

California Pacific Researching New Medications for Hepatitis B and C



Near-Term Hepatitis C Treatments

Trying to find a hepatitis C therapy with better long-term cure rates, California Pacific is testing PEG interferon monotherapy and combination therapy with ribavirin. More than 60 patients on PEG interferon have been evaluated, all of whom have had promising results.

Approximately 66% of patients treated with PEG interferon lose the hepatitis C virus RNA during treatment but some relapse when treatment is stopped. Overall, there is a 30% to 35% sustained response rate.

"Combination therapy with PEG interferon and ribavirin is encouraging and current data shows it may have a higher sustained response rate than PEG interferon monotherapy," explains Gish.

Future Possibilities

Longer-term treatment prospects being researched for hepatitis C include antiviral and immune therapies. Potential targets under exploration include NS3 protease, NS3 helicase and NS5B polymerase. Other antiviral developments include:

- Alpha glucosidase inhibitor that blocks viral packaging;
- Ribozymes that are synthetically engineered to act as "molecular scissors," cleaving target RNA to kill the virus and leaving it unable to produce more;
- VX-497—an IMPDH inhibitor in clinical trials that works similarly to ribavirin but may be more potent and have fewer side effects.

Immune therapies, which seek to directly alter the immune system or its harmful effects may also offer a treatment for hepatitis C. These therapies include: Interleukin 10— a treatment shown to reduce or block fibrosis in early studies; CD81 inhibition to block viral entry of hepatitis C; and Maximine in combination with interferon.

Ongoing Clinical Trials Offer Promising Therapies

With nearly a dozen trials underway to examine the effects of new drugs and drug combinations on hepatitis B and C, California Pacific Medical Center is helping to uncover innovative treatments for these viruses that result in better outcomes and fewer side effects.

"From our trials, it appears that PEG interferon with or without ribavirin is the next promising advance in treating hepatitis B and C," says Medical Director Robert Gish, MD.

The current standard of care for patients with hepatitis C is immediate treatment with interferon and ribavirin for at least six months. Interferon can prevent or delay the need for liver transplantation by reducing the amount of liver inflammation and scar tissue. The administration of ribavirin in combination with interferon results in a higher sustained response and, according to recent studies, 35% of patients are cured six months after stopping treatment.

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Ribozymes and alpha glucosidase inhibitors are also being investigated for use with hepatitis B and hepatitis C. Other future possibilities include DAPD and L-FMAU, nucleoside analogues in development to inhibit HBV replication.

Hepatitis B and C Research Trials Seek Participants

California Pacific is recruiting for the following research trials. If you are interested in learning more about these trials, further information is available at www.cpmc.org/liver/clinic.htm or through Research Nurse Linda Brooks at 415/202-1504 or brooksl@sutterhealth.org

Current Trials Seeking Enrollees:

1. Study of PEG interferon alfa-2a Monotherapy vs. Combination Therapy for patients with chronic Hepatitis C and HIV
2. Study of Pegasys™ plus Ribavirin, CellCept®, Amantadine or Amantadine plus Ribavirin for patients with chronic Hepatitis C who have not responded to Rebetron
3. Study of Adefovir Dipivoxil for the Treatment of Liver Disease due to Lamivudine Resistant Hepatitis B (HBV) in Liver Transplant Patients
4. Study of 52-weeks Treatment with Adefovir Dipivoxil and Lamivudine for Patients with Chronic Hepatitis B
5. Comparison of Three Doses of Entecavir vs. Lamivudine in Immunocompetent Subjects with Chronic Hepatitis B Infection

Hepatitis B

In comparison to hepatitis C, the hepatitis B virus (HBV) mutates less often, offering the body a better chance to fight it. This decreased mutation activity led to the development of a HBV vaccine to prevent transmission. However, for patients who are already infected with HBV, the vaccine is ineffective. Patients with HBV are typically treated with interferon therapy and after treatment, 40% have a fall in liver enzymes and/or disappearance of HBV DNA according to published studies.

According to Gish, "Patients most likely to respond to interferon are those who have had hepatitis B infection for less than four years, those with elevated liver enzymes or positive HBeAg and Hepatitis B DNA."

Oral medications such as lamivudine, famciclovir can be prescribed to suppress HBV infection or reduce post-transplant recurrence of HBV, however Gish stresses that these medications do not cure the disease. Sometimes, these medications are used with interferon because combination therapy has been suggested to increase the chance of a cure and decrease virus mutations.

New Therapies in Research

Because interferon is not always successful in controlling HBV and can be associated with severe flu-like symptoms, research is underway to find new therapies. Among the hepatitis B trials at California Pacific Medical Center include further research of nucleoside analogues—such as lamivudine—that may inhibit HBV replication.



Development of Fatty Liver

Steatosis and steatohepatitis are most commonly associated with obesity and in some people, even a small amount of excess body fat can increase the amount of fat stored in the liver. Under normal conditions, fat from the diet is metabolized by the liver and other tissues. If the amount of fat exceeds the body's requirement, abnormal fat accumulations may develop in the liver, causing an increase in liver enzymes and inflammation. This inflammation can cause scarring and hardening of the liver (cirrhosis) and results in decreased liver function.

While obesity is a major contributor to fatty liver, other causes include Hepatitis C virus, Wilson's disease, medications, chemical compounds, poor nutrition, hyperlipidemia or endocrine disorders.

Specific medications and substances that can cause fatty liver include alcohol, amiodarone, methotrexate, high doses of vitamin A, tetracycline, cortisone, phosphorus, prednisone and carbon tetrachloride. Of these substances, alcohol is by far the most common cause of fatty liver and even as little as one glass of wine or beer a week may contribute to this condition.

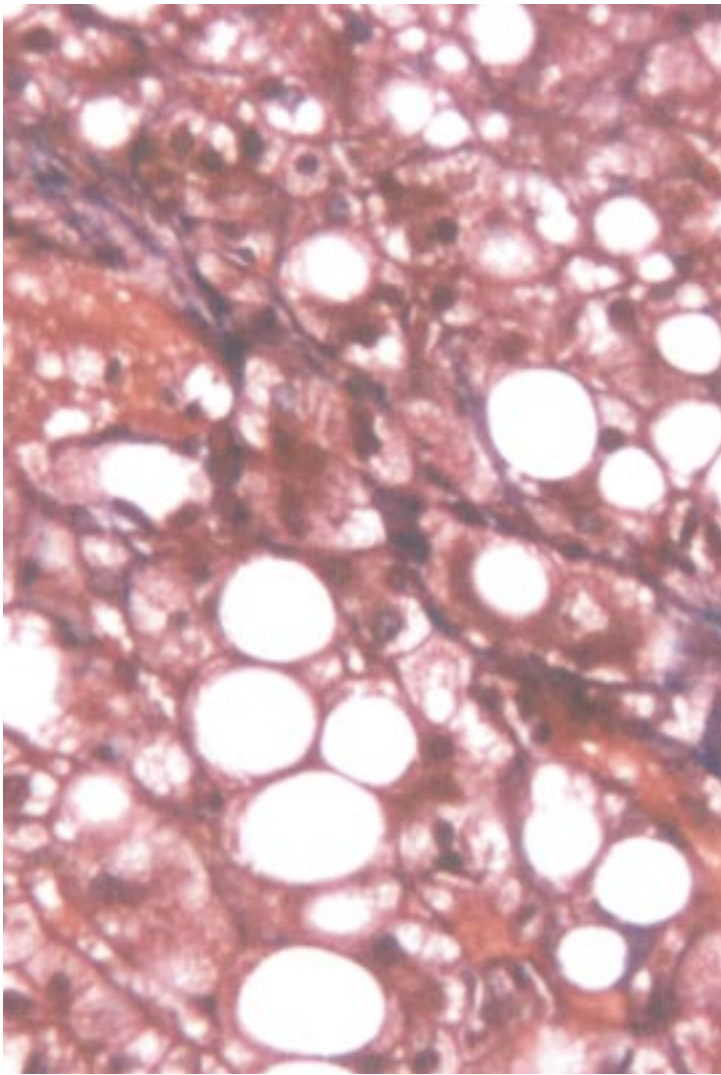
Controlling Fatty Liver

Treatment of fatty liver is determined based on its cause and typically, fat is decreased through weight loss, diabetes control or elimination of the offending substance or drug. By stopping alcohol consumption, the rate of metabolism and secretion of fat will increase, helping to reduce fat accumulations. Likewise, the removal of medications or chemical compounds associated with fatty liver can reverse the condition.

While drug therapy is not yet available for fatty liver, studies are underway on medications such as Actigall. In early research, this drug appears to reduce liver damage in cases of steatohepatitis but until data is confirmed, weight loss and elimination of alcohol and offending substances are critical. For more information on fatty liver or a patient handout, contact Dr. Robert Gish at 415/202-1530 or email: gishr@sutterhealth.org.

Tips to Avoid Fatty Liver

- Follow a low-fat and low-cholesterol diet
- Exercise regularly to maintain an ideal weight
- Do not drink alcohol to excess
- Review medications to ensure that they aren't hepatotoxic
- Have blood sugar, cholesterol and triglyceride levels checked regularly



MICROSCOPIC APPEARANCE OF FATTY LIVER

Recognizing Fatty Liver: Its Symptoms, Causes and Treatment

Fatty liver refers to the infiltration of triglycerides and other fats into the liver cells, causing abnormal liver tests, inflammation and possibly permanent liver damage when left untreated. Because of improved imaging tests and frequent blood testing, fatty liver is now being diagnosed more frequently and non-alcoholic steatohepatitis (NASH), a form of fatty liver, has become the third most common liver disease in U.S. adults who are evaluated for increased liver enzymes.

While patients don't usually experience symptoms from fatty liver, it can be detected through an ultrasound or CT scan and an elevation in liver chemistries. Occasionally, patients may experience fatigue or a dull pain in the upper right abdomen. To make an absolute diagnosis, a liver biopsy is performed.

If the liver enzyme tests and liver biopsy show inflammation and fibrosis, steatohepatitis is diagnosed. Patients with steatohepatitis have a 50% risk of developing cirrhosis that may lead to liver transplantation if end-stage liver disease develops. Steatohepatitis may be associated with alcohol use, but if the liver damage is unrelated to alcohol, the condition is called non-alcoholic steatohepatitis (NASH).

Fatty liver without inflammation—a more common diagnosis—is called steatosis and altogether, about 25% of the general population is affected by this form of fatty liver.

California Pacific's Liver Disease Management & Transplant Program

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California Pacific Medical Center offers one of the leading adult liver disease management and transplant programs with outcomes ranked at the top among U.S. transplant centers. By working in partnership with Northern California and Nevada gastroenterologists and internal medicine physicians, we provide clinical trials on hepatitis B and C, liver cancer and transplantation as well as complete evaluation and assessment for liver transplantation and end-stage liver disease.

Through more than 20 outreach clinics in Northern California and Nevada, we bring our specialists to local communities and support our comprehensive patient care with the latest advances and research. Since the liver program's inception in 1988, we have performed more than 880 liver transplants. We presently evaluate nearly 400 patients and perform more than 60 transplants annually, and continue to grow as a result of our excellent results and patient friendly services.

To learn more about our liver transplant services, please return the enclosed response card.

Robert Gish, MD, Medical Director
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Transplant Assessment Guide Available

California Pacific Medical Center's Liver Disease Management & Transplant Program has available a Liver Transplant Assessment Guide for use in determining a patient's Child-Turcotte Pugh (CTP) score and liver transplant status. This one-page guide includes a chart for physicians to calculate the severity of liver disease and an explanation of current listing criteria for transplantation.

For a copy of the Liver Transplant Assessment Guide, contact Laura Miyashita at 415/923-3596 or by email at miyashl@sutterhealth.org.



The Liver Disease & Transplant Program

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