

TUMORS OF THE LIVER

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N.B: RED !! → Important Point

STAR !! → Important Slide

BENIGN NEOPLASMS

1. Hemangioma
2. Hepatic (liver cell) Adenoma
3. Bile duct Adenoma

1- HEMANGIOMA

A benign tumor to the Blood Vessels in the Liver but
NOT TO LIVER TISSUE

- **The most common benign lesions:**

- ***Cavernous Hemangiomas***

blood vessel tumors identical to those occurring elsewhere

Appearance: discrete red-blue, soft nodules,
usually less than 2 cm in diameter, and often occur
directly beneath the capsule.

-Remember: Liver is a very common site of metastasis

-Cavernous hemangiomas: is a vascular disorder of the central nervous system

2- Liver cell adenomas

- If a **benign neoplasm** developed from **hepatocytes**, it is called: *liver cell adenoma*.
- These tend to occur in young women who have used oral contraceptives ((irreversible by stopping the use)).





2- Liver cell adenomas

Liver cell adenomas have clinical significance for three reasons:

1. When they present as an **intrahepatic mass**, they may be **mistaken for** the more malignant **hepatocellular carcinoma**.
2. **Subcapsular adenomas** have a tendency to **rupture**, particularly **during pregnancy** (under estrogen stimulation), causing severe intraperitoneal hemorrhage.
3. Rarely, they may **harbor hepatocellular carcinoma**

2- Liver cell adenomas: Morphology.

- **nodules (GROSS):**
are pale, yellow-tan **well demarcated**,
found anywhere in the hepatic substance but often
beneath the capsule.
- **On microscopic examination**
 - **liver cell adenomas** are composed of
sheets and cords of cells that may resemble
normal hepatocytes.
 - **Portal tracts are absent** (MOST IMPORTANT FEATURE);
instead, **prominent arterial vessels and draining**
veins are distributed through the substance of
the tumor.

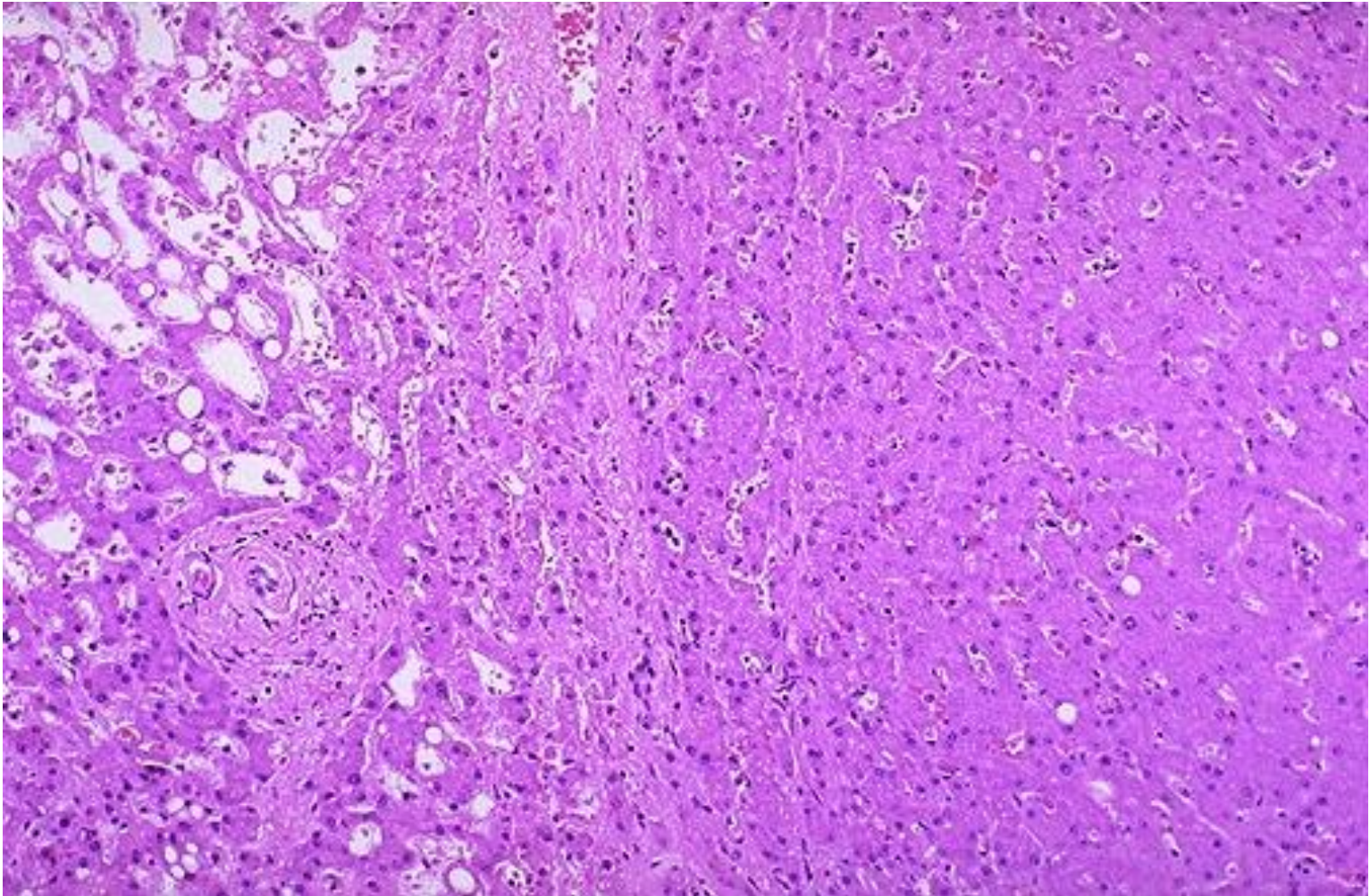
A well-circumscribed neoplasm that is arising in liver.
((hepatic adenoma))



The cut surface of the liver reveals the hepatic adenoma. Note how well circumscribed it is.



Normal liver with portal tract (left). Hepatic adenoma seen on right is made of cells that resemble normal hepatocytes, **but tissue is disorganized and does not show normal lobular architecture**



3- BILE DUCT ADENOMA

cholangiocarcinomas >>> malignant
Bile duct adenoma >>> benign

- GROSS:
small encapsulated spherical, yellow white nodules
(many small tumors appearing together)
- Microscopically:
multiple small acini lined by epithelium similar to that present in small bile ducts is seen and are surrounded by fibrous stroma.
- Unlike liver adenomas, these are more frequent in males.

لأنها أورام صغيرة ومنتشرة دائما يخلط بينها وبين
Metastasis cancers

MALIGNANT TUMORS

1. Hepatocellular Carcinomas
 - Fibrolamellar Carcinoma -
2. Cholangiocarcinoma
3. Metastatic Tumors

MALIGNANT TUMORS

- Metastatic Tumors

The **liver** and **lungs** are the visceral organs that are most often involved by **metastasis**.

(most liver's tumors are metastatic)

- Primary carcinomas :

Are relatively uncommon.

-Most arise from hepatocytes →

termed ***hepatocellular carcinoma (HCC)***.

- Much less common are carcinomas originated from bile duct →
termed ***cholangiocarcinomas***.

There are two rare forms of primary liver cancer :

- Hepatoblastomas (most common in babies/children)

- Angiosarcomas (in elderly).

((will speak about each seperately))





1- Hepatocellular Carcinomas (HCC)

- male predominance
- *More than 85% of cases of HCC occur in countries with high rates of chronic HBV infection.* In these regions, the HBV carrier state begins in infancy following vertical transmission of virus from infected mothers, conferring a 200-fold increased risk for HCC by adulthood
- In the Western world where HBV is not prevalent, cirrhosis is present in 85% to 90% of cases of HCC, usually in the setting of other chronic liver diseases;

Remember: HCC is one of the complications of liver cirrhosis

Pathogenesis of HCC

The following have been implicated in human hepatocarcinogenesis:

- 1) viral infection (**HBV, HCV**):
Extensive studies link chronic HBV and chronic HCV infection with liver cancer.
- 2) **Cirrhosis**:
the development of cirrhosis appears to be an important, but not necessarily a contributor to the emergence of HCC.
- 3) **Chronic alcoholism**.

Pathogenesis of HCC

The doctor said it's not an important slide



- 4) Food contaminants (primarily aflatoxins from aspergillus). High exposure to dietary aflatoxins derived from the fungus *Aspergillus flavus*. These highly carcinogenic toxins are found in "moldy" grains and peanuts.
- 5) Other conditions include tyrosinemia and hereditary hemochromatosis.

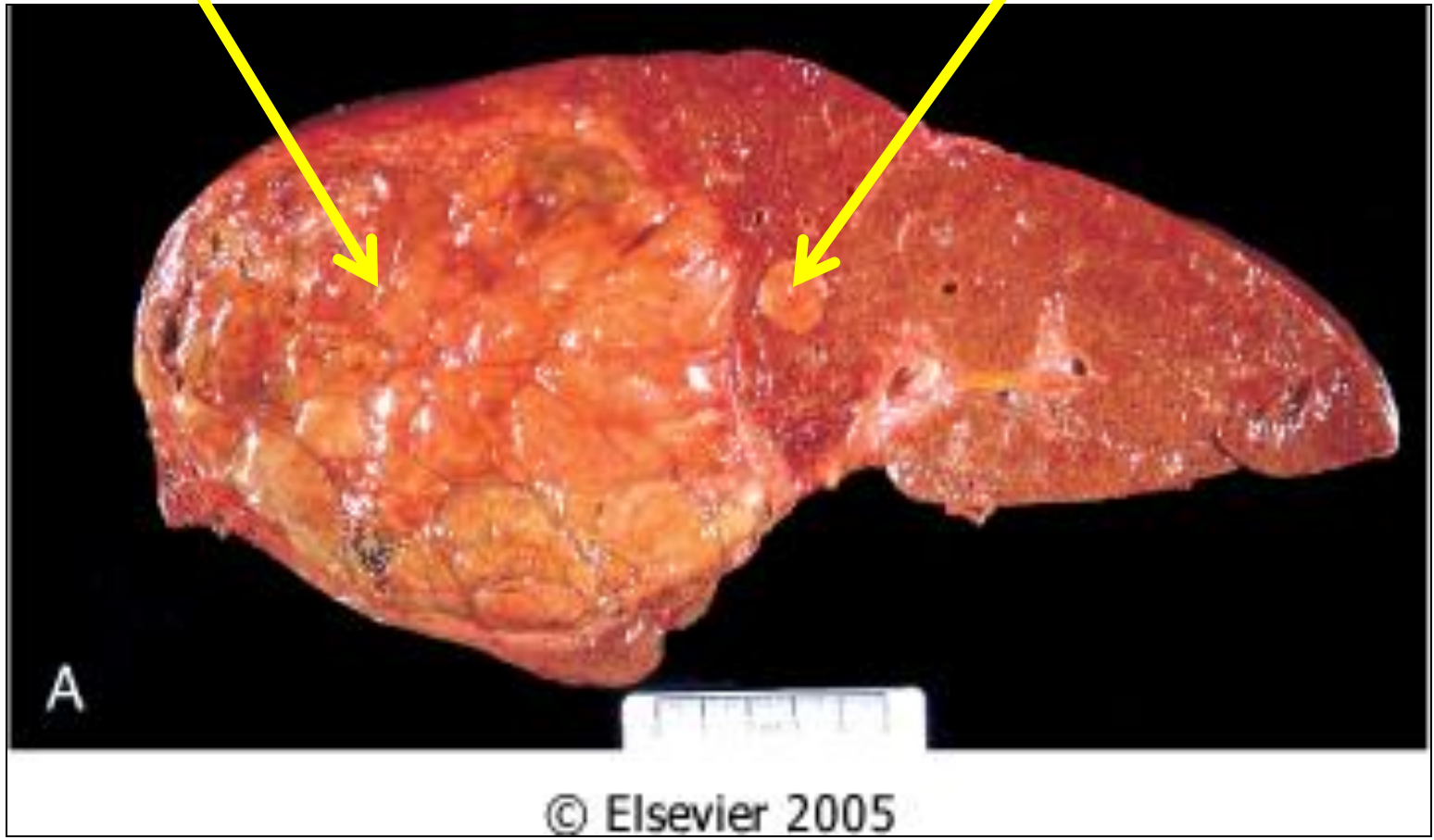


Morphology of HCC

- **GROSS:** either
 - (1) a **unifocal** mass
 - (2) **multifocal**, multiple nodules of variable size
 - or (3) a **diffusely infiltrative** cancer.
- All three patterns may cause liver enlargement.
All patterns of hepatocellular carcinomas have a strong propensity for invasion of vascular channels >> metastasis

HCC, unifocal, massive type

Satellite tumor nodule



Morphology of HCC

- Extensive intrahepatic metastases may occur
- tumor may invade the portal vein (with occlusion of the portal circulation) or inferior vena cava, extending even into the right side of the heart.
- **Lymph node metastases** to the perihilar, peripancreatic, and para-aortic nodes above and below the diaphragm can be present.
- **Hepatocellular carcinomas range from well-differentiated to highly anaplastic undifferentiated lesions.**

Morphology of HCC

- **In well-differentiated and moderately well-differentiated tumors**, cells that are recognizable as hepatocytic in origin.
Bile pigment is usually present (>> not metastasis).

The malignant cells may be
positive for alpha-fetoprotein
(tumor marker of HCC, present normally in a child)

- **In poorly differentiated forms**, tumor cells can take on a *pleomorphic appearance* with numerous *anaplastic giant cells*, can become small and completely undifferentiated cells.



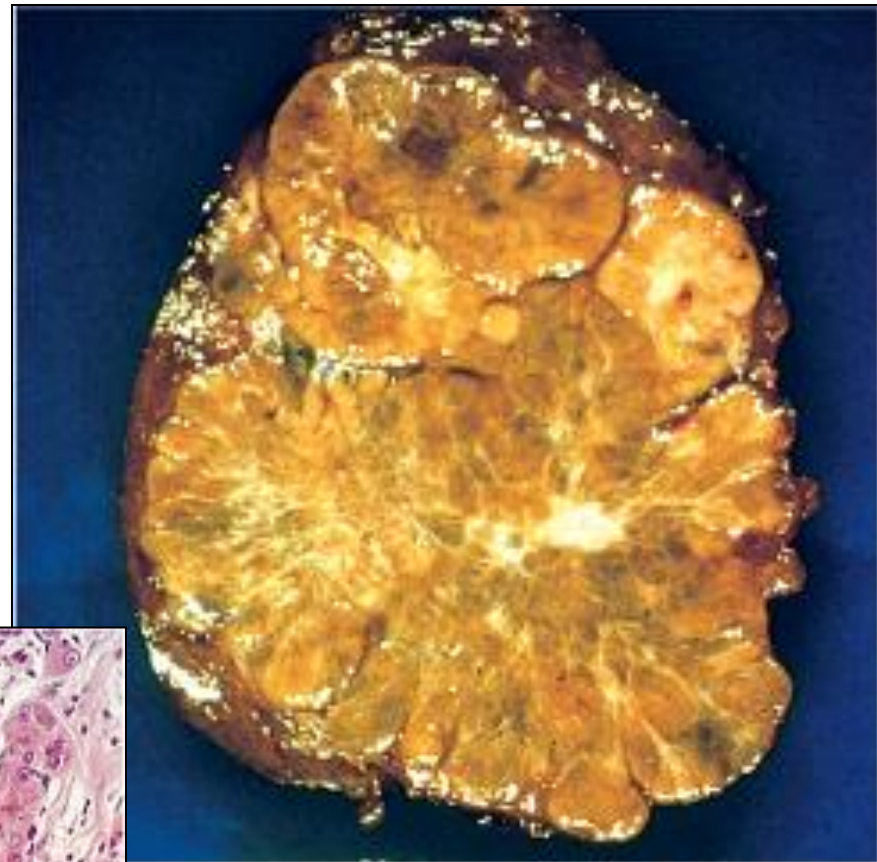
A famous type of HCC: Fibrolamellar Carcinoma

- A distinctive variant of hepatocellular carcinoma is the **fibrolamellar carcinoma**.
- **This tumor occurs in young male and female adults (20 to 40 years of age)**
has NO association with HBV or cirrhosis, and often has a better prognosis.
- **GROSSLY:**
It usually presents as single large, hard "scirrhous" tumor with **fibrous bands** coursing through it.
On microscopic examination,
it is composed of well-differentiated polygonal cells growing in nests or cords and **separated by parallel lamellae of dense collagen bundles**

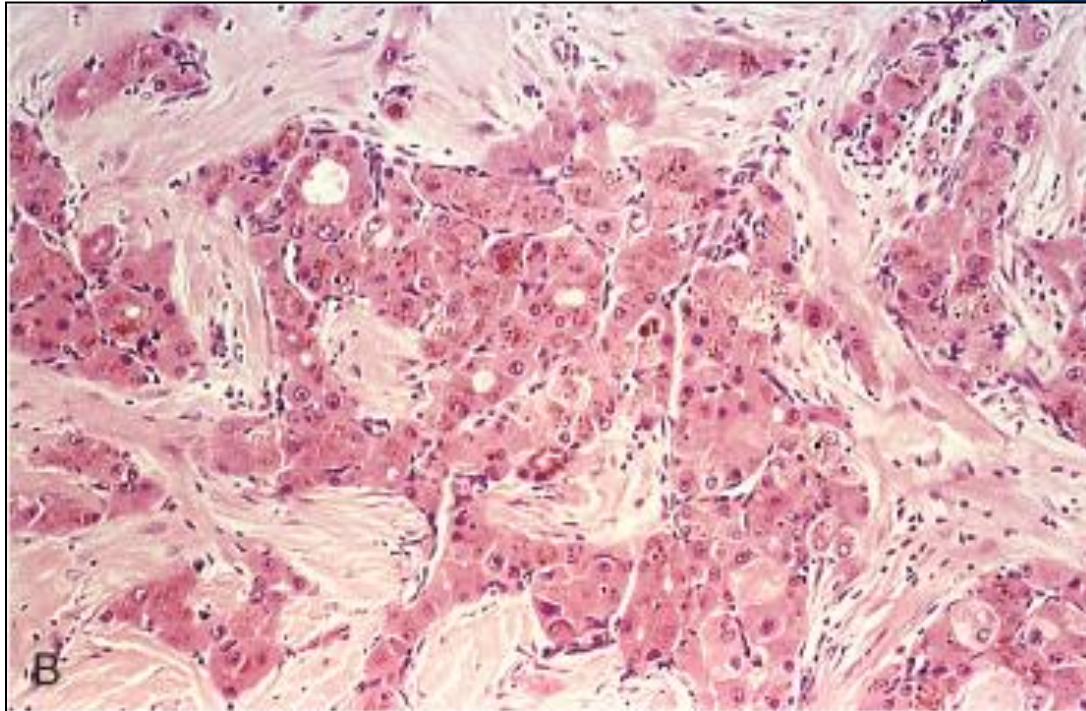
fibrolamellar carcinoma

Remember:

has no association with
cirrhosis or other risk
factors such as HBV



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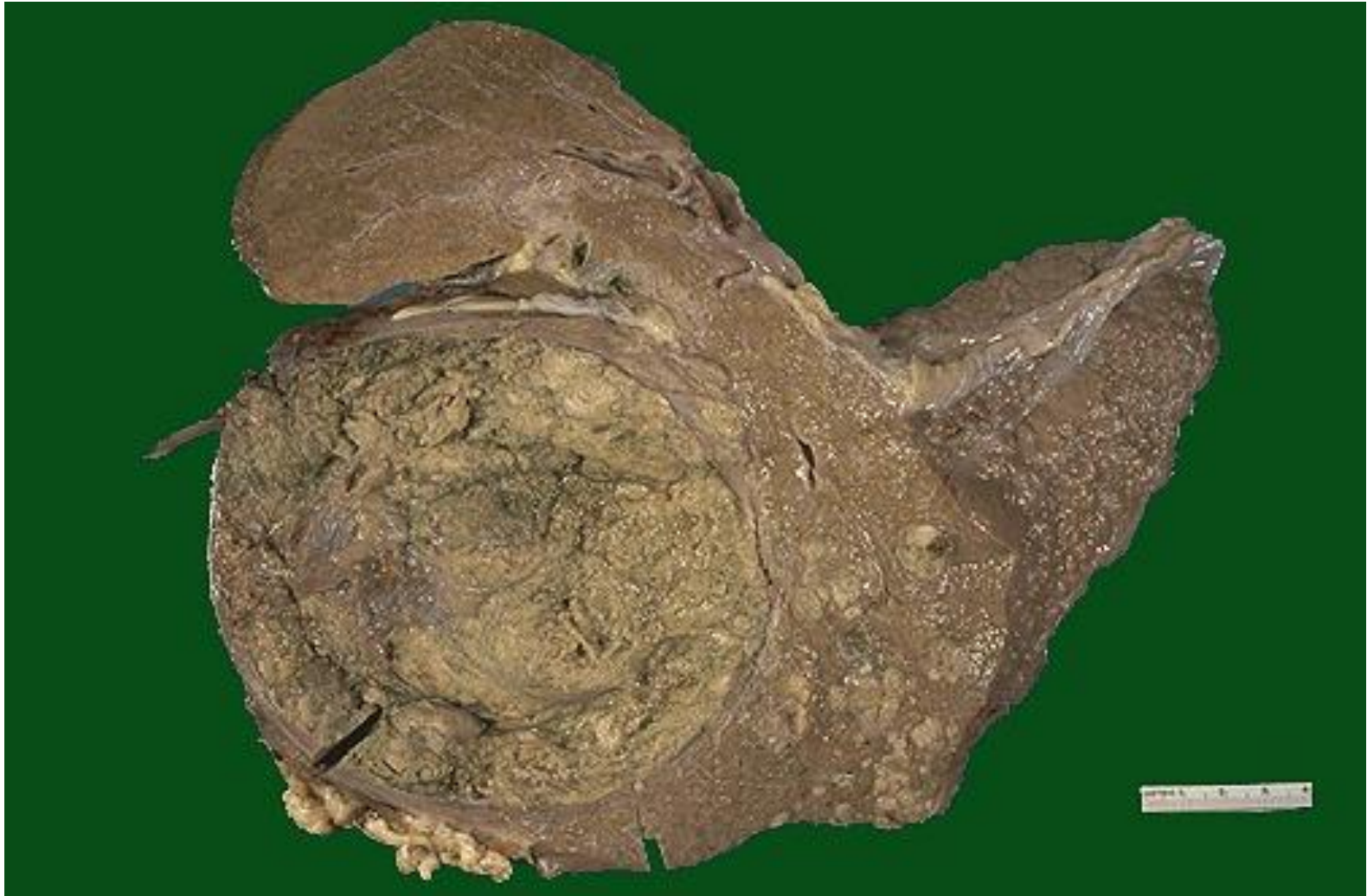


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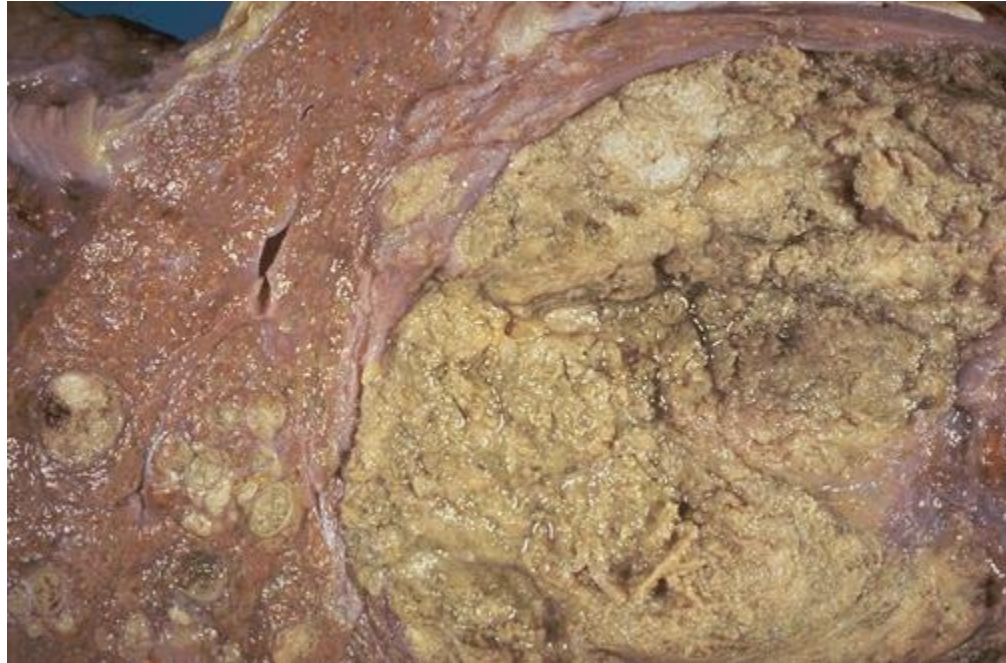
Hepatocellular carcinoma.

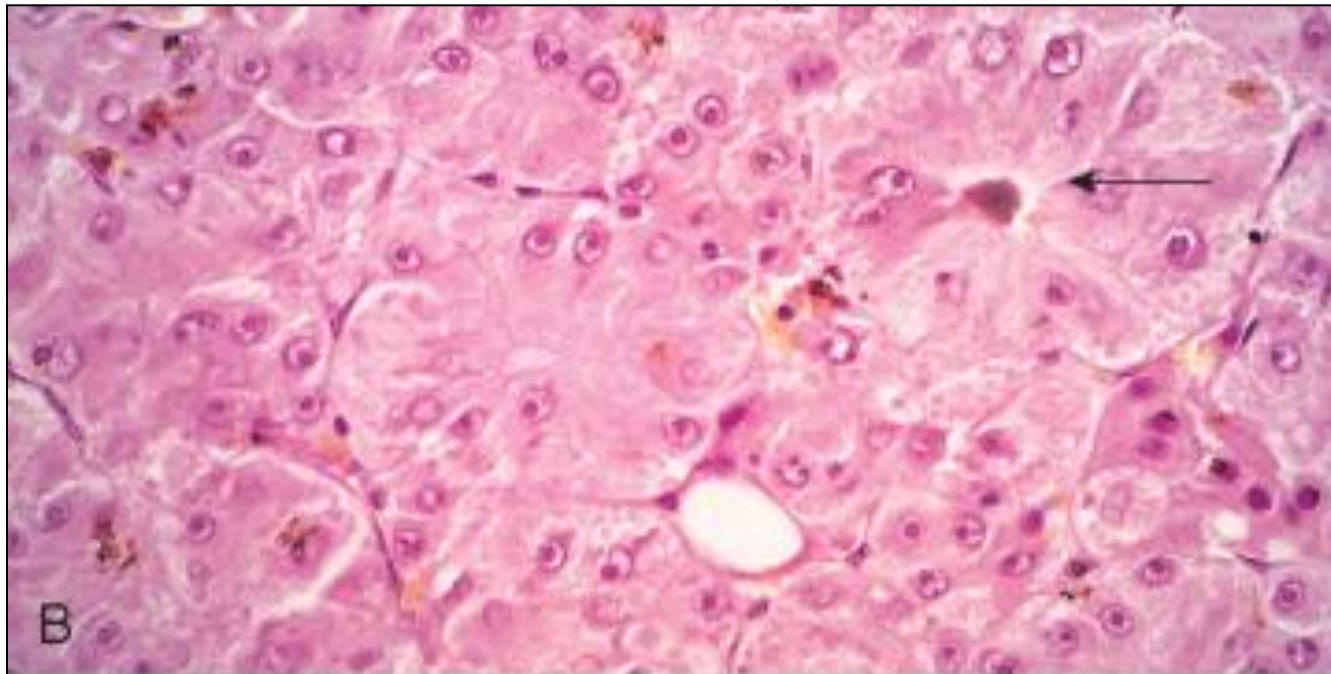
Such liver cancers arise in the setting of cirrhosis. Worldwide, viral hepatitis is the most common cause, but in the U.S. chronic alcoholism is the most common cause. The neoplasm is large and bulky and has a greenish cast because it contains bile.

To the right of the main mass are smaller satellite nodules.



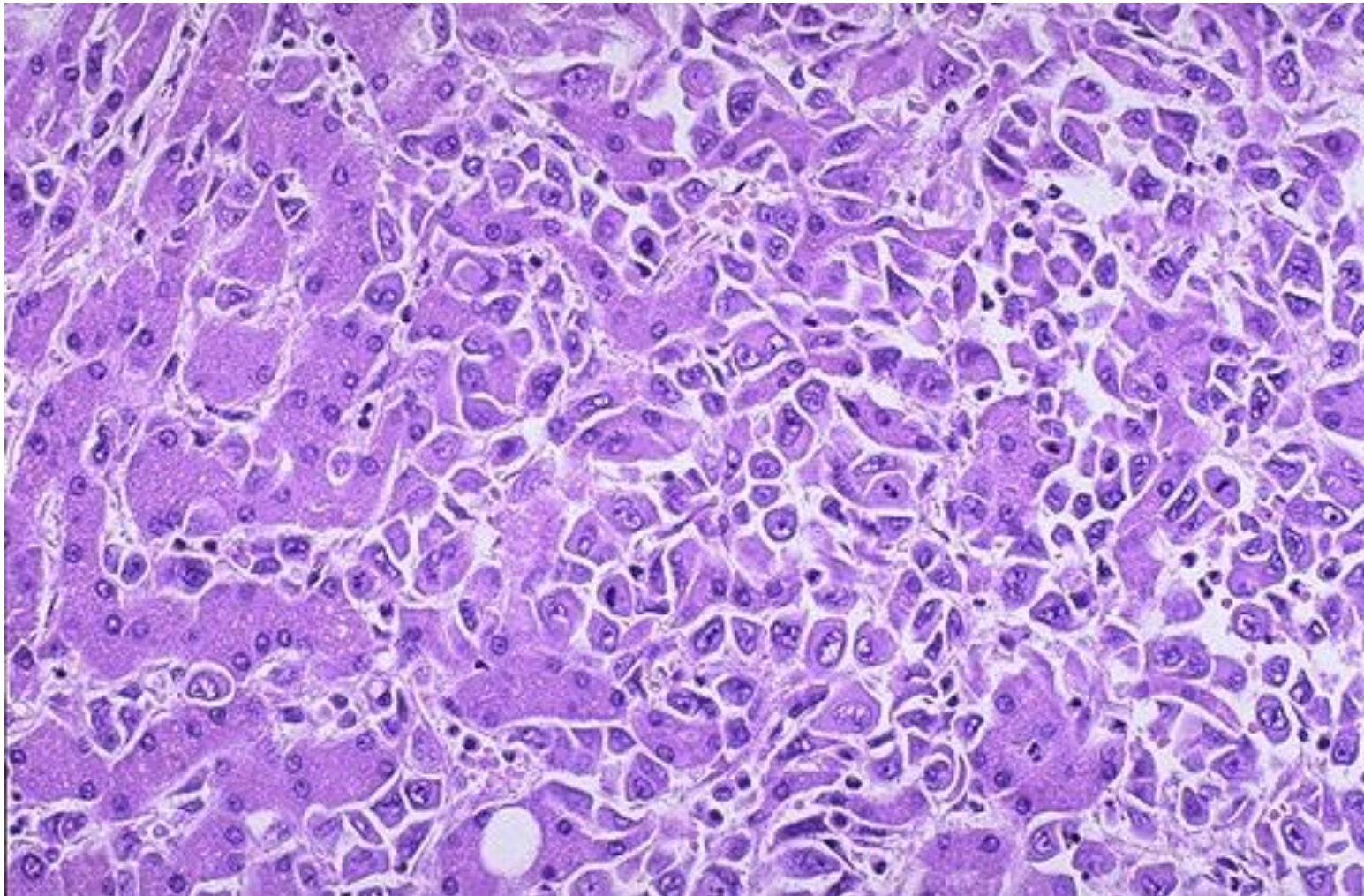
The satellite nodules of this hepatocellular carcinoma.






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Malignant cells of HCC (seen mostly on right) are well differentiated and interdigitate with normal, larger hepatocytes (seen mostly at left).



Clinical Features

- ill-defined upper abdominal pain, malaise, fatigue, weight loss, and feeling of abdominal fullness.
- In many cases, the enlarged liver can be felt on palpation. Jaundice and fever are uncommon.
- **Laboratory studies:**
 Elevated levels of serum α -fetoprotein are found in 50% to 75% of patients with HCC.



- Overall, death usually occurs from
 - (1) **Cachexia** (weight loss) وكأنه جلد على عظم
 - (2) gastrointestinal or esophageal **variceal bleeding**,
 - (3) **liver failure with hepatic coma**or, rarely,
 - (4) **rupture of the tumor with fatal hemorrhage.**

SUMMARY from the book

Liver Tumors



- The liver is the most common site of metastatic cancers from primary tumors of the colon, lung, and breast.
- The main primary tumors are hepatocellular carcinomas and cholangiocarcinomas; hepatocellular carcinomas are by far the most common.
- HCC is a common tumor in regions of Asia and Africa, and its incidence is increasing in the United States.
- The main etiologic agents for hepatocellular carcinoma are hepatitis B and C, alcoholic cirrhosis, hemochromatosis, and more rarely, tyrosinemia. In the Western population about 90% of hepatocellular carcinomas develop in cirrhotic livers; in Asia almost 50% of cases develop in noncirrhotic livers.
- The chronic inflammation and cellular regeneration associated with viral hepatitis may be predisposing factors for the development of carcinomas.
- Hepatocellular carcinomas may be unifocal or multifocal, tend to invade blood vessels, and recapitulate normal liver architecture to varying degrees.

2- Cholangiocarcinoma

- Cholangiocarcinoma is a malignancy of the biliary tree, arising from bile ducts within and outside of the liver.

The **risk conditions** for development of cholangiocarcinoma include

- **primary sclerosing cholangitis** (the most common risk factor), (remember: it's a complication of ulcerative colitis, & it's one of the causes of Liver cirrhosis)
- congenital fibropolycystic diseases of the biliary system (particularly Caroli disease and choledochal cysts),
- previous exposure to Thorotrast (formerly used in radiography of the biliary tract).
- In the Orient, the incidence rates are higher, and it is due to chronic infection of the biliary tract by the liver fluke *Opisthorchis sinensis*.

Morphology ((just read))

just know → it starts in one vessel then ends up reach the whole tree

- **Intrahepatic cholangiocarcinomas** occur in the non-cirrhotic liver and may track along the intrahepatic portal tract system to create a **treelike tumorous mass** within the liver or a massive tumor nodule. Lymphatic and vascular invasion are common.
- By microscopy, cholangiocarcinomas resemble adenocarcinomas arising in other parts of the body. Most are well to moderately differentiated. **Cholangiocarcinomas are rarely bile stained**, because differentiated bile duct epithelium does not synthesize bile.

Morphology

- Mixed variants occur, in which elements of both hepatocellular carcinoma and cholangiocarcinoma are present.
- Hematogenous metastases to the lungs, bones (mainly vertebrae), adrenals, brain. Lymph node metastases to the regional lymph nodes are also found

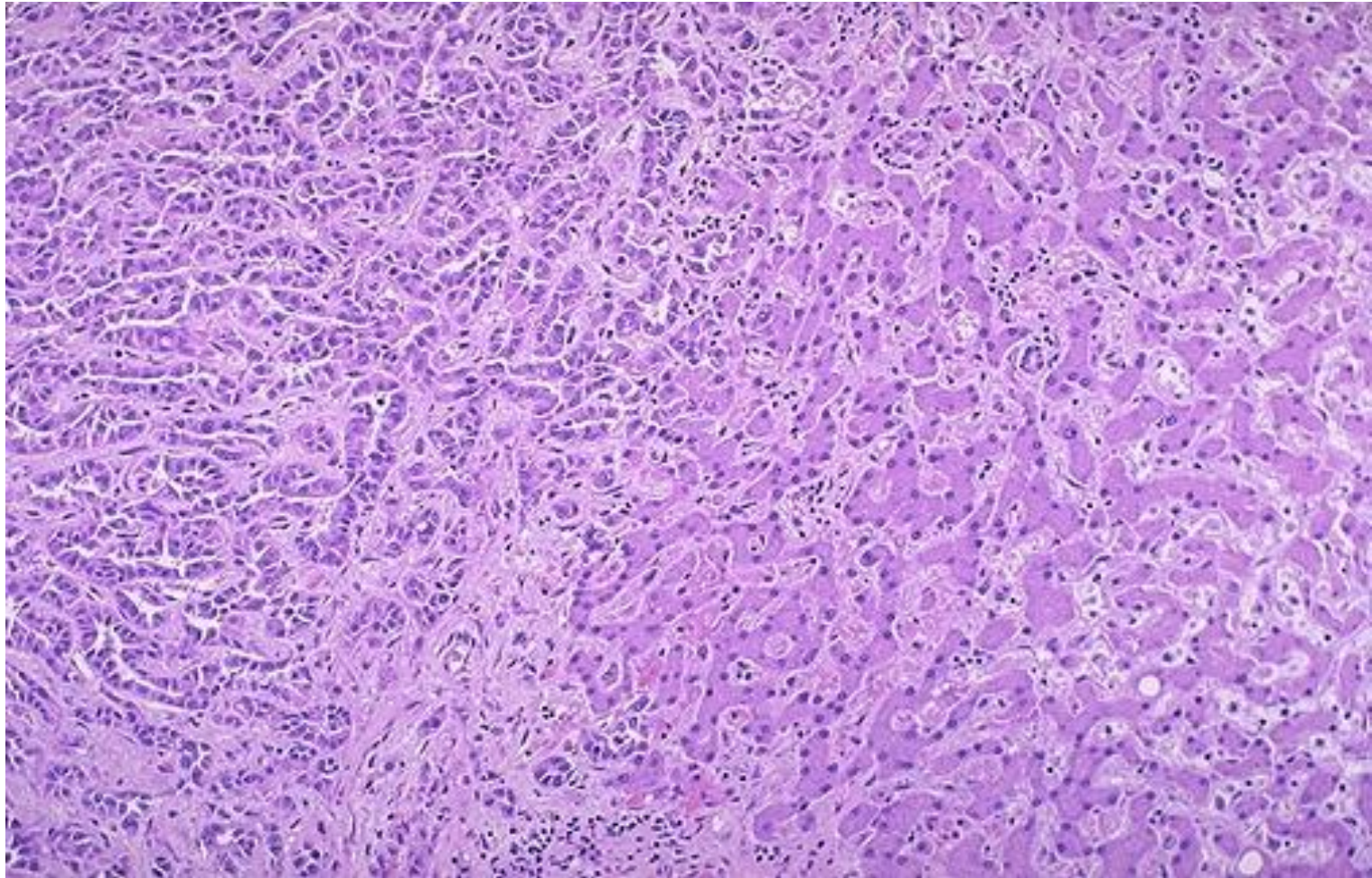


Cholangiocarcinoma.

A, Massive neoplasm in the right lobe and multiple metastases throughout the liver.

B, Tumor cells forming glandular structures surrounded by dense sclerotic stroma.

The carcinoma at the left has a glandular appearance. Cholangiocarcinomas do not make bile, but the cells do make mucin, and they can be almost impossible to distinguish from metastatic adenocarcinoma on biopsy or fine needle aspirate

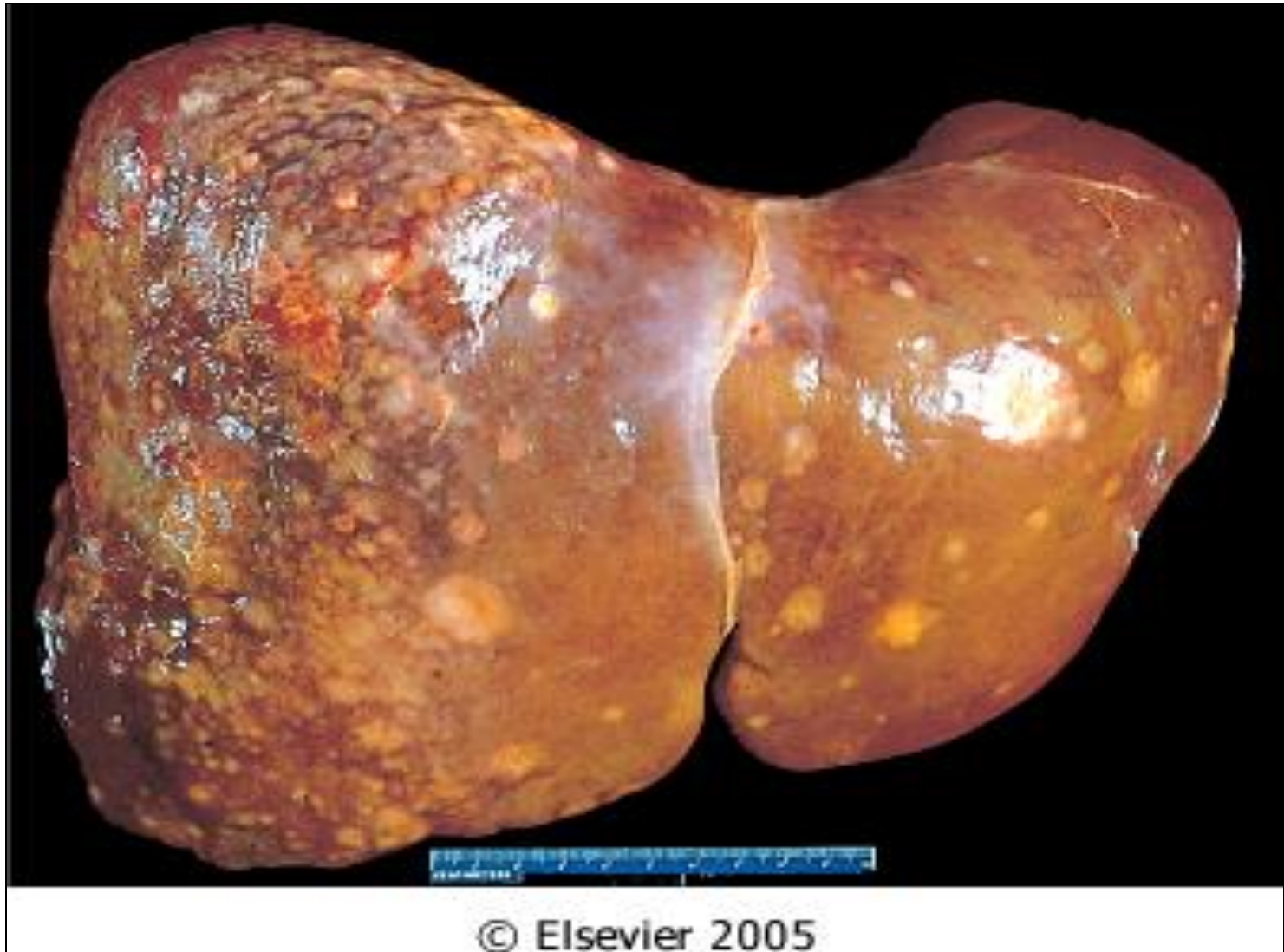


Clinical Features

- Intrahepatic cholangiocarcinoma is usually detected late in its course, either as the result of obstruction to bile flow through the hilum of the liver or as a symptomatic liver mass.
- Prognosis is poor **لأنه لا يكشف إلا متاخرا**.
The median time from diagnosis to death is 6 months. Aggressive surgery remains the only treatment offering hope for long-term survival.
- Alpha-fetoprotein is not elevated.

3- Metastatic tumors

- Metastatic involvement of the liver is far more common than primary neoplasia.
- **Although the most common primaries producing hepatic metastases are those of the breast, lung, and colon**, any cancer in any site of the body may spread to the liver, including leukemias and lymphomas.
- Typically, multiple nodular metastases are found that often cause striking hepatomegaly and may replace over 80% of existent hepatic parenchyma. The liver weight can exceed several kilograms.



Numerous mass lesions of variable size. Some of the larger ones demonstrate central necrosis. The masses are metastases to the liver.



ANGIOSARCOMA

Important to know:

**A malignant tumor to the blood vessels in the liver
(not Hemangioma) + know risk factors**

- This consists of **pleomorphic** endothelial cells with large hyperchromatic nuclei, giant cells in frequent mitosis and irregular anastomosing vascular channels.
- **Risk Factors**
 - The cells may appear spindle shaped and **cirrhosis** is present in 20% to 40% of the cases.
 - These have also been linked to **vinyl chloride and thorostrast exposure**.