Hepatitis C: everyone deserves a chance at cure

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New all-oral therapies for hepatitis C can permanently cure over 90 percent of infections in the United States. Health care providers in North Carolina must recognize patients who should be screened for hepatitis C infection, counseled about lifestyle interventions, and then linked to appropriate care for possible treatment with these remarkable new medications.

Many North Carolinians suffer from hepatitis C

It is estimated that nearly 2 percent of the U.S. population, or 3-4 million individuals, have been infected with hepatitis C[1,2]. In North Carolina, approximately 150,000 people may be living with hepatitis C infection. These figures likely underestimate the actual incidence of hepatitis C infection, since certain at-risk populations were not included in the major national epidemiologic studies. For many years, the impact of hepatitis C on morbidity and mortality has also been underestimated. Complications of hepatitis C include progression to cirrhosis, liver failure, and hepatocellular carcinoma (HCC). Chronic hepatitis C infection is driving the increased incidence of hepatocellular carcinoma in the U.S. The importance of hepatitis C as a public health concern is highlighted by recent data demonstrating that the annual age-adjusted mortality rate for hepatitis C is higher than for HIV infection[3].

All Baby Boomers should be tested for HCV

Even more striking is that over half of the patients infected throughout the U.S. are unaware that they have hepatitis C, despite the availability for more than 20 years of sensitive and specific tests for the diagnosis of this chronic viral disease. Until recently, screening strategies for hepatitis C focused on ascertainment of risk factors for infection (prior history of injecting drug use or blood transfusion prior to 1992 as the major risks for infection). However, the CDC and the U.S. Preventative Services Task Force have augmented this risk-based screening strategy with additional recommendations based upon the high prevalence of hepatitis C in the "Baby Boomer" generation: Any person born between 1945 and 1965 should have a one-time anti-HCV screening test for hepatitis C[4]. Patients testing positive should then be tested for HCV RNA to determine if the viral infection is still present. An alcohol assessment and counseling regarding the detrimental effects of alcohol use should be provided concurrent with linkage to HCV care.

Hepatitis C should be cured in order to improve patient outcomes

Sustained virological response (SVR) is defined as the absence of HCV RNA in blood when measured 12 weeks after the end of treatment and is considered as evidence of cure of HCV infection. Long-term follow-up studies have demonstrated that this short-term surrogate endpoint used in clinical trials of antiviral drugs is durable and that the likelihood of HCV relapse beyond this time frame is nil. The benefits of achieving SVR are myriad[5,6].

Hepatitis C can be cured with all-oral regimens and minimal side effects

Treatments for hepatitis C have evolved rapidly over the last several years with new drugs developed specifically to inhibit replication of the hepatitis C virus. These direct acting antiviral agents (DAAs) are focused on three specific regions of the hepatitis C virus that are critical to viral functions. Thus, NS3 protease inhibitors, NS5A replication complex inhibitors, and NS5B polymerase inhibitors have been combined with or without ribavirin in order to achieve all oral therapeutic with high rates of sustained virological response. Combining drugs from different classes is very important in order to hit multiple targets to increase the efficacy of these drugs and also to diminish the risk of viral resistance. These drugs should never be used as single agents due to the immediate risk of selecting for resistant virus.

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It is anticipated that two all-oral regimens will be approved in the last quarter of 2014. Sofosbuvir is a nucleotide polymerase inhibitor that has been combined with ledipasvir (NS5A inhibitor) to achieve a once-daily single pill regimen for the treatment of hepatitis C. SVR was achieved in 94 to 99 percent of patients who were treated for only 12 weeks in phase III clinical trials of sofosbuvir and ledipasvir[1,2]. Another regimen that combined ABT-450 (protease inhibitor, boosted with ritonavir), with ombitasvir (NS5A inhibitor), dasabuvir (non-nucleoside polymerase inhibitor), and ribavirin, yielded SVR rates between 92 and 96 percent[3,4]. At least two other all-oral regimens are in late stage clinical trials but are not expected for FDA approval until sometime in 2015.

These all-oral therapies are extremely well tolerated with low rates of generally mild adverse events (headache, fatigue, nausea, possibly anemia with ribavirin) or treatment discontinuations and represent major advances in HCV therapeutics. Indeed, few patients will have contraindications to this new generation of antiviral therapy, in glaring contrast to the rigorous interferon-based regimens for which many patients were not suitable candidates or preferred not to experience the harsh adverse effects.

Evidence continues to accrue about the substantial improvements in hepatic and non-hepatic outcomes among patients who are cured from chronic hepatitis C. The availability of simplified all-oral regimens that minimize adverse events and achieve near universal SVR will encourage health care providers to screen appropriate patients for HCV infection and will lead to more patients undergoing successful, and potentially life-saving, antiviral therapy.

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Hepatitis C (HCV) screening recommendations

- All adults born during 1945 through 1965 should be tested once (without prior ascertainment of HCV risk factors)
- HCV-testing is recommended for those who:
  - Currently inject drugs
  - Ever injected drugs, including those who injected once or a few times many years ago
  - Have certain medical conditions, including persons:
    - who received clotting factor concentrates produced before 1987
    - who were ever on long-term hemodialysis
    - with persistently abnormal alanine aminotransferase levels (ALT)
    - who have HIV infection
  - Were prior recipients of transfusions or organ transplants, including persons who:
    - were notified that they received blood from a donor who later tested positive for HCV infection
    - received a transfusion of blood, blood components or an organ transplant before July 1992
  - HCV-testing based on a recognized exposure is recommended for:
    - Healthcare, emergency medical, and public safety workers after needle sticks, sharps, or mucosal exposures to HCV-positive blood
    - Children born to HCV-positive women

Note: For persons who might have been exposed to HCV within the past 6 months, testing for HCV RNA or follow-up testing for HCV antibody is recommended.

Persons for Whom Routine HCV Testing is of uncertain need

- Recipients of transplanted tissue (e.g., corneal, musculoskeletal, skin, ova, sperm)
- Intranasal cocaine and other non-injecting illegal drug users
- Persons with a history of tattooing or body piercing
- Persons with a history of multiple sex partners or sexually transmitted diseases
- Long-term steady sex partners of HCV-positive persons

Persons for Whom Routine HCV Testing is Not Recommended (unless other risk factors present)

- Health-care, emergency medical, and public safety workers
- Pregnant women
- Household (nonsexual) contacts of HCV-positive persons
- General population

Source: U.S. Centers for Disease Control and Prevention