

## Risk Factor Information for Liver and Intrahepatic Bile Duct Cancers

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### How to Use this Factsheet

This risk factor summary was developed to serve as a general fact sheet. It is an overview and should not be considered exhaustive. For more information on other possible risk factors and health effects being researched, please see the References section.

A risk factor is anything that increases a person's chance of developing cancer. Some risk factors can be controlled while others cannot. Risk factors can include *hereditary conditions, medical conditions or treatments, infections, lifestyle factors, or environmental exposures*. Although risk factors can influence the development of cancer, most do not directly cause cancer. An individual's risk for developing cancer may change over time due to many factors, and it is likely that multiple risk factors influence the development of most cancers. Knowing the risk factors that apply to specific concerns and discussing them with your health care provider can help to make more informed lifestyle and health care decisions.

For cancer types with environmentally-related risk factors, an important factor in evaluating cancer risk is the route of exposure. This is particularly relevant when considering exposures to chemicals in the environment. For example, a particular chemical may have the potential to cause cancer if it is inhaled, but that same chemical may not increase the risk of cancer through skin contact. In addition, the dose and duration of time one might be exposed to an environmental agent is important in considering whether an adverse health effect could occur.

Gene-environment interactions are another important area of cancer research. An individual's risk of developing cancer may depend on a complex interaction between their genetic make-up and exposure to an environmental agent (for example, a virus or a chemical contaminant). This may explain why some individuals have a fairly low risk of developing cancer as a result of an environmental factor or exposure, while others may be more vulnerable.

### Key Statistics

The liver is a vital organ located beneath your right lung. It serves several critical functions in the body, including filtering toxic substances from the blood and storing nutrients absorbed from the intestines. The bile duct is a thin tube that delivers bile fluid from the liver to the small intestine. The fluid helps break down the fats in food. The parts of the bile duct that begin in the liver are called intrahepatic bile ducts (IBD). Liver and IBD cancers are fairly rare in the United States. The American Cancer Society estimates 35,660 individuals will be diagnosed with liver and IBD cancer in the U.S. in 2015: 25,510 men and 10,150 women.<sup>1,2,5</sup> In Massachusetts, these cancers accounted for about 1.6% of all cancers diagnosed from 2007 to 2011.<sup>8</sup> Liver and IBD cancers are more common in men than women.<sup>1</sup> More than 95% of individuals diagnosed with liver and IBD cancer are older than 45 years of age, with an average age at diagnosis of 63 years.<sup>2</sup> Asian Americans and Pacific Islanders have the highest incidence rates in the

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U.S., followed by American Indians/Alaska Natives and Hispanics/Latinos, African Americans, and whites.<sup>2</sup> Incidence rates in the U.S. have been slowly rising for several decades.<sup>2</sup> These cancers are much more common in countries in sub-Saharan Africa and Southeast Asia than in the U.S. and are the most common type of cancer in many of these countries.<sup>2,5</sup>

### **Types of Liver Cancer**

The term "cancer" is used to describe a variety of diseases associated with abnormal cell and tissue growth. Cancers are classified by the location in the body where the disease originated (the primary site) and the tissue or cell type of the cancer (histology).

Liver and IBD tumors can be either malignant (cancerous) or benign (non-cancerous). Both primary and secondary tumors can arise in the liver and IBD. Secondary liver and IBD tumors are more common. These tumors generally originate elsewhere in the body and metastasize, or spread, to the liver. Hepatocellular carcinoma (HCC), which includes several subtypes, is the most common type of primary liver cancer and accounts for about 80% of all diagnoses. Intrahepatic cholangiocarcinomas start in the parts of the bile duct that branch into the liver and account for approximately 10% to 20% of all primary liver cancers.<sup>2</sup> Rarer forms of malignant liver and IBD cancers include angiosarcoma, hemangiosarcoma, and hepatoblastoma, the last of which usually develops in children under the age of 4.<sup>2</sup>

### **Established Risk Factors**

#### *Hereditary Conditions*

Certain inherited metabolic diseases can lead to cirrhosis (a disease in which liver cells become damaged and are replaced by scar tissue), which in turn increases the risk of liver and IBD cancer. For example, individuals with hemochromatosis are more likely to develop cirrhosis due to high iron levels in their liver.<sup>12</sup> Other inherited metabolic diseases that increase the risk of liver and IBD cancer include tyrosinemia,  $\alpha$ 1-antitrypsin deficiency, porphyria cutanea tarda and Wilson disease.<sup>2,12</sup>

#### *Medical Conditions/Treatments*

Cirrhosis is a major risk factor for the development of liver and IBD cancers. Most cirrhosis in the U.S. occurs as a result of heavy alcohol consumption or chronic (long-term) infection of the hepatitis B virus (HBV) or hepatitis C virus (HCV).<sup>2</sup> Additional causes include certain types of inherited metabolic diseases (as previously discussed) and some types of autoimmune diseases.

Exposure to thorium dioxide (Thorotrast) raises the risk of angiosarcoma of the liver and may also increase the risk of developing cholangiocarcinoma and HCC. Thorotrast is no longer used, but had been in the past for certain x-ray tests.<sup>2,12</sup>

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### *Infections*

Chronic infection with HBV or HCV is the most significant risk factor for developing liver and IBD cancers. Infection with HCV is the most common cause of HCC in the United States, whereas infection with HBV is more commonly the cause in Asia and developing countries. HBV and HCV can be spread through intravenous drug use (e.g., sharing contaminated needles), unprotected sexual intercourse, childbirth, or transfusion of and contact with unscreened blood and blood products (though this has rarely happened in the U.S. since the start of blood product testing for these viruses). Since the early 1980s, a vaccine has been available to help prevent infection with HBV.<sup>2, 12</sup>

### *Environmental Exposures*

Long-term exposure to aflatoxins is a major risk factor for liver and IBD cancers.<sup>12</sup> These carcinogenic (cancer-causing) substances are produced by a fungus that grows in warm, moist environments and is commonly found in tropical countries.<sup>12</sup> Individuals may be exposed to aflatoxins by consuming contaminated foods such as peanuts, wheat, soybeans, ground nuts, corn, and rice. Developed countries such as the U.S. and those in Europe regulate the content of aflatoxins in foods through testing.<sup>2</sup>

Exposure to vinyl chloride, a chemical used in making some kinds of plastics, raises the risk of angiosarcoma of the liver and may also increase the risk of developing cholangiocarcinoma and HCC.<sup>2, 12</sup> Exposure of workers to vinyl chloride is now strictly regulated.<sup>2</sup> Furthermore, chronic exposure to drinking water contaminated with naturally occurring arsenic increases the risk of some types of liver and IBD cancer.<sup>12</sup> The chance of being exposed to arsenic depends on where you live and whether your water comes from a well or from a system that meets the standards for arsenic content.<sup>2</sup>

## **Possible Risk Factors**

### *Medical Conditions*

Diabetes may increase the risk of liver and IBD cancers, particularly in individuals who have additional risk factors such as heavy alcohol consumption and/or chronic viral hepatitis.<sup>1, 2, 4</sup>

### *Infections*

Infection of the bile duct with a parasite called a liver fluke may contribute to intrahepatic cholangiocarcinomas. These parasites are common in Asia and the Middle East.<sup>4, 11, 12</sup>

### *Lifestyle Factors*

Alcohol consumption has been linked to cirrhosis, a major risk factor for the development of liver and IBD cancers (as previously discussed). It is unclear whether alcohol is related to the development of liver and IBD cancers independent of cirrhosis.<sup>12</sup> Since

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obesity can contribute to fatty liver disease and cirrhosis, it may increase the risk of developing liver and IBD cancers.<sup>12</sup> In addition, long-term use of anabolic steroids may slightly increase the risk of HCC.<sup>2, 12</sup>

### Other Risk Factors That Have Been Investigated

#### *Infections*

Although the hepatitis A virus and the hepatitis E virus can cause hepatitis, individuals infected with these viruses do not have an increased risk of liver and IBD cancer.

#### *Lifestyle Factors*

Some studies have found a link between smoking and liver cancer, but the extent of this association is not known.<sup>2, 12</sup> Oral contraceptives (birth control pills) are a cause of benign tumors called hepatic adenomas but it is not known if they increase the risk of HCC.<sup>12</sup> Some studies have suggested there may be a link, but the types and doses of estrogens in the pills that were investigated differ from those that are currently used. It is not known if newer birth control pills increase the risk of developing liver cancer.<sup>2</sup> Unlike anabolic steroids, long-term use of cortisone-like steroids (such as hydrocortisone, prednisone, and dexamethasone) does not increase the risk of liver and IBD cancer.<sup>2</sup>

### Liver and Intrahepatic Bile Duct Cancers in Children

Liver and IBD cancers were the least commonly occurring cancers among Massachusetts children and adolescents younger than 20 years of age between 2000 and 2009, accounting for 1.5% of all childhood cancers in the state.<sup>9</sup> Hepatoblastoma is a very rare type of liver cancer that usually develops in children under the age of 4.<sup>2</sup>

### For More Information / References

*Much of the information contained in this summary has been taken directly from the following sources. This material is provided for informational purposes only and should not be considered as medical advice. Persons with questions regarding a specific medical problem or condition should consult their physician.*

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