

August 2006 HepTalk Listserv

Again in the month of August we welcome many new members to the HepTalk Listserv! Our concentration for this month is **Liver Cancer and Hep B and C**. We present two articles in full and three abstracts:

1. **Deadly Liver Cancer Creeps In** “[Primary liver cancer] cases are rising as rapidly as 4.5 percent among black men and **5 percent among Hispanic women**...The striking increase in liver cancers here and in other developed countries is a result of chronic and usually silent infections by the hepatitis B and C viruses, which are spread by blood and attack the liver.”
2. **Liver Transplants** “The most common indications for liver transplantation in the United States are hepatitis C virus (30%) and alcoholic liver disease (18%).”
3. **Regular Surveillance for Hepatocellular Carcinoma Improves Survival** “‘The big deal is catch them early so they are still candidates for a curative therapy which is transplantation,’ said Alan Hemming, MD.”
4. **The contributions of hepatitis B virus and hepatitis C virus infections to cirrhosis and primary liver cancer worldwide.** “Globally, 57% of cirrhosis was attributable to either HBV (30%) or HCV (27%) and 78% of HCC was attributable to HBV (53%) or HCV (25%).”
5. **Systemic Therapy of Advanced Hepatocellular Carcinoma: How Hopeful Should We Be?**

For those of you just joining, be sure to check the Listserv Archives at <http://www.migrantclinician.org/excellence/hepatitis/listservarchive>, or email the listserv administrator, Kath Anderson, at dempander@earthlink.net to have a previous edition e-mailed directly to you. You can also contact the listserv administrator if others at your clinic would like to be on the listserv, or if you have questions about the listserv or resources listed here, or if you would like to add something to the posts, or to unsubscribe from the list. The following is a list of the monthly topics in 2006:

- o **January 2006:** Updated Advisory Committee on Immunization Practices (ACIP) of the US Centers for Disease Control and Prevention (CDC) comprehensive guidelines for the eradication of hepatitis B virus (HBV) in the United States.
- o **February 2006:** Update on Hepatitis C.
- o **March/April 2006:** Cross cultural communication.
- o **April 2006:** Hepatitis A and prevention, with guest editor Amy Liebman, MPA.
- o **May 2006:** two successful adult immunization programs, one in Pennsylvania and one in New York. Each involves cooperation between state and local health departments and community clinics in order to provide immunizations, including Hepatitis A and B, to migrant seasonal farmworkers. The Pennsylvania program works with a HepTalk clinic participant.
- o **June /July 2006:** Cultural Competency and Hepatitis, with guest editor Dr. Jennie McLauren
- o **July 2006:** Hepatitis B Updates

1. **Deadly Liver Cancer Creeps In**

<http://www.theledger.com/apps/pbcs.dll/article?AID=/20051018/NEWS/510180304/1021>

Published Tuesday, October 18, 2005

You don't hear much about liver cancer, but its incidence is increasing faster than that of any other cancer in the United States. That increase is expected to continue for two more decades.

Liver cancer is also one of the most deadly cancers, typically fatal within a year of diagnosis, unless, as rarely occurs, it is found very early. This fact alone suggests that people at high risk of developing the cancer may want to consider periodic screening with whatever tests are available.

That in turn suggests that people at high risk should know that they are and find out whether screening will be effective.

Many people are confused about liver cancer. Only cancers that originate in the liver are liver cancers. Cancers of the colon, lung or breast, among others, often spread to the liver, prompting the confusion. But every cancer, regardless of where it may spread, retains the name and cellular characteristics of its origin.

Liver cancer is one of the most common cancers in the world, especially prevalent in Southeast Asia and sub-Saharan Africa. In the last quarter-century, Japan, for example, has experienced an epidemic of liver cancer, now the third leading cause of cancer deaths among its men and the fifth leading cause among the women.

A RISING SCOURGE

Primary liver cancer is still relatively rare in the United States, where it is the 20th most common type of cancer. But earlier this month, The Associated Press reported, cases are rising as rapidly as 4.5 percent among black men and 5 percent among Hispanic women.

Because liver cancer is usually not found before symptoms of advanced disease develop, it is also the eighth most common cause of cancer deaths in this country.

The striking increase in liver cancers here and in other developed countries is a result of chronic and usually silent infections by the hepatitis B and C viruses, which are spread by blood and attack the liver. These viral infections, which damage liver cells, can lead to primary liver cancer 30 years or more after an infection takes hold.

Genetic material of the hepatitis B virus incorporates itself into the DNA of liver cells, subverting normal functions and, ultimately, causing cancer. The hepatitis C virus works differently: It is believed to disrupt the action of a gene called P53 that normally suppresses tumor formation.

Like hepatitis B, chronic hepatitis C infections can also cause cirrhosis, a scarring of the liver. When the damaged liver tries to repair itself, mutations can occur that result in uncontrolled cell growth. About 5 percent of people with cirrhosis from any cause eventually develop liver cancer.

But with screening of blood supplies for hepatitis B virus in place since the late 1980s and with current immunizations of infants and some adults with hepatitis B vaccine,

the incidence of liver cancer brought on by this virus should be reduced in years to come.

Although potential blood donors and donations are now checked for the hepatitis C virus, many people became infected before the virus was identified. No vaccine has been developed against this infection.

Many people continue to put themselves at risk of developing a hepatitis C infection through exposure to contaminated needles as a result of drug use, tattooing and body piercing, and unprotected sex with people who may carry the virus. Hepatitis C accounts for half the cases of primary liver cancer in the United States.

Another important cause of liver cancer is alcohol abuse. Alcohol damages the liver and over the years can result in cirrhosis. In fact, cirrhosis from chronic alcohol consumption, especially when combined with a chronic hepatitis C infection, is the most common cause of liver cancer in the developed world.

Further, it is more likely to develop a decade or more after a person with alcohol-induced cirrhosis stops drinking, when the liver generates new cells to repair the damage caused by alcohol. Of course, people who continue to abuse alcohol risk an early demise from liver failure.

Other factors known to cause liver cancer are exposure to certain industrial chemicals like vinyl chloride and a poison called aflatoxin B, produced by a fungus, *Aspergillus flavus*, that can grow on foods like peanuts and other nuts, rice, soybeans, corn and wheat.

The Food and Drug Administration monitors the American food supply for this toxin. But in southern China and sub-Saharan Africa, chronic consumption of aflatoxin B, believed to suppress the P53 gene, is a leading cause of liver cancer.

Concerns have also been raised about substances like estrogen and anabolic steroids that can cause the development of benign liver tumors, which may ultimately become malignant.

A genetic disease called hemochromatosis, which causes excess iron to accumulate in the liver and other organs, also results in liver cancer in up to 30 percent of the people with this disorder.

Other risk factors include smoking, diabetes and mutations in the genes BRCA1 and 2, which are most often linked to breast and ovarian cancers.

As with the viral infections that can cause it, liver cancer is often a silent disease. Symptoms typically result only when the cancer grows to a size that cannot be cured by simple surgery or when it spreads to other organs. After that point, it cannot be cured.

The symptoms include pain in the upper right side of the abdomen, possibly extending to the back and shoulder; a swollen abdomen; weight loss; loss of appetite and feelings of fullness; weakness or fatigue; nausea and vomiting; fever; and jaundice, evidenced by yellowing of the skin and eyes and by dark urine.

People at high risk of developing liver cancer are not likely to want to wait until they have symptoms to find out that cancer -- most likely advanced cancer -- is the cause.

FLAWS IN SCREENING

Far better to find a liver cancer while it is still a silent disease, because early detection

is crucial. Liver cancer grows quickly, doubling in size every four months.

There is still no completely accurate screening test for liver cancer. A blood test for alphafetoprotein (AFP) is sometimes used, though other conditions, including noncancerous liver diseases, can cause AFP levels to increase.

Abdominal ultrasound, a noninvasive test that does not involve exposure to radiation or dyes, can sometimes reveal an early liver tumor. A CT scan, with or without a dye, uses X-rays to produce cross-section images of the liver, and an MRI can create a similar image.

If a suspicious lesion is found, a biopsy can determine whether it is cancer. If the liver is not cirrhotic and the tumor is small, confined to one lobe of the liver and not near a main artery, vein or bile duct, surgery can be curative.

If the cancer is more advanced, treatments like chemotherapy, radio frequency ablation and alcohol injection into the tumor can slow its progress. The surest cure for an early liver cancer is a liver transplant. The patient's entire liver is removed and replaced with a healthy liver from a cadaver or a lobe from a living donor. Because the liver regenerates, the donor and recipient soon have full-size livers.

About 18,000 patients are waiting for liver transplants, but only 4,000 cadaver organs become available each year. Often while patients wait for donor organs, their cancers become too large to be cured by transplants.

Jane Brody covers science and biology for The New York Times.

2. Liver Transplants June 30, 2006 Author: Lemi Luu, MD, Staff Physician, Section of Emergency Medicine, Yale-New Haven Hospital

Background

Application and success of orthotopic liver transplantation (OLT) has continued to grow, and liver transplantation has become accepted therapy for several causes of irreversible liver disease. As of 2005, 76,575 liver transplants had been reported to the United Organ Sharing network since it created a national database in 1988. In 2005, 6,444 liver transplants were performed and 17,645 patients were on the waiting list for transplantation. With the increased number of transplants, chances are greater that a transplant patient will present to the ED. Basic knowledge of medical care involved in treatment of the transplant patient will assist ED physicians in evaluation.

The most common indications for liver transplantation in the United States are hepatitis C virus (30%) and alcoholic liver disease (18%). Others include idiopathic/autoimmune liver disease (12%), primary biliary cirrhosis (10%), primary sclerosing cholangitis (8%), acute liver failure (7%), hepatitis B virus (6%), metabolic liver disease (eg, inborn errors of metabolism) (3%), cancer (3%), and others (3%). Biliary atresia is a common indication in pediatric patients. Chances of survival following orthotopic liver transplantation are good, with a 5-year survival rate of 72%. The most common causes of death in liver transplant patients (beyond the early in-hospital transplant period) are infection, rejection, and malignancy.

3. Regular Surveillance for Hepatocellular Carcinoma Improves Survival

Katherine Kahn, DVM July 31, 2006 (Boston) World Transplant Congress 2006: Abstract 776. Presented July 26, 2006. J Hepatol. 2006 Jun 23; [Epub ahead of print]

Routine surveillance for hepatocellular carcinoma (HCC) in patients with cirrhosis results in earlier diagnosis of HCC, improves access to liver transplantation, and improves survival times, a new study reveals. Richard Stravitz, MD, associate professor of medicine in hepatology at the Virginia Commonwealth University in Richmond, presented the findings here at the World Transplant Congress.

"Before liver transplantation there wasn't much you could do with a diagnosis of HCC," Dr. Stravitz told Medscape. "Now that we have liver transplantation, the question is whether surveillance detects cancers earlier so that we can transplant patients and have improved outcomes."

To examine this further, Dr. Stravitz and coinvestigators retrospectively reviewed the records of 296 patients with cirrhosis and HCC that had been diagnosed and treated between 1997 and 2005 at the Virginia Commonwealth University Medical Center and its Veterans Affairs affiliate. Of these patients, 86% were men, 62% were white, and 76% were younger than 65 years.

The researchers assigned patients to 1 of 3 groups, representing different levels of quality of surveillance. The standard-of-care surveillance group included patients who had received an ultrasound or other abdominal imaging at least once in the year prior to HCC diagnosis. The substandard surveillance group included patients who were known to have cirrhosis but did not undergo imaging in the year prior to a HCC diagnosis. The unrecognized cirrhosis group included patients who received no surveillance prior to a HCC diagnosis.

The majority of patients (63%) had underlying hepatitis C as the cause of cirrhosis, with 41% having alcohol abuse as a contributing factor in addition to hepatitis C. Eleven percent had alcoholic cirrhosis and 10% had nonalcoholic steatohepatitis or cryptogenic cirrhosis. Nine percent had cirrhosis from other causes, and 7% had cirrhosis from hepatitis B virus.

Half of the patients had stage I (9%) and stage II (41%) HCC at time of diagnosis, while half had stage III (19%) and stage IV (31%) HCC.

The quality of surveillance was strongly linked to tumor stage at diagnosis. Whereas almost 70% of patients who underwent standard-of-care surveillance had stage I or II HCC at initial diagnosis, only 35% of those who received substandard surveillance had stage I or II. "Still, even substandard surveillance was better than no surveillance, since fewer than 20% of patients with unrecognized cirrhosis had HCC within Milan criteria at diagnosis," Dr. Stravitz said during his presentation.

Not surprisingly, survival was closely linked with the tumor stage at diagnosis, with mean survival for stage I patients near 60 months and decreasing to a mean of 26 months for stage II, 14 months for stage III and 5 months for stage IV.

Quality of surveillance also significantly correlated with whether a patient underwent liver transplantation. While 32% of the standard-of-care group received liver transplants, 13% of the substandard surveillance group and 7% of the group that had no surveillance received liver transplants ($P < .001$).

Those patients who underwent liver transplantation ($n = 60$) had a much greater increase in mean survival time compared with those who did not receive liver transplants ($n = 205$), with 81% of those receiving transplants having a mean survival of 3 years vs 12% for those not transplanted ($P < .001$).

Survival also correlated significantly with quality of surveillance. "Mean 3-year survival

in patients who received standard-of-care surveillance was 40% as compared to 27% in those with substandard surveillance, but only 12% in patients with unrecognized cirrhosis," Dr. Stravitz said.

Session cochair William Chapman, MD, commented to Medscape, "Even in our best medical centers, surveillance programs fail frequently. Even among transplant centers and physicians that treat patients with liver disease, we do not have a systematic approach to surveillance." Dr. Chapman is chief of the abdominal transplantation section at Washington University School of Medicine in St. Louis, Missouri.

"The big deal is catch them early so they are still candidates for a curative therapy which is transplantation," said Alan Hemming, MD, session cochair and chief of the division of transplantation and hepatobiliary surgery at the University of Florida in Gainesville. "But it's hit or miss ~ even in our program. Although we apply set criteria and patients get screened at set intervals, that interval may not be adequate."

Dr. Stravitz and colleagues were surprised to find that more than 80% of patients who did not receive surveillance did have laboratory markers for cirrhosis that went unrecognized. "The bottom line is if a physician sees laboratory abnormalities in a patient such as thrombocytopenia, low platelet count, an AST/ALT ratio of greater than 1 ~ and these may be subtle ~ then that patient needs to be referred for surveillance," he told Medscape.

The study was independently funded. The authors report no relevant financial relationships.

4. The contributions of hepatitis B virus and hepatitis C virus infections to cirrhosis and primary liver cancer worldwide. Perz JF, Armstrong GL, Farrington LA, Hutin YJ, Bell BP. Centers for Disease Control and Prevention, National Center for Infectious Diseases, Division of Viral Hepatitis, Epidemiology Branch, Atlanta, GA 30333, USA.

BACKGROUND/AIMS: End-stage liver disease accounts for one in forty deaths worldwide. Chronic infections with hepatitis B virus (HBV) and hepatitis C virus (HCV) are well-recognized risk factors for cirrhosis and liver cancer, but estimates of their contributions to worldwide disease burden have been lacking. **METHODS:** The prevalence of serologic markers of HBV and HCV infections among patients diagnosed with cirrhosis or hepatocellular carcinoma (HCC) was obtained from representative samples of published reports. Attributable fractions of cirrhosis and HCC due to these infections were estimated for 11 WHO-based regions. **RESULTS:** Globally, 57% of cirrhosis was attributable to either HBV (30%) or HCV (27%) and 78% of HCC was attributable to HBV (53%) or HCV (25%). Regionally, these infections usually accounted for >50% of HCC and cirrhosis. Applied to 2002 worldwide mortality estimates, these fractions represent 929,000 deaths due to chronic HBV and HCV infections, including 446,000 cirrhosis deaths (HBV: n=235,000; HCV: n=211,000) and 483,000 liver cancer deaths (HBV: n=328,000; HCV: n=155,000). **CONCLUSIONS:** HBV and HCV infections account for the majority of cirrhosis and primary liver cancer throughout most of the world, highlighting the need for programs to prevent new infections and provide medical management and treatment for those already infected.

PMID: 16879891 [PubMed - as supplied by publisher]

5. Systemic Therapy of Advanced Hepatocellular Carcinoma: How Hopeful Should We Be? Andrew X. Zhu Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston, Massachusetts, USA The Oncologist, Vol. 11, No. 7, 790-800, July 2006; doi:10.1634/theoncologist.11-7-790

<http://theoncologist.alphamedpress.org/cgi/content/full/11/7/790>

Correspondence: Andrew X. Zhu, M.D., Ph.D., Tucker Gosnell Center for Gastrointestinal Cancers, Massachusetts General Hospital Cancer Center, 100 Blossom Street, Cox 640, Boston, Massachusetts 02114, USA. Telephone: 617-724-0786; Fax: 617-724-3166; e-mail: azhu@partners.org. Received April 3, 2006; accepted for publication May 10, 2006.

ABSTRACT Worldwide, hepatocellular carcinoma (HCC) is the fifth most common cancer and the third most common cause of cancer-related death. In the U.S., 18,510 new cancers of the liver and intrahepatic bile duct are expected in 2006, with an estimated 16,200 deaths. The incidence rates for HCC in the U.S. continued to rise steadily through 1998 and doubled during the period 1975-1995. Unresectable or metastatic HCC carries a poor prognosis, and systemic therapy with cytotoxic agents provides marginal benefit. A majority of HCC patients (>80%) presents with advanced or unresectable disease. Even for those with resected disease, the recurrence rate can be as high as 50% at 2 years. Because of the poor track record of systemic therapy in HCC, there has been a sense of nihilism for this disease in the oncology community for decades. However, with the arrival of newly developed molecularly targeted agents and the success of some of these agents in other traditionally challenging cancers, like renal cell carcinoma, there has recently been renewed interest in developing systemic therapy for HCC. This review attempts to concisely summarize the historical perspective and the current status of systemic therapy development in HCC.

HepTalk is a project of the Migrant Clinicians Network and Community Health Education Concepts. HepTalk is funded by the Centers for Disease Control and Prevention. The goal of HepTalk is to help clinicians serving migrants and recent immigrants engage in productive discussions about hepatitis risks with their clients and help them make prevention plans. The HepTalk listserv is a support service for clinics participating in the project. This is a post-only listserv and postings will come from HepTalk staff about once a month. If others at your clinic would like to be on the listserv, or if you have questions about the listserv or resources listed here, or if you would like to add something to the posts, please contact Kathryn Anderson, HepTalk training and education coordinator and listserv administrator, at dempander@earthlink.net. You can also contact the listserv administrator if you would like to unsubscribe from the list.