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The Specter of Liver Disease

NETWORK

HCH providers see many patients with liver disease, mainly secondary to hepatitis C (HCV). While the incidence of newly acquired HCV infection has decreased in the United States, over 4 million Americans are estimated to have been infected.¹ A disproportionate number of homeless people (22%–53%) have the virus^{2,3}– indeed, incarcerated and homeless individuals are not included in the National Center for Health Statistics count and are thought to number another million.⁴ Clinicians find it difficult to get patients the special care they need when they lack stable housing, engage in chronic alcohol or drug use, or are mentally unstable. Many clients progress untreated to end-stage liver disease and fill medical respite facility beds. The following articles discuss the pathophysiology of liver disease, the preponderance of hepatitis among homeless and incarcerated people, and treatment options.

The liver is the body's workhorse — its largest functional organ. Located in the upper right quadrant of the abdomen, the liver is protected by the diaphragm, a connective tissue capsule, and the rib cage. Its dual blood supply consists of one quarter arterial inflow from the aorta and the rest from the portal vein, which provides venous blood rich in nutrients from the intestines. Inside liver lobules, hepatic sinuses are surrounded by sheets of liver cells serviced by a maze of bile ducts and blood and lymph vessels.

This factory of metabolic activity makes bile to aid digestion; changes food into energy; cleanses toxins, old blood cells, and alcohol from the blood; secretes; stores; regulates; synthesizes; and excretes. All is well until a widespread significant insult causes cellular failure or blocks blood flow resulting in portal hypertension, which is the main event in most liver diseases. Fortunately, the liver's functional redundancy is strong enough to maintain its operations on as little as 20% of capacity; the downside is that early disease states are often asymptomatic and unrecognized.⁵

CLIENT EDUCATION HCH clinicians concur that client education about liver disease is an important harm-reduction technique. Chronic alcohol use, intravenous drug use, HIV infection, inadequate personal hygiene, and malnutrition place some homeless people at high risk for liver disease. These clients need to understand the long-term consequences of untreated chronic hepatitis (often contracted through use of contaminated needles): scarring of the liver (cirrhosis), brain and nervous system damage (hepatic encephalopathy), excess fluid in the abdomen (ascites), abnormally enlarged veins in the esophagus that can rupture (esophageal varices), and liver cancer (hepatocellular carcinoma). Emphasis should be placed on:

- Testing for hepatitis B and C;
- Benefits of vaccination against hepatitis A and B;
- Dangers of sharing needles or other drug paraphernalia;
- Need for protection from blood and other bodily fluids during sex, while getting a tattoo, or sharing toothbrushes or razors;
- Abstinence from alcohol and reduction of other drug use; and
- The importance of good nutrition.

SIGNS & SYMPTOMS Jaundice can be one of the first symptoms of liver disease, signaling isolated disorders of bilirubin metabolism (hyperbilirubinemia) or obstruction of the bile ducts (by gallstones, inflammation, infection, or tumors). The 10% to 20% of individuals with acute hepatitis C who present with jaundice are often sicker but resolve sooner and are more likely to experience spontaneous viral clearance than others whose nonspecific symptoms include fatigue, nausea, and vomiting.⁶

Individuals with chronic hepatitis are often asymptomatic and may harbor the disease for 20 years before encountering symptoms that include fatigue, joint pain, burning or prickling sensations, muscle pain, itching, depression, nausea, anorexia, abdominal discomfort, and difficulty concentrating, but seldom jaundice. Those whose disease progresses to cirrhosis are at high risk for serious complications.⁶

How a Normal Liver Works⁵

Digestive Functions

- Secrete bile salts for fat digestion
- Process and store fats, carbohydrates, and proteins absorbed by the intestines
- Process and store vitamins and minerals

Endocrine Functions

- Metabolize glucocorticoids, mineralocorticoids, and sex hormones
- Regulate carbohydrate, fat, and protein metabolism

Hematologic Function

- Store blood temporarily
- Synthesize bilirubin from blood breakdown products
- Synthesize blood clotting factors

Excretory Functions

- Excrete bile pigment
- Excrete cholesterol via bile
- Synthesize urea
- Detoxify drugs and other foreign substances

INTERVENTIONS Individuals with advanced liver disease are very ill and may survive as long as 5 to 10 years without treatment. Concrete steps that health care providers can take to arrest the progression of disease or ameliorate its effects include testing high-risk patients (e.g., those with HIV infection) for HCV, immunization against HAV

and HBV, and encouraging other harm-reduction practices (including abstinence from alcohol, which is like pouring gasoline on a fire⁷). In addition, patients with advanced liver disease who are homeless need assistance with applications for disability benefits, health insurance, and housing (which are often prerequisites of antiviral treatment).

Liver Disorders Commonly Seen by HCH Providers

A variety of pathological conditions inhibit liver function. Among those of particular concern to clinicians serving poor and homeless people in the US are the following:

ABSCESS Liver abscesses are generally associated with abdominal (upper right quadrant) or right shoulder pain, fever, nausea, vomiting, and weight loss. Common causes are:

- **Bacterial cholangitis** (obstruction of bile ducts),
- **Portal vein bacteremia** (following bowel inflammation or organ perforation), and
- *Amebiasis* (infestation with the parasite *E. histolytica*; people at highest risk include immigrants from tropical areas, individuals living in unsanitary conditions, and men who have sex with men).

TRAUMA Liver trauma can be lethal because of heavy blood loss, requiring careful monitoring and often surgical resection.

- **Penetrating injuries** are associated with knife or gunshot wounds; greater missile velocity causes increased damage.
- **Blunt injuries** from falls or automobile accidents can cause lacerations or hematomas under the liver capsule.

TUMORS Primary tumors originating in the liver include hepatic adenomas (benign) and hepatocellular carcinoma (malignant). Most malignant liver tumors are metastatic, spreading directly from adjacent organs by cell migration and seeding onto the liver capsule or via arterial and portal venous blood flow into the liver.

- *Hepatic adenomas* are benign, but must be taken seriously because they may rupture, causing hemorrhage. Nearly 90% occur in women and are associated with oral contraceptive use.⁸
- Hepatocellular carcinoma (HCC) is becoming more common in the US as a complication of HBV, HCV, cirrhosis, and the use of anabolic steroids.

According to Lucinda Yates, RN, patient educator at the University of New Mexico

Medical Center Hepatitis C Treatment Clinic in Albuquerque where HCH clients are referred, "patients with cirrhosis have a 1 in 4 chance of developing HCC every year. So we screen cirrhosis clients at six month intervals with an ultrasound of the liver and an alpha fetal protein tumor marker to catch tumors while they are still small and localized."

Magnetic resonance elastography (MRE) has been shown to be highly accurate in differentiating between benign and malignant liver tumors, possibly eliminating the need for biopsy.⁹

"The liver has become my deep interest because all my clients are so sick and liver disease is so prevalent among them."
— Tina Carlson, APRN, BC, Clinical Nurse Specialist, Psychiatry, Albuquerque Health Care for the Homeless, Inc.

HEPATITIS Inflammation of the liver (hepatitis) may be caused by viruses, toxins, drugs, alcohol, or other chemicals. If hepatitis is not spontaneously cleared from the body or treated, it can progress to cirrhosis.

Acute viral hepatitis is classified as hepatitis A through E. In the United States, HAV, HBV, and HCV are the most prevalent types. Hepatitis D (delta) only co-infects with HBV in the presence of hepatitis B surface antigen.

- *HAV* is transmitted via the small intestine from contaminated food or water. Acute hepatitis A can be treated with gamma globulin and inactivated HAV vaccine.
- HBV, spread through contact with infected blood, blood products, and other body fluids, is more serious. Children in the US are routinely vaccinated against HBV. Acute HBV is more common among adults. Hepatitis B vaccine is available for all age groups to prevent HBV infection. After exposure, HBV vaccine and HB immune globulin should be given concurrently for best protection.
- Acute **HCV** is seldom seen clinically because it is mostly asymptomatic. As

mentioned previously, individuals who are the sickest and who may also exhibit telltale jaundice tend to recover completely. "If 100 people have acute hepatitis C, 30 will clear the virus completely on their own. That's the good news," Yates observes.

Chronic viral hepatitis, however, can be a much greater health challenge. Patients who have not cleared HBV or HCV within 6 months are considered to have chronic disease. "Most patients never know they have hepatitis until they develop cirrhosis," says Yates. "Of the 70% who develop chronic infection, 20% will progress to cirrhosis with significant risk for major complications that include ascites, liver cancer, varices, encephalopathy, and end-stage liver disease."

Because concurrent infections are more serious, susceptible patients need to be vaccinated against HAV and HBV. There is currently no vaccine for HCV. Treatment modalities for chronic viral hepatitis are difficult for patients to endure, but outcomes are often very good.

The newly revised treatment algorithm for chronic HBV management relies on better understanding of treatments, more sensitive molecular diagnostic tests, and the licensure of new therapies to suppress serum HBV DNA to low or undetectable levels. Preferred first-time treatment choices are entecavir, peginterferon alfa-2a, and tenofovir.¹⁰

Treatment for HCV infection is formidable, requiring strong patient motivation and commitment to adherence. Weekly injections of long-acting pegylated interferon are reinforced with daily oral doses of ribavirin; the two drugs act synergistically in patients to achieve sustained virologic response (SVR).^{7,11,12} The course of treatment is generally 24 to 48 weeks, depending on the patient's disease genotype, or longer if suspended to clear up side effects which include:^{7,11,12}

• Flu-like symptoms (fever, headache, fatigue, joint and muscle pain)

- Respiratory tract manifestations (bronchitis, pneumonia)
- Hematologic abnormalities (low blood count)
- Neuropsychiatric symptoms
- Gastrointestinal symptoms
- Dermatologic manifestations (severe itching)
- Overwhelming fatigue

Treatment outcomes are mixed. Individuals with HCV genotype 1 (75% of HCV-infected patients in the US) often experience treatment resistance over a 48-week course of therapy, obtaining a SVR rate of 40% to 50%; those with genotypes 4 to 6 have similar responses.¹³ Patients with genotype 2 or 3 have better outcomes over 24 weeks; some achieve satisfactory results with only a 12- to 14-week course of medication.⁷

Patients who do not achieve viral clearance may at least achieve stabilization or reversal of their liver damage during therapy.⁷ "All therapy should be individualized; some clients may continue therapy [beyond the standard course]," adds Yates.

CIRRHOSIS This chronic and progressive condition is marked by scarring (fibrosis) of liver tissue and the formation of nodules that interrupt vascular and lymphatic flow and block bile duct channels. Viral hepatitis and alcohol and drug toxicity are the primary causes, although other liver insults may also lead to cirrhosis. Chalasani and colleagues working with the Drug-Induced Liver Injury (DILI) Study Group have recently shown antibiotics to be "the single largest class of agents that cause drug-induced liver injury"; antimicrobials account for 45.5% and central nervous agents, for 15% of DILI.¹⁴

Even though cirrhosis is irreversible, residual liver function can be maximized through a good diet high in protein, rest, and careful monitoring to minimize complications:

• *Malnutrition*, one of the most serious complications of cirrhosis, should not be allowed to accelerate the patient's decline. In addition to the metabolic imbalance induced by cirrhosis, the following side effects can diminish nutrient intake: nausea and anorexia (often alcohol-induced), early satiety, abdominal compression in response to ascites, change in the source of dietary calories, and altered gastric motility (slower

emptying of the stomach).^{15,16} Dietary assessment, use of preventive dietary measures, and correction of dietary deficits can go a long way toward improving disease control and patient quality of life.

- **Portal hypertension** is the increased pressure in portal circulation that results from decreased blood flow in the liver due to fibrosis and ongoing degeneration of tissue. The corresponding venous congestion in gastrointestinal track drainage leads to dilatation of the esophageal, abdominal wall, and rectal veins. Increased venous pressure makes veins swell and distend (varices), creating risk of rupture and lifethreatening hemorrhage.
- Ascites result from accumulation of peritoneal fluid in the abdomen exacerbated by sodium retention and osmotic plasma pressure. Increased abdominal pressure and liver compression, ineffective shallow breathing and impaired gas exchange add to patient discomfort. Although usually related to liver disease, in 15% of patients ascites may be secondary to peritoneal carcinomatosis, peritoneal tuberculosis, or heart failure.⁶
- Hepatic encephalopathy is caused by the inability of a diseased liver to metabolize and excrete ammonia as urea. This results in increasing concentrations of ammonia in the blood stream and cerebrospinal fluid. An associated continuum of neuropsychiatric symptoms range from reduced alertness to confusion to stupor, seizures, and coma.

ALCOHOLIC LIVER DISEASE Ingestion of large quantities of alcohol can lead to alcoholic fatty liver (90%) and alcoholic hepatitis (10%–35%), which are reversible with complete abstinence and good nutritional support.¹⁷ Goals of medical nutrition therapy include:

- Adequate calories, protein, and other nutrients for hepatocyte regeneration;
- Frequent, small meals to compensate for reduced glycogen storage;
- Gradual loss of weight (in obese patients) through diet, exercise, and behavior modification; and
- Short bouts of aerobic activity (walking and lifting weights) to increase muscle mass.

Alcoholic liver disease leads to chronic alcoholic hepatitis; 70% of patients may eventually develop cirrhosis.¹⁸ Of 27,530

deaths in the US attributable to chronic liver disease and cirrhosis in 2005, 12,928 (47%) were due to alcoholic liver disease.¹⁹

FATTY LIVER DISEASE One of the most common metabolic diseases of the liver, this condition is caused by infiltration of lipids (triglycerides, cholesterol, phospholipids), resulting in liver enlargement, stenosis, and decreased function. In addition to alcoholic liver disease, other predisposing factors are obesity, diabetes mellitus, and various nutritional conditions.

Lucinda Yates, RN, of the UNM Hepatitis Treatment Center, says, "We see lots of folks with fatty liver disease, and before they can be considered for Hep C therapy, they often have to lose as much as 50 pounds." Indeed, research shows that hepatic steatosis (fatty change in cells) affects 40% to 86% of patients with chronic HCV. Concurrent nonalcoholic fatty liver disease, HCV, and insulin resistance have clinical implications for increased disease progression, decreased response to viral treatment, and elevated risk of hepatocellular carcinoma.²⁰

LIVER TRANSPLANT Progressive liver disease eventually reaches end-stage liver disease (ESLD)—a point when the organ can no longer function effectively as a result of cirrhosis and related complications. At this stage the only solution is a liver transplant.

"Often these patients are so sick that they must have respite care," says **Robert Donovan**, **MD**, a physician with the HCH Cincinnati Health Network. "The University of Cincinnati Hepatitis Program insists that clients who need a liver transplant have stable life situations. Our staff tries to help patients accomplish those life changes, but it's a very difficult road."

Transplant Centers also require 6 months of documented abstinence from alcohol and other drug use and substance abuse treatment in order to be placed on the transplant waiting list. In 2005, more than 17,000 people in the US were awaiting a liver transplant.²¹

HCV Care for Homeless Clients

Hepatitis C is often called a silent disease because of its elusive nature. The most common blood-borne illness in the United States, HCV is asymptomatic but deadly for growing numbers of Americans; over 4 million have been infected with the virus and over 3 million have chronic HCV infection. These numbers do not include incarcerated and homeless people, accounting for an additional million people who are disproportionately affected by the disease.^{1,2,4,7}

Four to five times more widespread than HIV infection, chronic HCV can progress to cirrhosis, the most common reason for liver transplantation, and results in 8,000 to 12,000 deaths annually.^{7,11} Since the prevalence of HCV is highest among people under 50 years of age, the disease burden is bound to increase over the next 10 to15 years.¹¹ These factors make HCV a major public health problem in the United States.^{17,11-13}

"At the Tom Waddell Health Center in San Francisco, about one-third of our primary care patients have HCV," says Medical Director **Barbara Wismer, MD**. "We also have a large percentage of HIV patients, 50% of whom have comorbid HCV." Unlike HIV infection, however, which eventually causes severe illness in all those infected, many millions of people with chronic HCV will live full lives with few consequences of the disease, observes **Barry Zevin, MD**, also at Tom Waddell.⁴

NATURAL HISTORY OF HCV The reasons why some people with chronic HCV infection remain asymptomatic for 20 years and why 80% of infections do not result in progressive liver disease are not yet fully understood. Nevertheless, clinical investigators point to increased understanding of the natural history of the disease, its risk factors, and infection levels found among various demographic groups.²²⁻³⁰ Factors associated with greater morbidity in people with chronic HCV include:^{7,11,12}

- Male gender
- Older age at initial infection
- Concurrent HBV infection
- Immunocompromise (HIV infection)
- Alcohol use (30 g/day for men, 20 g/day for women)

Given the serious consequences of hepatitis C infection for public health, for the health care system in general, and for medically underserved people in particular, determining the best interventions for infected individuals with different acuity levels is a high priority.

According to Diana Sylvestre, MD, Executive Director of Organization to Achieve Solutions in Substance-Abuse (OASIS) in Oakland, CA, developing a plan of care is initially a matter of triage and figuring out how to identify and help folks who are in the most danger as well as teaching everyone infected with HCV how to help themselves. "It's about empowerment," she says.

EDUCATION & SELF HELP Helen Speer is just about halfway through HCV antiviral therapy and is having a really tough time, probably exacerbated by her co-occurring bipolar disease. She says, "It's

very important for the patient to know as much about his or her disease and treatment as possible and have it repeated again at various intervals."

"I had no idea how hard the treatment would be.
I'm really thankful to have this chance to get well—but it took
9 months just to get my viral load down.
I'll be on interferon for at least 21 months. And the shots aren't getting easier. I just don't feel like me anymore."
— Helen Speer, hepatitis C patient

Care providers can start by giving patients information about HCV transmission and how to prevent it, the stage of their illness, what symptoms to expect, how to prevent progression, and options for antiviral treatment. To prevent complications and progression of liver disease:⁴

- Suggest vaccination against hepatitis A and B.
- Advise abstinence from alcohol, which increases liver inflammation and decreases the effectiveness of therapy.
- Inform patients about substance abuse treatment, safer injection practices, and how to obtain harm-reduction services including access to sterile syringes.
- Recommend testing for HIV because co-infection speeds progression of liver disease.
- Help patients avoid hepatotoxic medications.

"The OASIS approach is a little different," says Sylvestre. "We emphasize that recovery is a process rather than an event. We don't exclude patients from HCV treatment simply because they are using drugs. If they demonstrate their commitment by attending our education program every week, we will offer HCV treatment even to active injectors. It's not that we don't address drug use; it's a matter of doing both simultaneously. And sometimes success with HCV precedes success with recovery."

Sylvestre continues: "We like to get the word out and educate. Hepatitis C University (<u>www.hcvu.org</u>) is an education and mentoring program for medical professionals, and we have parlayed our success with peer-to-peer counseling³¹ into an anonymous phone chat program, HepC:411." (1–800-391–1709, every Tuesday from 7:00 to 7:30 pm PST, Bridge code 888185).

DIAGNOSIS Following the 2002 National Institutes of Health Consensus Development Conference statement on the management of hepatitis C, which recommended that active injection drug users not be excluded from viral therapy, the OASIS Clinic begins HCV care with diagnostic testing:^{7,32}

- Base screening on risk status (Most infected individuals only have nonspecific symptoms.)
- Antibody-mediated immunoassay (75% of antibody-positive patients have chronic HCV; the rest have spontaneously cleared their infection.)
- Polymerase chain reaction test to differentiate antibody-positive patients

- *Liver biopsy* to check for liver damage (Typically patients require treatment only if the disease is causing significant liver damage or symptoms are severe.)
- Blood test (Determine HCV genotype as the basis for selecting HCV medication dosage and length of treatment.)

ANTIVIRAL TREATMENT As discussed previously, HCV therapy relies on a combination of pegylated interferon reinforced by ribavirin and has an array of difficult side effects. Perhaps the most difficult are fatigue and insomnia because they wear the patient down. Psychiatric reactions related to interferon occur in 33% of patients and may include severe depression, mania, and psychosis.⁷ Because of these side effects some clinicians hesitate to treat HCV patients with co-occurring mental illness; however, research indicates that with monitoring and individualized dosing, such patients can achieve outcomes similar to those of HCV-infected individuals without mental illness.^{7,33}

In addition to onerous side effects, interferon treatment is expensive (typically \$15,000–\$25,000 per treatment course) but the drugs are generally available free or at reduced cost from medical assistance programs for uninsured and low-income patients.⁷

"Our patients—particularly those who are marginalized and needy without a circle of friends and family—need to hear messages of hope," adds Sylvestre. "Regular moral support within the structure of an addiction treatment program can go a long way toward helping a patient stay the course of treatment and reap the best possible results."

ADAPTING OASIS TO A HOMELESS SHELTER Catherine

Rongey, MSHS, MD, is a former Robert Wood Johnson Scholar and current GI Fellow at the University of California. Her two-year RWJ fellowship focused on a community sensitive participatory health care research project modeled in part on the OASIS program. "I worked with homeless patients at the HCH Weingart Center on Skid Row in

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Los Angeles to determine the seroprevalence of HCV in a primary care setting," explains Rongey. "We went to Oakland to observe the OASIS program and used many of their methods, which are so very empowering for patients. The Weingart Center has the benefit of supportive residential services that are extremely important to individuals who are so ill that shelter status becomes a tenuous part of their road to recovery."

Managing Side Effects of Antiviral HCV Treatment ⁷	
SIDE EFFECT	MANAGEMENT STRATEGIES
Flu-like symptoms	Increased water intake, acetaminophen, nonsteroidal antiinflammatory medications
Nausea	Adjustment to ribavirin dosing schedule, H2 blockers, promethazine
Fatigue	Light exercise, more water, improved sleep hygiene
Insomnia	Improved sleep hygiene, diphenhydramine, trazodone, amitriptyline
Skin problems	Emollients, increased water intake
Depression	Antidepressant medication (e.g., SSRIs [Prozac, Paxil, Zoloft, Lexapro, Effexor])
Mania	Mood-stabilizing agents (e.g., olanzapine, quetiapine, lithium)
''Brain fog''	Increased water intake, improved sleep hygiene
Anemia	Reduced ribavirin dosage, erythropoietin
Neutropenia	Reduced interferon dosage, granulocyte colony- stimulating factor
Thrombocytopenia	Reduced interferon dosage, interleukin-11
Hypothyroidism	L-thyroxine

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For a related Homeless Health Care Case Report: Decompensated Chronic Liver Disease with Comorbid Treatable Aplastic Anemia in a Homeless Adult Male, see the National Health Care for the Homeless Council's website: www.nhchc.org/CaseReportLiverDisease121208.pdf

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