

## **RISK FACTOR INFORMATION FOR SELECTED CANCER TYPES**

---

### **Liver Cancer**

An estimated 17,550 people in the U.S. (12,130 men and 5,420 women) will be diagnosed with liver cancer in 2005, accounting for approximately 1% of all new cancers (ACS, 2005). Hepatocellular carcinoma (HCC) is the most common primary cancer of the liver, accounting for about 75% of all cases. Rarer forms of malignant liver cancer include cholangiocarcinomas, angiosarcomas, and hepatoblastomas in children. Although HCC is approximately ten times more common in developing countries in East and Southeast Asia and Africa, incidence is rapidly increasing in the United States (ACS, 2001). Rates of HCC in the U.S. have increased by 70% over the past two decades (Yu et al., 2000). Similar trends have been observed in Canada and Western Europe. The primary reason for the higher rates observed in recent years is the increase in hepatitis C virus infection, an important factor related to liver cancer (El-Serag, 2001; El-Serag and Mason, 2000). Men are at least two to three times more likely to develop liver cancer than women (Yu et al., 2000). Incidence rates are also higher among African Americans than whites. Although the risk of developing HCC increases with increasing age, the disease can occur in persons of any age (London and McGlynn, 1996).

Several important risk factors for liver cancer have been identified. Chronic infection with hepatitis B virus (HBV) and hepatitis C virus (HCV) are the most significant risk factors for developing liver cancer (ACS, 2001). It is estimated that 80% of HCC cases worldwide can be attributed to HBV infection (Yu et al., 2000). However, HBV accounts for only about a quarter of the cases in the U.S. and infection with HCV plays a much larger role in the incidence of this cancer. HBV and HCV can be spread through intravenous drug use (e.g., the sharing of contaminated needles), unprotected sexual intercourse, and transfusion of and contact with unscreened blood and blood products. In addition, mothers who are infected with these viruses can pass them on to their children at birth or in early infancy (ACS, 2001).

Cirrhosis is also a major risk factor for the development of liver cancer. Cirrhosis is a progressive disease that causes inflammation and scar tissue to form on the liver, which can often lead to cancer. Researchers estimate that 60% to 80% of HCC cases are associated with cirrhosis. However, it is unclear if cirrhosis itself causes liver cancer or if the underlying causes of cirrhosis contribute to the development of this disease (Garr et al., 1997). Most liver cirrhosis in the U.S. occurs as a result of chronic alcohol abuse, but HBV and HCV are also major causes of cirrhosis (ACS, 2001). In addition, certain inherited metabolic diseases, such as hemochromatosis, which causes excess iron accumulation in the body, can lead to cirrhosis (ACS, 2001). Some studies have shown that people with hemochromatosis are at an increased risk of developing liver cancer (Fracanzani et al., 2001).

Epidemiological and environmental evidence indicates that exposure to certain chemicals and toxins can also contribute significantly to the development of liver cancer. For example, chronic consumption of alcoholic beverages has been associated with liver cancer (Wogan, 2000). As noted above, it is unclear if alcohol itself causes HCC or if underlying cirrhosis is the cause (London and McGlynn, 1996). However, it is clear that alcohol abuse can accelerate liver disease and may act as a co-carcinogen in the development of liver cancer (Ince and Wands, 1999). Long-term exposure to aflatoxin can also cause liver cancer. Aflatoxins are carcinogenic agents produced by a fungus found in tropical and subtropical regions. Individuals may be exposed to aflatoxins if they consume contaminated peanuts and other foods that have been stored under hot, humid conditions (Wogan, 2000). Vinyl chloride, a known human carcinogen used in the

## RISK FACTOR INFORMATION FOR SELECTED CANCER TYPES

---

manufacturing of some plastics, and thorium dioxide, used in the past for certain x-ray tests, are risk factors for a rare type of liver cancer called angiosarcoma (ACS, 2001; London and McGlynn, 1996). These chemicals may also increase the risk of HCC, but to a lesser degree. The impact of both thorium dioxide and vinyl chloride on the incidence of liver cancer was much greater in the past, since thorium dioxide has not been used for decades and exposure of workers to vinyl chloride is now strictly regulated in the U.S. (ACS, 2001). Drinking water contaminated with arsenic may increase the risk of liver cancer in some parts of the world (ACS, 2001; ATSDR, 2001).

The use of oral contraceptives by women may also be a risk factor in the development of liver cancer. However, most of the studies linking oral contraceptives and HCC involved types of oral contraceptives that are no longer used. There is some indication that the increased risk may be confined to oral contraceptives containing mestranol. It is not known if the newer oral contraceptives, which contain different types and doses of estrogen and different combinations of estrogen with other hormones, significantly increase the risk of HCC (ACS, 2001; London and McGlynn, 1996). Long-term anabolic steroid use may slightly increase the risk of HCC; however, a definitive relationship has not been established (ACS, 2001; London and McGlynn, 1996). Although many researchers believe that cigarette smoking plays a role in the development of liver cancer, the evidence for this is still inconclusive (Mizoue et al., 2000; London and McGlynn, 1996).

### References

- Agency for Toxic Substance and Disease Registry. 2001. ToxFAQs: Arsenic. U.S. Department of Health and Human Services, CAS #7440-38-2.
- American Cancer Society. 2005. Cancer Facts & Figures 2005. Atlanta: American Cancer Society, Inc.
- American Cancer Society. 2001. Liver Cancer. Available at: <http://www3.cancer.org/cancerinfo/>.
- El-Serag HB. 2001. Epidemiology of hepatocellular carcinoma. *Clin Liver Dis* 5(1):87-107.
- El-Serag HB, Mason AC. 2000. Risk factors for the rising rates of primary liver cancer in the United States. *Arch Intern Med* 160(21):3227-30.
- Fracanzani AL, Conte D, Fraquelli M, Taioli E, Mattioli M, Losco A, Fargion S. 2001. Increased cancer risk in a cohort of 230 patients with hereditary hemochromatosis in comparison to matched control patients with non-iron-related chronic liver disease. *Hepatology* 33(3):647-51.
- Garr BI, Flickinger JC, Lotze MT. Cancer of the Liver. In: *Cancer: Principles and Practice of Oncology*, Fifth Edition, edited by Devita V, Hellman S, Rosenberg S. Lippincott-Raven Publishers, Philadelphia 1997. P. 1271-1297.
- Ince N, Wands JR. 1999. The increasing incidence of hepatocellular carcinoma. *NEJM* 340(10):789-9.
- London WT, McGlynn KA. 1996. Liver cancer. In: *Cancer Epidemiology and Prevention*. 2<sup>nd</sup> Ed, edited by Schottenfeld D, Fraumeni. JF. New York: Oxford University Press: 1996.

## **RISK FACTOR INFORMATION FOR SELECTED CANCER TYPES**

---

Mizoue T, Tokui N, Nishisaka K, Nishisaka S, Ogimoto I, Ikeda M, Yoshimura T. 2000. Prospective study on the relation of cigarette smoking with cancer of the liver and stomach in an endemic region. *Int J Epidemiol* 29(2):232-7.

Wogan GN. 2000. Impacts of chemicals on liver cancer risk. *Semin Cancer Biol.* 10(3):201-10.

Yu MC, Yuan JM, Govindarajan S, Ross RK. 2000. Epidemiology of hepatocellular carcinoma. *Can J Gastroenterol* 14(8):703-9.