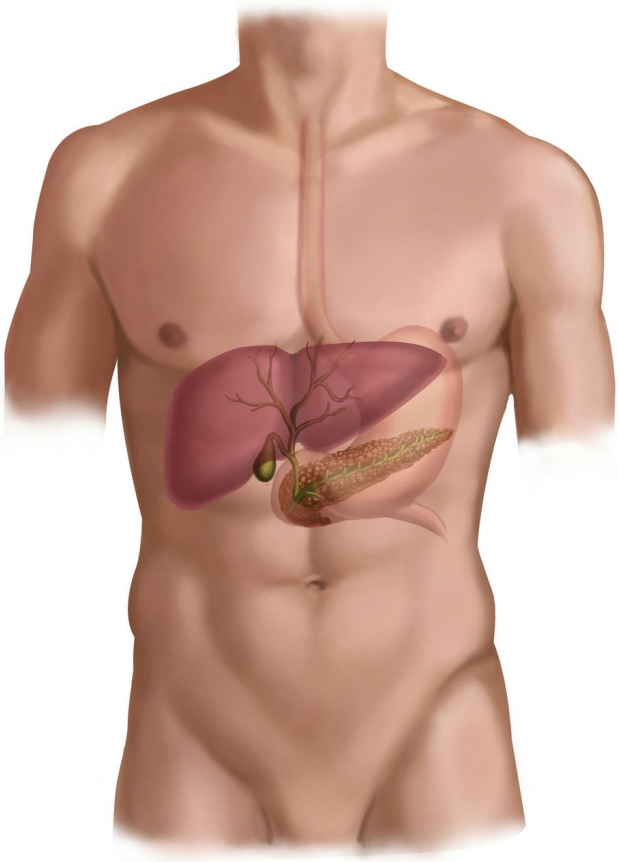
Cancer of liver and pancreas



Objectives:

- Describe hepatocellular and cholangiocarcinoma.
- Understand the frequency of metastatic disease to the liver.
- Recognize the rarity of primary liver neoplasms in children.
- Recognize all aspects of pancreatic carcinoma.

Important note: **Please check out this link before viewing the file to know if there are any additions or changes. The same link will be used for all or our work: Pathology Edit.**

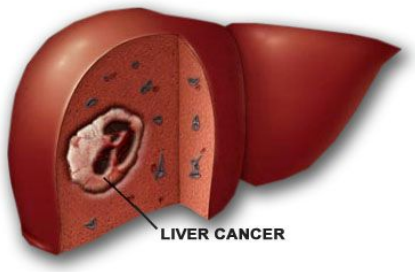
Introduction

Cancer can occur anywhere in the body. Broadly, cancers are classified as either solid (for example: breast, lung, or prostate cancers) or liquid (blood cancers, e.g: leukemia). Cancer is further classified according to the tissue in which it arises from to:

A- Carcinomas:

Are cancers that originates in the **epithelial (lining) tissues**, and they comprise 80% to 90% of all cancers. And are divided into:

- **Pancreas**: Pancreatic carcinoma is almost always of the adenocarcinoma type and is highly lethal.
- **Liver**: Mostly arises from hepatocytes and are termed hepatocellular carcinoma (HCC).
- **Colon and rectum**: Nearly all malignancies of the colon and rectum are either *adenocarcinoma* or *squamous cell carcinoma*.
- Oral: (mostly squamous-cell carcinoma)
- Lung: (it comprises >98% of all lung cancers).
- Breast: (nearly all are ductal carcinoma).
- Prostate: (mostly adenocarcinoma).
- Ovaries.



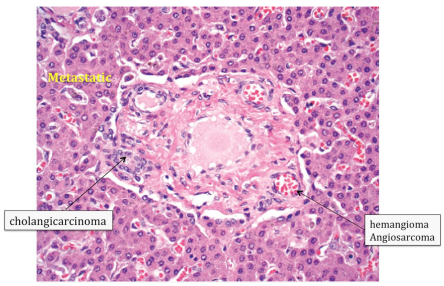
B- Sarcomas:

Arises from transformed cells of mesenchymal origin occur in connective tissue like the bones, cartilage, fat, blood vessels, and muscles. And they are further divided into two groups:

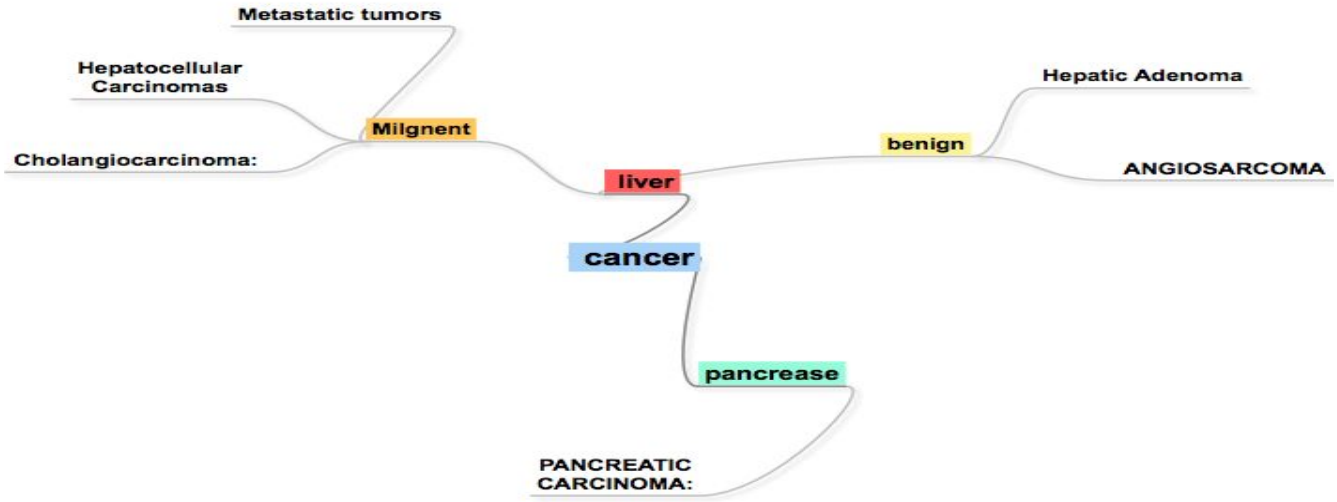
1. Bone sarcoma: (such as osteosarcoma and Ewing's sarcoma)
2. Soft tissue sarcoma: (such as **Angiosarcoma**[1], liposarcoma and many more)
3. **Myelomas** are cancers that occur in plasma cells in the bone marrow.
4. **Leukemias** are blood cancers of the bone marrow.
5. **Lymphomas** are cancers of the immune system cells.
6. **Mixed** cancers arise from more than one type of tissue.

Malignant tumors of the liver.

- The liver and lungs are the visceral organs that are most often involved by **metastatic tumors.**
- Primary carcinomas of the liver are relatively uncommon.
- Most arise from hepatocytes and are termed **hepatocellular carcinoma (HCC).** Much less common are carcinomas of bile duct origin, **cholangiocarcinomas.**
- There are two rare forms of primary liver cancer: hepatoblastomas[2] (a childhood hepatocellular tumor) and angiosarcomas



[1] Cancer of the inner lining of blood vessels, and it can occur in any area of the body.
[2] Primary malignant liver tumour in children



Hepatocellular Carcinomas:

General features

- Male predominance.
- Malignant tumors of hepatocytes.
- More than 85% of cases of HCC occur in countries with high rates of chronic **HBV** infection (asian countries:korea,taiwan,southeast china and sub saharan Africa) in these regions, the HBV carrier state begins in infancy following vertical transmission of virus from infected mothers (during pregnancy, at the time of delivery, or during the first 28 days after birth), 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.**
- Worldwide, **viral hepatitis** is the most common cause, but in the U.S., chronic alcoholism is the most common cause.

Etiologies: (The following have been implicated in human hepatocarcinogenesis)

Viral infection (HBV, HCV)	Cirrhosis	Chronic alcoholism	Food contaminants	Other conditions
Extensive studies link chronic HBV and chronic HCV infection with liver cancer.	The development of cirrhosis appears to be an important, but not requisite, contributor to the emergence of HCC.	alcohol abuse → cirrhosis(indirectly) → HCC (or might directly without cirrhosis)	High exposure to dietary **aflatoxins** derived from the fungus ***Aspergillus flavus*** (induce mutations of P53). These highly carcinogenic toxins (aflatoxins) are found in "moldy" grains and peanuts.	- Tyrosinemia[3]. - Hereditary hemochromatosis[4] - Alpha 1 antitrypsin deficiency

[3] Is an error of metabolism, usually inborn, in which the body cannot effectively break down the amino acid tyrosine.
[4] Excess iron accumulates in tissues and organs disrupting their normal function.

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:

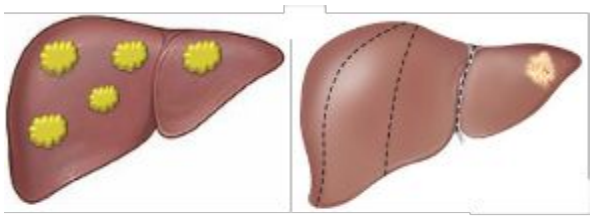
1. **Cachexia:** weakness and wasting of the body due to severe chronic illness.
2. Gastrointestinal or **Esophageal variceal** bleeding.
3. Liver failure with hepatic coma (portosystemic encephalopathy→ due to portosystemic venous shunting)
4. **Rupture** of the tumor with fatal hemorrhage.

Tumor are often detected late because symptoms are masked by cirrhosis; poor prognosis.

Morphology:

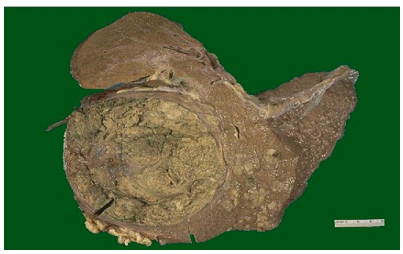
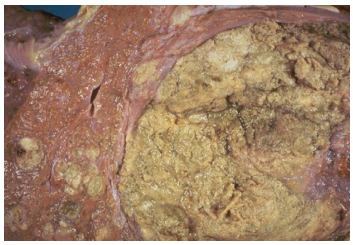
Gross appearance:

1. Unifocal mass.
2. Multifocal, multiple nodules of variable size
3. Diffusely infiltrative cancer (sometimes involving the entire liver).



Multifocal Unifocal

- All three patterns may cause **liver enlargement.**
- All patterns of hepatocellular carcinomas have a strong propensity[5] for invasion of vascular channels.
- 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.

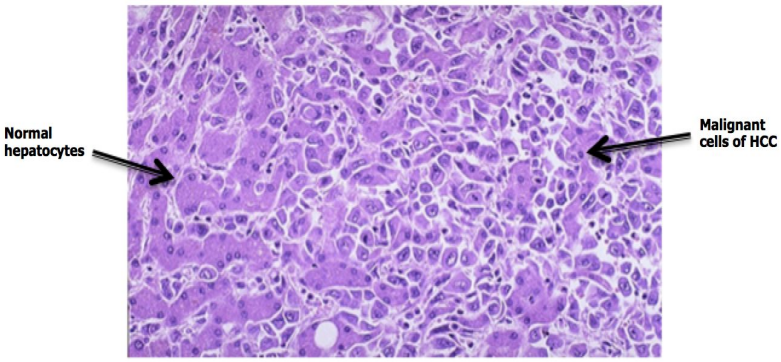
Gross	
	
The neoplasm is large and bulky and has a greenish cast because it contains bile.	**Satellite nodules** (Moon-like appearance).

[5] Tendency.

Microscopic appearance:

Hepatocellular carcinomas range from **well-differentiated** to highly **anaplastic undifferentiated** lesions.

Well-differentiated and moderately well-differentiated tumors	Poorly differentiated forms
• Cells that are recognizable as hepatocytic in origin. • Bile pigment is usually present. • The malignant cells may be positive for **alpha-fetoprotein**.	Tumor cells can take on a pleomorphic appearance with numerous **anaplastic giant cells**, can become small and completely undifferentiated cells.

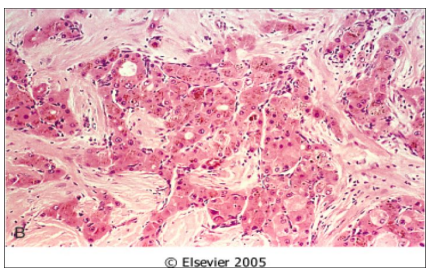


Fibrolamellar carcinoma: (Fibro = fibrous tissue, lamellar= layers → in hepatic tissue)

- 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).
- It has **no association** with HBV or cirrhosis, and often has a better prognosis.

Gross appearance: It usually presents as single large, hard "scirrhous" tumor with fibrous bands coursing through it.

Microscopic appearance: it is composed of well-differentiated polygonal cells growing in **nests or cords** and separated by parallel lamellae of **dense collagen bundles.**



Hepatic Adenoma (Benign tumor of hepatocyte.)

- Occurs as a solitary, sharply demarcated mass up to 40 cm
- It is a complication of **Oral Contraceptive use in women** and estrogens pills too. (regress upon cessation of drug)
- In about 30% of patients, the tumor tends to **bleed** (especially during pregnancy) into the peritoneal cavity, inducing **hypovolemic shock** that requires emergency treatment .

Cholangiocarcinoma: (adenocarcinoma)

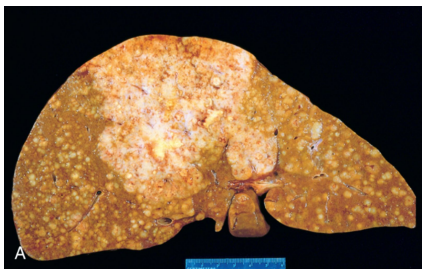
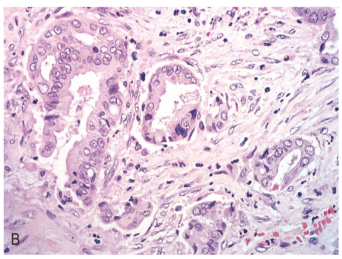
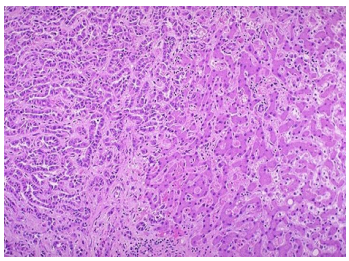
Cholangiocarcinoma is a malignancy of the biliary tree, arising from bile ducts within (intrahepatic) and outside of the liver (extrahepatic).

Risk factors:

- Primary sclerosing cholangitis (inflammation lead to scar in bile duct).
- 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).
- Chronic infestation of **Opisthorchis sinensis** and ***Clonorchis sinensis*** (both are parasite) (clonorchiasis) ,so the incidence rates high In the Orient[6].

All of these → chronic cholestasis → mutation → activating KRAS and BRAF oncogene and inhibition of TP53.

Morphology:

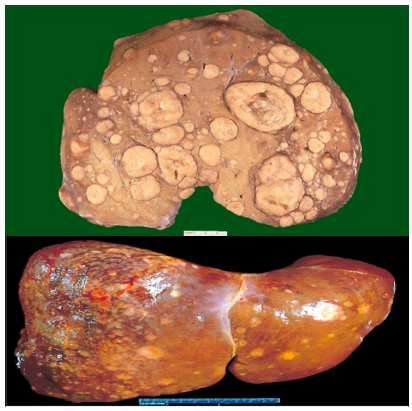
Gross	Microscopic	
		
• **Intrahepatic** cholangiocarcinomas occur in the non-cirrhotic liver → may track intrahepatic portal tract system to → treelike **tumorous mass** within the liver or a **massive tumor nodule.** • **Lymphatic and vascular invasion** are common.	• **Resemble adenocarcinomas** (typical adenocarcinoma) arising in other parts of the body. • Most are **well to moderately differentiated.** • **Rarely bile stained,** because differentiated bile duct epithelium does not synthesize bile. • Mixed variants occur, in which elements of both hepatocellular carcinoma and cholangiocarcinoma are present.	

[6] The countries of Asia, especially eastern Asia.

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.** 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.**(if it was elevated it might be mixed in which both variant is present)
- **Hematogenous metastases** to the lungs, bones (mainly vertebrae), adrenals, brain. Lymph node metastases to the regional lymph nodes are also found.
- Intrahepatic cholangiocarcinoma presence with weight loss ,anorexia ,pain and ascites while the extrahepatic with jaundice **. alcoholic stools , nausea and vomiting.**

Metastatic tumors:



- **Metastatic involvement of the liver is far more common** than primary neoplasia (the most common neoplasms in liver).
- Most commonly from (breast, lung, and colon, any cancer in the body ,including leukemias and lymphomas)**.**

Gross appearance:

Result **Multiple nodular** metastases are found → cause **hepatomegaly** and may replace over 80% of existent hepatic parenchyma. Liver weight can exceed several kilograms.

ANGIOSARCOMA → malignancy of the inner lining of blood vessels associated with exposure to **Thorotrast**, vinyl chloride and arsenic.

.Microscopic appearance

- Pleomorphic[7] endothelial cells with large hyperchromatic nuclei.
- Giant cells in frequent mitosis.
- Irregular anastomosing vascular channels.
- Cells may appear spindle shaped.

- These have also been linked to **vinyl chloride**[8] and **thorotrast** exposure.
- Cirrhosis is present in 20% to 40% of the cases.

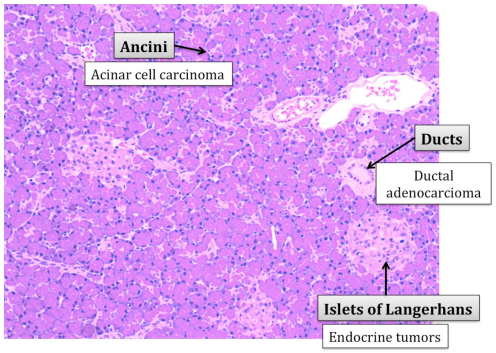
[7] Variability in the size and shape.
[8] Toxic gas.

PANCREATIC CARCINOMA:

Carcinoma of the **exocrine** pancreas that arises from **ductal epithelial cells**. (Majority are ductal adenocarcinomas).

Characteristic

- **Highly invasive.**
- Elicits an intense non-neoplastic host reaction called a "desmoplastic response"[9].
- Lymph nodes are frequently involved (Peripancreatic, gastric, mesenteric, omental, and porta hepatis).
- Distant metastases → principally to the lungs and bones.
- Less common variants of pancreatic cancer include:
- Acinar cell carcinomas,
- Adenosquamous carcinomas
- Undifferentiated carcinomas with osteoclast-like giant cells.



Pathogenesis:

Risk factors → Mutations → activating KRAS (oncogene and inactivation p16/CDKNA2A, SMAD 14 , TP53 (tumor suppressors)

Epidemiology:

- One of the **highest mortality** rates of any cancer.
- **6th to 8th decade**
- blacks > white.
- **Males > females.**
- diabetics > non-diabetics.

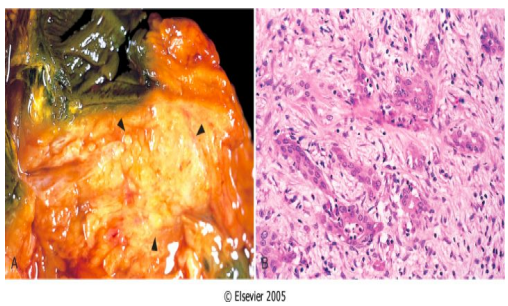
Clinical features:

- **Jaundice** → resulting from blockage of the bile ducts.
- Weight loss
- Pain
- Massive metastasis to liver
- Migratory thrombophlebitis.[10]

Morphology:

- Mainly arising from the head of the gland (60% of cases).
- Less common the body (15%) or the tail (5%).
- It might involve the **entire gland.** (20%)

Usually hard, stellate, gray-white, poorly defined masses. (the hardness because of the desmoplastic response).



[9] The growth of fibrous or connective tissue secondary to an insult.
[10] Inflammation of the wall of a vein with associated thrombosis.

Summary

	Incidence	Etiology	Morphology	Prognosis
Hepatocellular Carcinomas	- Male. - More than 85% of cases of HCC → chronic HBV infection. - Western: cirrhosis 85-90% + chronic liver diseases	1. HBV & HCV. 2. Cirrhosis. 3. Chronic alcoholism. 4. Aflatoxins from aspergillus. 5. Tyrosinemia & hemochromatosis	- In well-differentiated tumors, cells that are recognizable as hepatocytic in origin. - Positive for alpha-fetoprotein - Satellite nodules & greenish cast	Death occurs from: 1. Cachexia. 2. Variceal bleeding. 3. Liver failure with hepatic coma. 4. Rupture of the tumor with hemorrhage
Fibrolamellar carcinoma	- A distinctive variant of hepatocellular carcinoma. - Young male and female adults (20 to 40 years of age).	No association with HBV or cirrhosis	well-differentiated polygonal cells growing in nests or cords and separated by parallel lamellae of dense collagen bundles	**Better prognosis**
Hepatic adenoma	-	**Oral contraceptive drugs.**	Solitary, sharply demarcated mass up to 40 cm.	30% peritoneal cavity bleeding → hypovolemic shock → emergency treatment.
Cholangio-carcinoma	malignancy of the biliary tree, arising from bile ducts	- Primary sclerosing cholangitis. - Congenital fibropolycystic - Exposure to Thorotrast. - In the Orient : Clonorchis sinensis	- Cholangiocarcinoma resemble adenocarcinomas. - Well to moderately differentiated. - Rarely bile stained	- **Late detection:** as obstruction to bile flow or as a symptomatic liver mass - Prognosis is poor - Alpha-fetoprorein is not elevated
Angiosarcoma	Malignant tumor of endothelial cells	- Cirrhosis 20-40% - exposure to vinyl chloride and thorotrast	-	-
pancreatic carcinoma	- Ductal epithelial cells. - Most common: ductal adenocarcinoma. - Less common: 1. Acinar cell carcinomas. 2. Adenosquamous carcinomas. 3. Undifferentiated carcinomas.	- 6^{th} to 8^{th} decade. - Blacks. - Males. - Diabetics. - Cigarette smoking. - K-RAS mutation.	60% arise in the head of the gland - Highly invasive. - Desmoplastic response	- One of the highest mortality rates of any cancer. - Jaundice, weight loss, pain ,massive metastasis to liver and migratory thrombophlebitis.

MCQ's

1-A 51-year-old man presents with slowly progressive jaundice, weight loss, and upper abdominal pain that radiates to his mid back. Physical examination finds an enlarged gallbladder in the right upper quadrant of his abdomen, and a CT scan shows an irregular mass involving the head of the pancreas. Histologic sections from this mass are most likely to reveal which of the following abnormalities?

A-Adenocarcinoma
B-Clear cell carcinoma
C-Medullary carcinoma

2-Man came to emergency department with upper abdominal pain, malaise, fatigue.the enlarged liver can be felt on palpation. The patient Elevated levels of serum α-fetoprotein.

What's the most likely diagnosis?

A- fibrolamellar carcinoma
B- Hepatic Adenoma
C- Hepatocellular Carcinomas

3-A distinctive variant of hepatocellular carcinoma is the:

A- Fibrolamellar carcinoma
B-Hepatic Adenoma
C-Hepatocellular Carcinomas

4-Which one of these Result Multiple nodular are found?

A- Fibrolamellar carcinoma
B- Metastatic tumors :the answer:
C-Hepatocellular Carcinomas

5-Patient came to the ER with migratory thrombophlebitis, Jaundice and weight loss what's the most likely diagnosis ?

A- Metastatic tumors
B-Hepatocellular Carcinoma
C-Pancreatic carcinoma

6-What is the common etiology for Hepatic adenoma?

A-HBV & HCV
B-Primary sclerosing cholangitis
C-Oral contraceptive drugs

Answers:
1-A
2-C
3-A
4-B
5-C
6-C

Done by:

For any suggestions or questions please don't hesitate to contact us on: Pathology434@gmail.com
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Ask us: www.ask.fm/Pathology434

GOOD LUCK !!

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