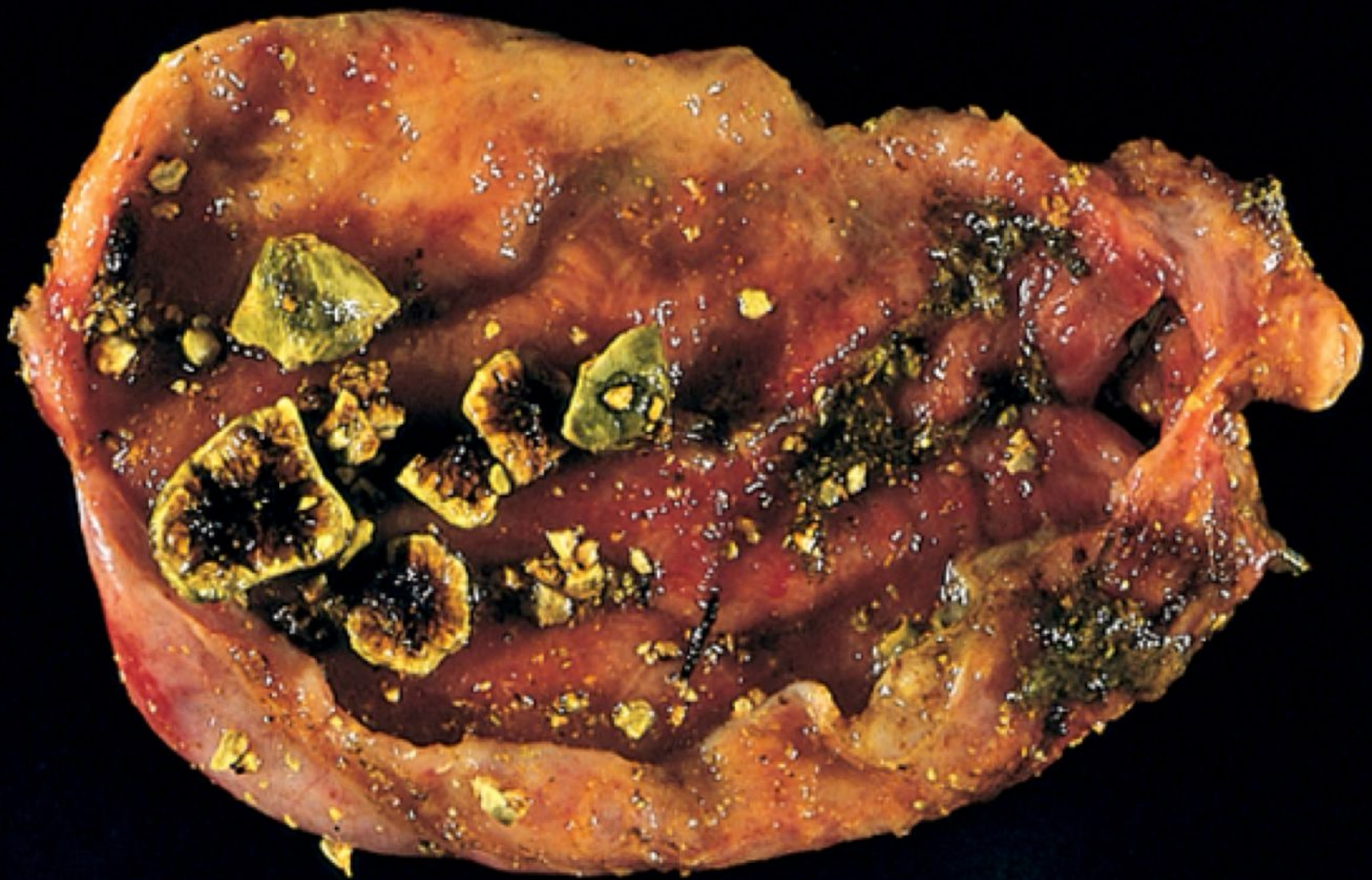
Metastatic carcinoma

GI Pathology Outline

- Esophagus
- Stomach
- Intestine
- Liver
- Gallbladder
 - Cholelithiasis
 - Cholecystitis

Cholelithiasis

- Common! (10% of adults in US)
- Cholesterol stones: Female, Fat, Fertile, Forty
- Pigment (bilirubin) stones: Asian countries, hemolytic anemia and biliary infections
- Symptoms: None, or excruciating pain
- Complications: cholecystitis (inflamed gallbladder), perforation, obstruction, pancreatitis



Cholesterol gallstones



Pigmented gallstones

GI Pathology Outline

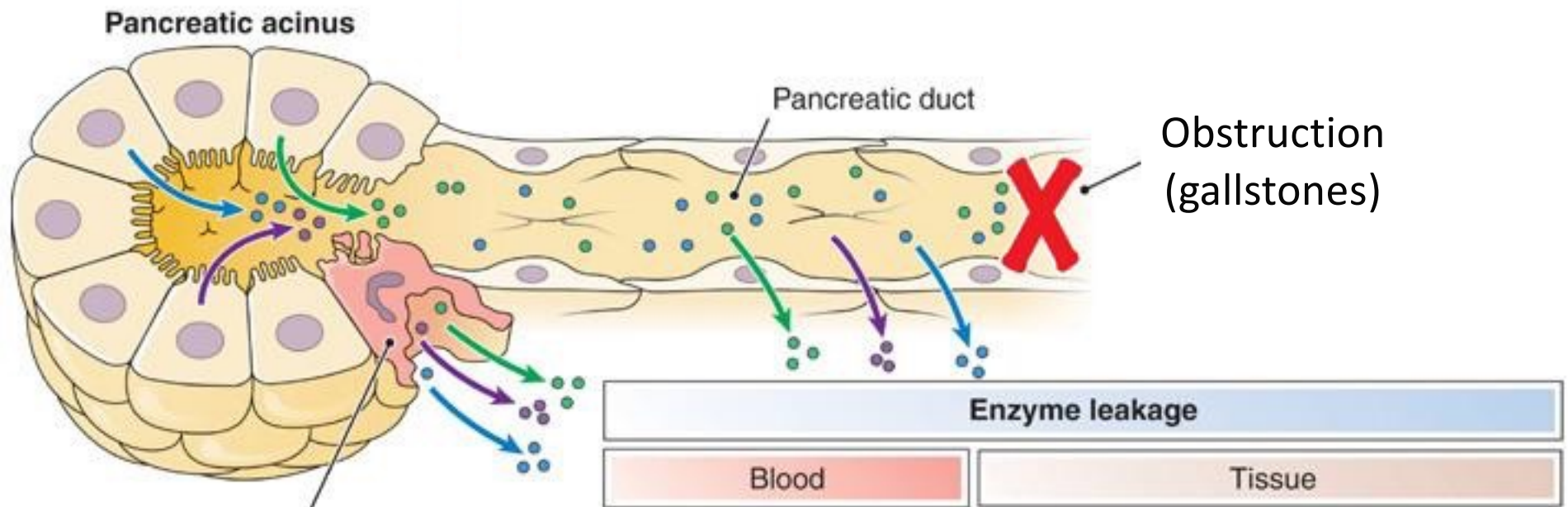
- Esophagus
- Stomach
- Intestine
- Liver
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- Pancreas
 - Pancreatitis
 - Carcinoma

Normal Pancreas

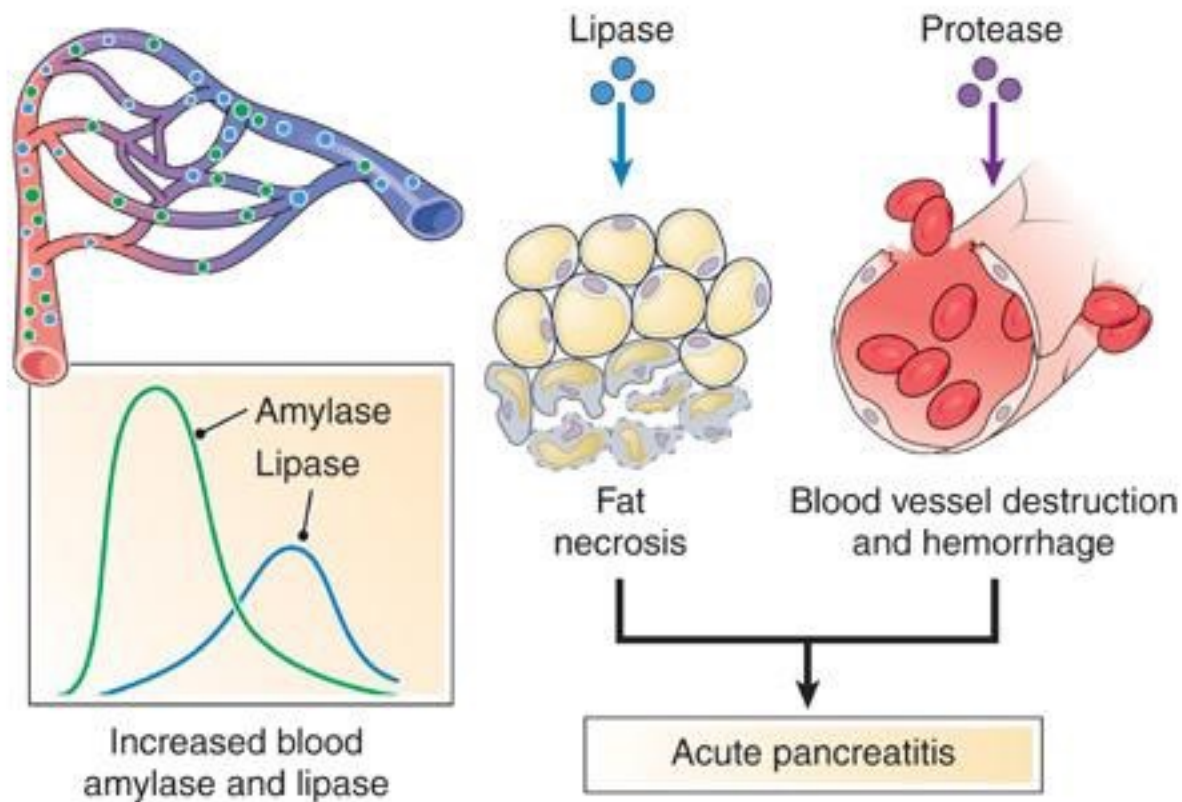
- Exocrine pancreas
 - Makes enzymes for digestion
 - Diseases: pancreatitis, cystic fibrosis, tumors
- Endocrine pancreas
 - Makes insulin, glucagon, other hormones
 - Diseases: diabetes, tumors

Acute Pancreatitis

- Acute inflammation and reversible destruction of pancreas
- Symptoms: abdominal pain radiating to back
- Main causes: alcoholism, gallstones
- Labs: elevated serum amylase and lipase
- Prognosis: Most recover, but 5% die in first week



Cell injury (alcohol)

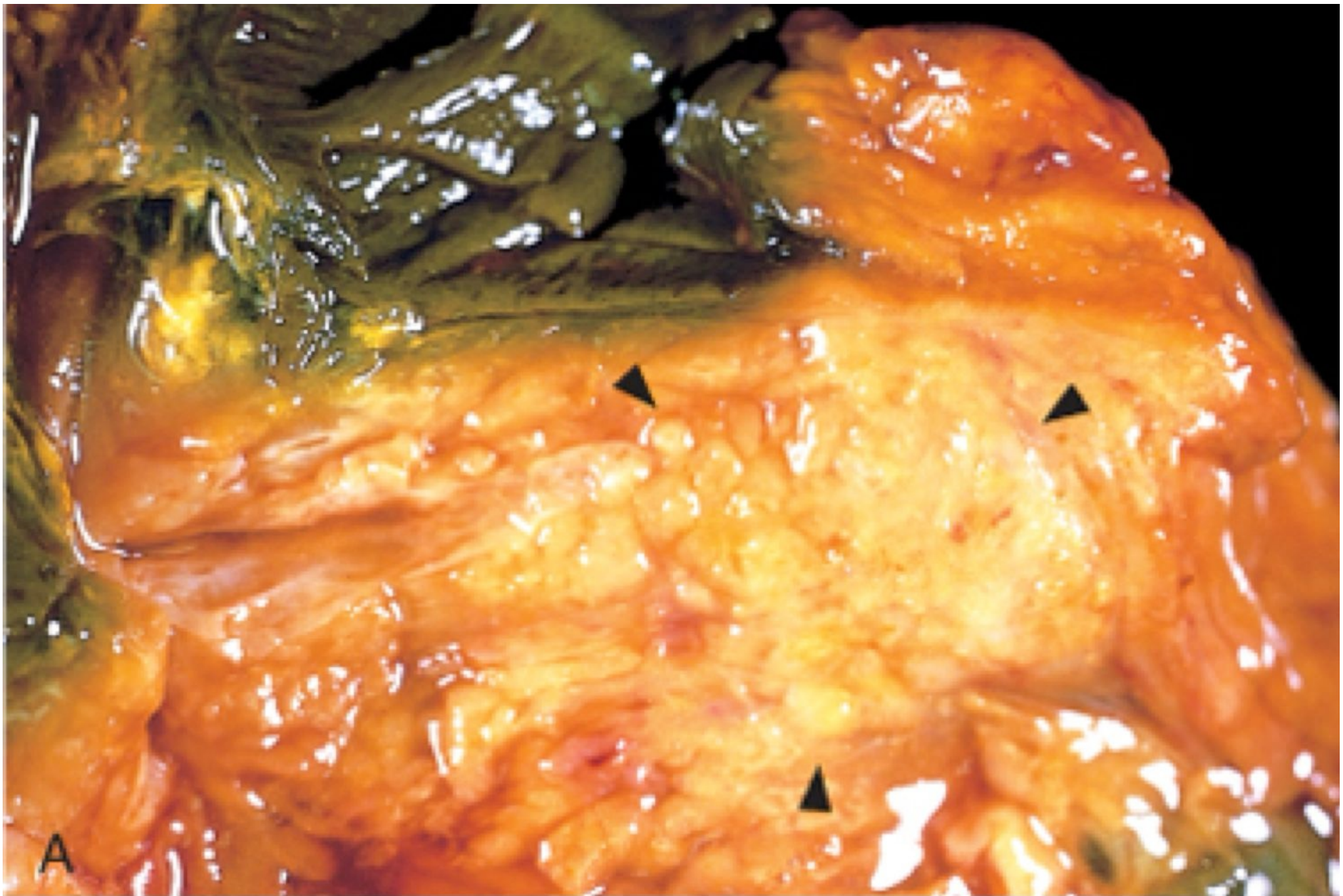


Chronic Pancreatitis

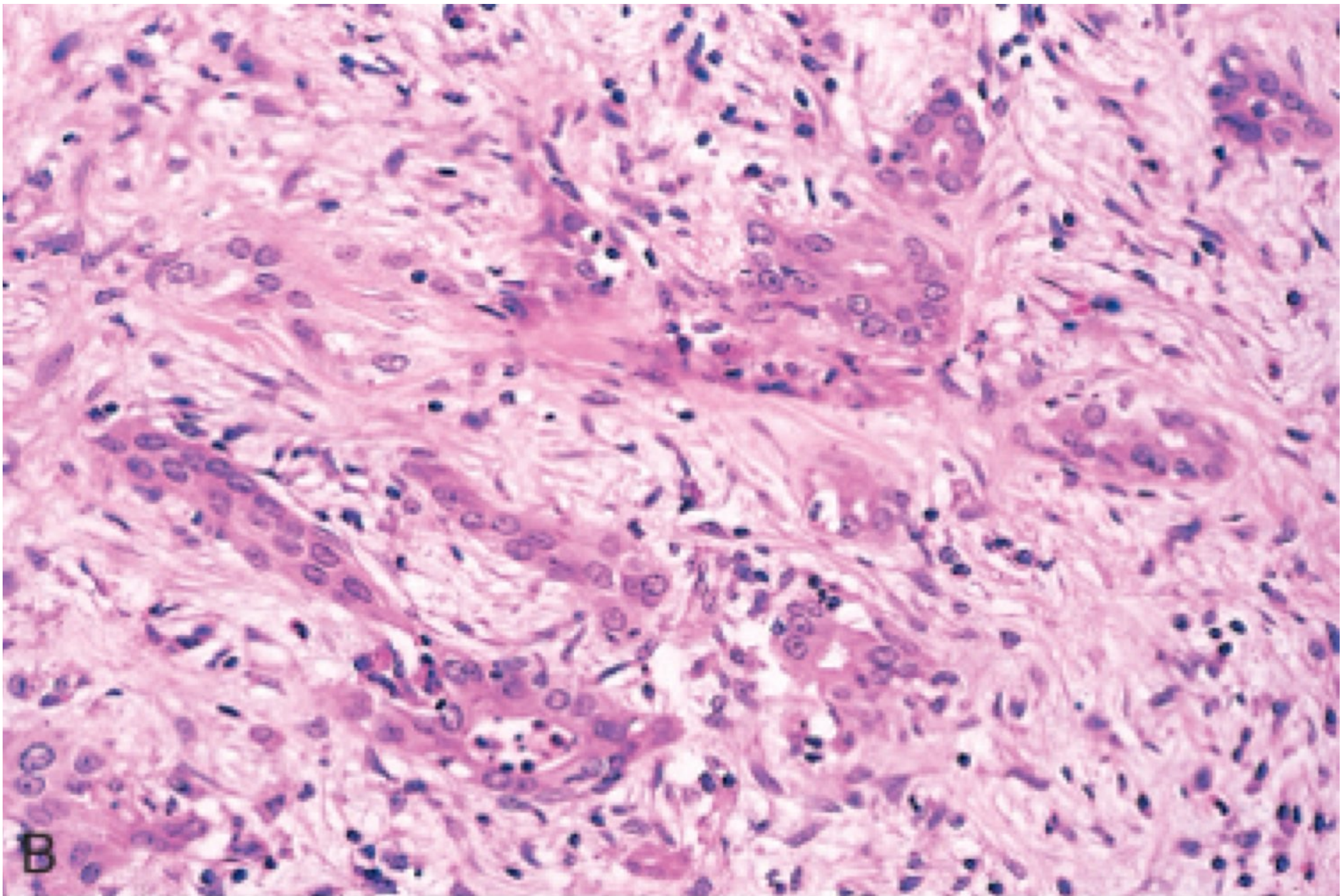
- Longstanding, irreversible pancreatic destruction
- Most are alcohol related, some idiopathic
- Symptoms: silent, or bouts of jaundice and pain
- Prognosis: poor (50% mortality over 20 years)

Pancreatic Carcinoma

- 4th leading cause of cancer death in US
- Biggest risk factor: smoking
- Highly invasive
- Silent until late; then pain, jaundice
- Very high mortality: 5ys <5%



Pancreatic carcinoma



Pancreatic carcinoma