

Treatment of Hepatitis C Virus Infection: Is It Time for the Internist to Take the Reins?

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For the first time since the identification of hepatitis C virus (HCV) in 1988, communitywide eradication of HCV infection seems possible. With the U.S. Food and Drug Administration's approval in late 2013 of simeprevir and sofosbuvir, 2 direct-acting oral anti-HCV drugs, the time has come to launch major initiatives to reduce the effect of this infection on individuals and on our communities. Who should lead the charge to initiate and manage treatment: subspecialists, internists, or both?

Globally, 230 million persons are infected with HCV, including 2.7 to 3.9 million persons in the United States (1, 2). Spontaneous resolution occurs in only 20% of HCV-infected individuals, and many chronically infected persons progress to cirrhosis (20% over 25 years) and develop hepatocellular carcinoma (20% of cirrhotic patients). Over the past 2 decades, HCV infection was treated first with parenteral interferon- α alone, then with pegylated interferon- α plus oral ribavirin, and more recently with oral boceprevir or telaprevir added to pegylated interferon plus ribavirin. Although each successive regimen incrementally reduced long-term complications of HCV infection, the regimens were lengthy (24 to 48 weeks), were only modestly effective, and were poorly tolerated (often because of depression and anemia and leukopenia). Thus, fewer than 10% of eligible patients have received treatment (3, 4).

In addition to simeprevir and sofosbuvir, many direct-acting oral anti-HCV drugs are in late development stages. Direct-acting regimens without interferon and ribavirin, administered for only 6 to 12 weeks, have yielded response rates greater than 90% with excellent tolerability and safety (5–7). These results are stunning triumphs for translational medicine if further trials confirm and extend these findings, although much remains to be learned about specific host, viral, and drug factors that influence treatment outcomes. The Infectious Diseases Society of America and the American Association for the Study of Liver Diseases have jointly released recent dynamic online clinical guidance for providers that accommodates rapid updates (www.hcvguidelines.org).

Internists have long played a unique and critical role on the forefront of HCV infection care by counseling, testing, and identifying patients with this disease. However, for treatment, most patients have been referred to hepatologists. If a cure for and communitywide eradication of HCV infection become realistic goals, will there be enough subspecialists to treat all infected patients? Is subspecialty expertise necessary for managing all HCV-infected patients?

Overseeing treatment of HCV infection in 2 to 4 million persons in the United States would probably overwhelm the country's 1800 hepatologists. Even if all 7000 practicing infectious disease subspecialists in the United States focused on this disease, it would not be sufficient. The subspecialist workforce would be overtaxed even if the 2 to 4 million persons eligible for treatment were prioritized to begin therapy over 5 to 10 years.

As treatment of HCV infection becomes more straightforward and does not require invasive diagnostic tests, such as liver biopsy, internists can and should take a more active role in treating most patients except those with advanced cirrhosis. Subspecialty referral should be unnecessary for many HCV-infected persons, especially those without advanced fibrosis, severe extrahepatic manifestations of HCV infection, or substantial comorbid conditions.

Once criteria are developed for subspecialist referral and prioritization of treatment, internists should be able to quickly develop the expertise to screen for relevant HCV-drug-resistance mutations, assess stage of liver disease, and determine which patients require subspecialist care and which patients with uncomplicated HCV infection they can treat using breakthrough drugs. Thus, internists should be leaders in this unprecedented opportunity to cure this chronic and morbid viral disease.

Internists, subspecialists, and public health authorities will need to work together to address barriers to adherence—as well as such issues as emergence of viral resistance—and the effect of reinfection, cost, and access (8). Finding funds to launch and operationalize widespread testing programs, persuade asymptomatic persons to be tested, link infected individuals to stable medical care, provide psychosocial support to patients with special needs, and persuade patients to receive therapy for an infection that often remains completely asymptomatic will pose considerable challenges.

We can learn from our 25 years of experience with HIV and AIDS. Our successes in reducing the effect of this infection in the United States have had some notable victories, but far more success is needed in important areas. Only 25% of HIV-infected patients are receiving stable care and have suppressed viral loads (9), which is sobering.

However, the HIV and HCV infection epidemics have some prominent differences. HIV requires lifelong therapy. In contrast, the ability to cure a life-threatening HCV infection with only 6 to 12 weeks of therapy is likely to make programmatic successes far easier in this condition than in HIV and AIDS. Internists must be leaders in educating all stakeholders about these opportunities and in transition

ensuring the from patient identification to patient cure and community eradication (7).

Even if testing and linkage to care were readily available for all infected persons, the cost of acquisition for the new direct-acting oral anti-HCV drugs is sobering. The current market price for 1 recommended regimen, simeprevir plus sofosbuvir for 12 weeks, is \$150 000 (10). Whether this price is cost-effective, let alone affordable or reasonable, requires careful analysis.

Patients with early disease could be counseled and monitored for years instead of being treated immediately. However, although market competition may decrease drug acquisition costs and multidrug combination regimens may allow progressively shorter regimens, it will be important to identify patients who need treatment sooner rather than later and thus those for whom current drug costs are warranted.

Treatment of HCV infection has entered a new era in which the cure of individual patients is eminently feasible and communitywide eradication is conceivable. A robust debate is accelerating about whom and when to treat and what fraction of our resources should be devoted to HCV infection. As advocates for their patients and communities, internists must have a strong voice in this debate to assure that those patients in imminent danger of HCV infection—related illness can access these promising drugs. The time for internists to embrace delivering therapeutic interventions for HCV infection in their practices is now.

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