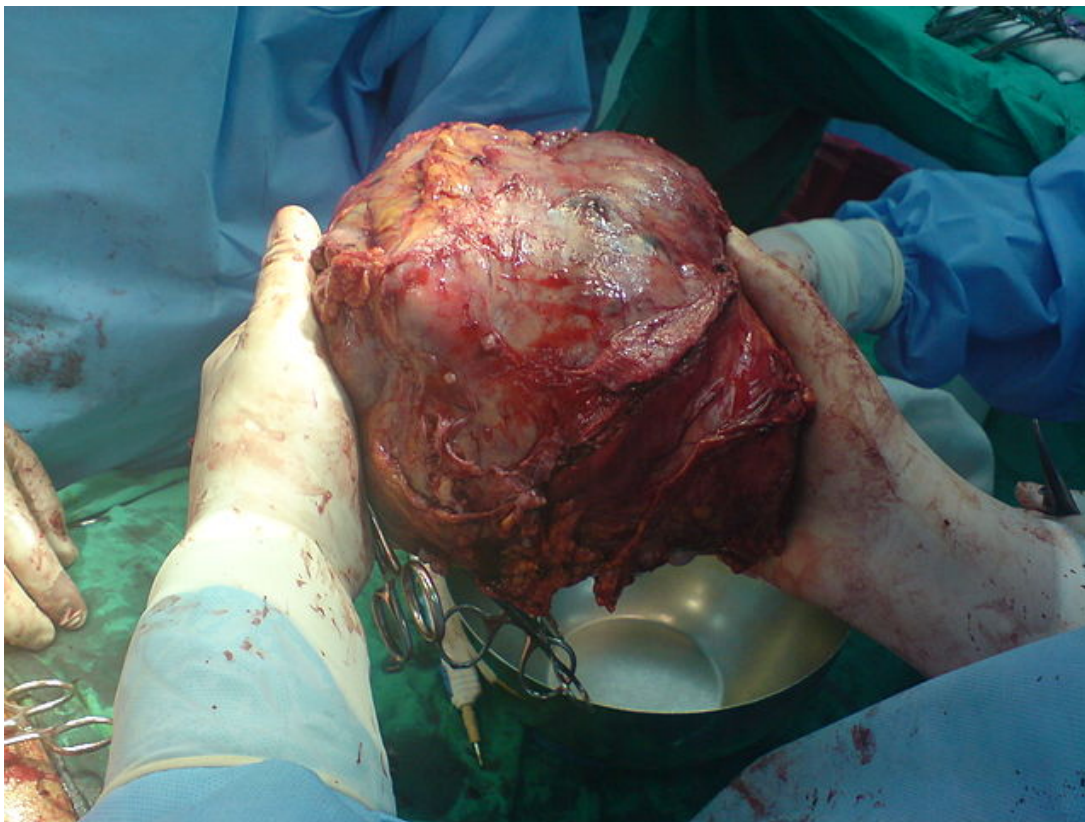


Liver Cancer: Types of Hepatobiliary Tumors

[See online here](#)

Liver tumors are common neoplasms and are classified as either primary or secondary. Management depends on several factors including the type and size of the tumor, and the extent of cancer's spread. This article outlines key facts about tumors of the liver including incidence, pathology, clinical features, diagnosis, and treatment.



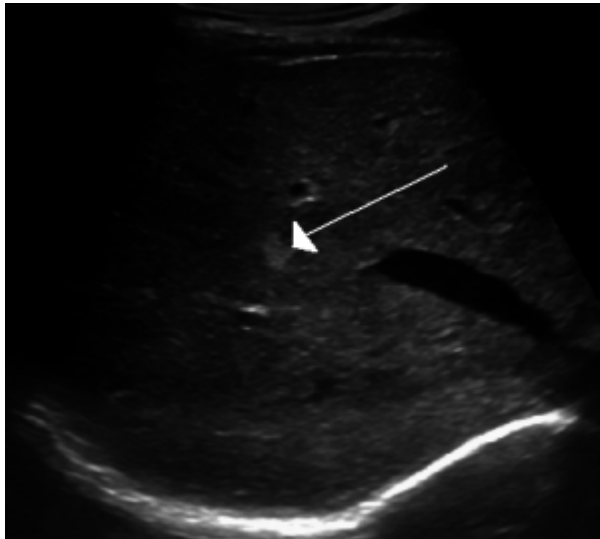
Types of Hepatobiliary Tumors

Tumors of the liver can either be primary or secondary. Although secondary tumors are more common, primary tumors are not uncommon.

Primary hepatic neoplasms arise from liver cells and are usually malignant. Secondary liver tumors are metastases of malignant neoplasms from other parts of the body, especially the gastrointestinal tract, breast, or bronchus. They usually present as multiple small liver lesions, whereas primary neoplasms usually present as a single large lesion.

Benign Liver Tumors

Cavernous hemangiomas



[Image](#): "Hemangioma of the liver as seen on ultrasound" by James Heilman, MD. License: [CC BY-SA 3.0](#)

Cavernous hemangiomas are the most common type of benign primary tumor of the liver. They occur within the blood vessels and can often be mistaken for metastatic tumors. These tumors are often **asymptomatic** and **found incidentally** during surgery, radiological examination (ultrasound, computed tomography [CT] scan, magnetic resonance imaging [MRI]), or at autopsy. They appear as a red, spongy mass lying below the capsule of the liver.

Needle biopsy should never be done if a hepatic hemangioma is suspected because they have a very high risk of bleeding.

Hepatic adenoma

Hepatic adenomas are benign tumors that develop from hepatocytes. These tumors are rare, with an incidence of about 1 in 100,000. They are usually associated with women who take **oral contraceptive pills** and athletes who abuse **anabolic steroids**. They generally shrink when these drugs are stopped.

Hepatic adenomas are clinically significant because:

- They are commonly mistaken for hepatocellular carcinomas.
- Their subcapsular adenomas (capsules under the liver) tend to rupture, especially in high-estrogen states such as pregnancy. Rupture can result in life-threatening hemorrhage within the peritoneum.
- There is a small risk that they **can become malignant**.

Pathophysiology

Although there is a relationship between hormonal stimulation and the development of hepatic adenomas, the exact cause is not yet known. However, mutations in some genes involved in transcription factors HNF1 alpha and beta-catenin have been identified in 50% and 15% of hepatic adenomas, respectively.

Clinical Presentation and Management

Patients often present with a mass, sudden onset of right upper quadrant pain, or bleeding due to rupture of the liver capsule.

Although they are benign, these tumors are usually resected due to the risk of malignant transformation.

Focal nodular hyperplasia

Focal nodular hyperplasia is not a true neoplasm. It is a hyperplastic mass lesion of the liver and is also associated with the use of oral contraceptive pills. These lesions are frequently solitary, subcapsular, well circumscribed, and rarely larger than 5 cm in size. On cut section, a gray-white central area with fibrous bands radiating to the periphery is seen. These are benign lesions and **treatment is not recommended**.

Malignant Liver Tumors

Malignant tumors of the liver can be either be primary or secondary. Primary liver tumors are not common in North America and Western Europe but fairly common in other parts of the world. Approximately 20%–40% of liver tumors are primary.

Malignant tumors of the liver can arise from:

1. Hepatocytes: **hepatocellular carcinoma (HCC)**
2. Intrahepatic bile ducts: **cholangiocarcinoma**
3. Mesenchymal structures such as the blood vessels: **angiosarcoma** or **hemangioendothelioma**

Hepatocellular carcinoma (HCC)

Incidence

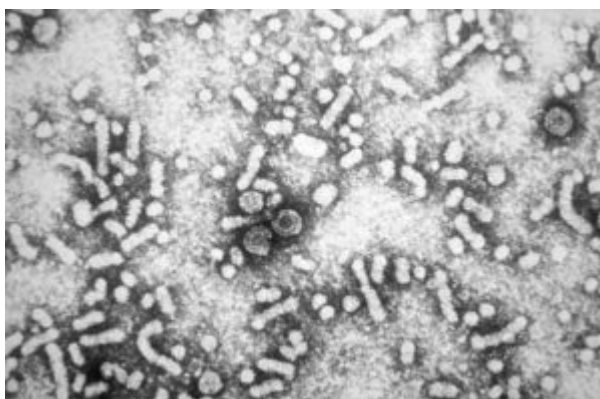


Image: "This electron micrograph reveals the presence of hepatitis-B virus HBV "Dane particles", or virions. The infective hepatitis-B (HBV), virions are also known as Dane particles. These particles measure 42nm in their overall diameter, and contain a DNA-based core that is 27nm in diameter." by CDC. License: Public Domain

HCC is the fifth most **common cancer worldwide** and the third most frequent cause of cancer deaths. Approximately 82% of cases that occur in developing countries are associated with chronic hepatitis B virus (HBV) infections. The incidence of HCC is higher among males, with a ratio to females of 2.4:1.

Etiology

The exact cause of HCC is unknown, although several risk factors have been identified. The four major risk factors associated with HCC are:

1. Chronic viral infection (Hepatitis B and Hepatitis C virus infection)

Carriers of HBV are at extremely high risk of developing HCC. In areas where HBV infection is prevalent, 90% of HCC cases are positive for HBV infection. HCC is common in Africa and countries in the far east, where a greater proportion of the population are hepatitis carriers. This may be due to vertical transmission of the virus from mother to child. The risk of HCC in HCV carriers is higher than in those with HBV.

2. Chronic alcoholism

More than 80% of patients who develop HCC in developed countries (where HBV is not as prevalent) have cirrhosis of the liver.

3. Non-Alcoholic Steatohepatitis (NASH)

4. Aflatoxins

Aflatoxin is a toxic product of the fungus *Aspergillus flavus*, which grows on peanuts and grains. Aflatoxins are toxic to liver cells as they can bind covalently to cellular DNA and cause specific mutations. Chronic ingestion of aflatoxins may be partially responsible for the development of HCC.

Pathology

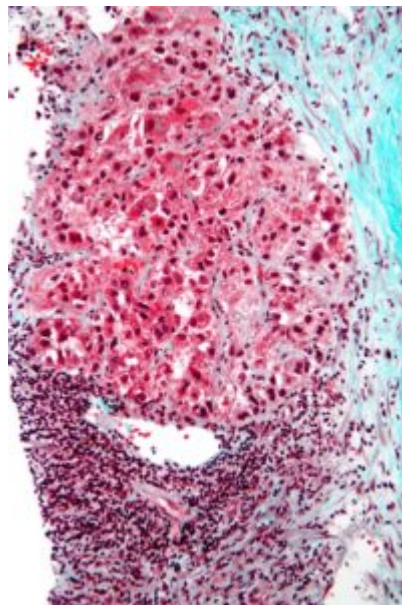


Image: "Intermediate magnification micrograph of hepatocellular carcinoma the most common form of primary liver cancer, i.e. the most common form of cancer to arise in the liver." by Nephron. License: [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/)

Hepatocellular carcinoma may present as:

1. A large solitary mass
2. A multinodular lesion with nodules of variable sizes
3. Diffusely infiltrative cancer sometimes involving the entire liver

All of these forms can result in enlargement of the liver and thus present with symptoms similar to other liver diseases.

Under microscopic examination, this cancer will show abnormal liver cells with variable degrees of differentiation. The well-differentiated cells will look similar to hepatocytes, arranged in cords that are separated by sinusoids. They can also have a green discoloration, which indicates that these cells are so well differentiated that they are capable of producing bile.

The undifferentiated cells will appear as sheets of anaplastic cells. It is often difficult to distinguish a poorly differentiated HCC from a metastatic tumor.

These cancers can metastasize extensively through the hepatic or portal veins to the lymph nodes, bones, and lungs. Metastasis to regional lymph nodes tends to occur early in the lymphatic system. Hematogenous spread to the lung occurs late in the disease.

Occasionally, long, snake-like masses of the tumor spread along the portal vein or the hepatic vein to the inferior vena cava and up to the right atrium.

HCC commonly secretes alpha-fetoprotein (AFP) into the blood. Elevated serum AFP levels are found in over 50% of patients with HCC, making it an important diagnostic test.

Fibrolamellar carcinoma is a variant of HCC and has a better prognosis. It usually does not have an underlying chronic liver cell disease. This tumor occurs in both men and women equally, usually between the ages of 20 and 40 years. It presents as a hard, scirrhous tumor with fibrous bands throughout it. Histologically, it appears as well-differentiated polygonal cells separated by dense collagen bands.

Clinical features

Clinical features include:

- Weight loss
- [Anorexia](#)
- Fever
- Right upper quadrant pain
- Ascites

If the above symptoms newly appear in a patient known to have cirrhosis, then HCC should be suspected.

Diagnosis

- **Serum alpha-fetoprotein concentration:** may be **increased** but can be normal in one-third of the patients.
- Ultrasound
- Enhanced CT: helps identify HCC but not usually helpful for small lesions less than 1 cm.
- MRI
- Tumor biopsy under ultrasound guidance: not used frequently even though it helps with diagnosis as imaging techniques are often sufficient to make a diagnosis of HCC.

Treatment

- **Surgical resection - considered if the lesion is a solitary nodule measuring less than 5 cm in size or there are up to 3 lesions, each**

measuring less than 3 cm. Although there is a risk of recurrence, surgical resection of the tumor provides a median survival of 5 years.

- **Liver transplantation** - the only option available that provides a complete cure for patients with a small primary tumor.
- **Transarterial embolization or radiofrequency ablation** - although less successful than surgical excision, this treatment can prolong the survival period in patients with small primary tumors and good liver function.
- **Antiangiogenic compounds such as sorafenib** - helps prolong survival in patients with nonresectable tumors.

Cholangiocarcinoma (CCA)



Image: "CT scan showing cholangiocarcinoma." by Samir.
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Cholangiocarcinoma is the second-most common malignant primary liver tumor. It arises from the bile ducts within and outside of the liver and is not associated with liver cirrhosis.

The risk factors for CCA include primary sclerosing cholangitis, congenital fibropolycystic diseases of the biliary system, and HCV infection.

CCAs are classified as either intrahepatic or extrahepatic; 80%-90% of all CCAs are extrahepatic.

Extrahepatic CCAs are usually small at the time of diagnosis. They appear as firm, gray nodules within the bile duct wall. Most are adenocarcinomas and may or may not secrete mucin. The presence of mucin in the cytoplasm helps distinguish CCA from HCC.

Intrahepatic CCAs occur in noncirrhotic livers and move down the portal tracts, forming a tree-like tumor within the liver.

Patients with CCA often present in a similar way as those with HCC. However, jaundice is more frequent in those with CCA because of bile duct obstruction. In these patients, surgical resection is rarely possible and the prognosis is poor (mean survival is 6 months from diagnosis).

Liver metastasis (secondary hepatic carcinoma)

Metastatic (secondary) tumors of the liver are most common type of hepatic neoplasm. They include cancers of the **colon, breast, lung, and pancreas**. However, any malignant tumor can metastasize to the liver.

In metastatic cancers, multiple lesions are usually seen with massive hepatomegaly.

It is very difficult to distinguish between HCC and metastatic liver tumor.

Features that can help differentiate between these two types include the following:

1. Often, the nodules of the liver show central necrosis and umbilication seen macroscopically.
2. The presence of cirrhosis favors HCC.
3. Increased levels of AFP are diagnostic of HCC.
4. If the tumor has invaded the hepatic veins, HCC is the more likely diagnosis.

References

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