What's Hepatitis C Reinfection Got to Do With It?

Ending the epidemic is going to require addressing the fact that certain individuals are at high risk of reinfection after a cure.

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The World Health Organization (WHO) has set the ambitious goal of eliminating hepatitis C virus (HCV) as a public health threat by 2030. Thankfully, the pharmacological tools to make that dream a reality are now available: highly effective, well-tolerated direct-acting antiviral (DAA) treatments for the virus.

Getting these medications to the estimated 70 million people living with hep C worldwide—and paying the substantial associated cost—is another matter. In the United States in particular, the price tag for curing hep C is in the tens of thousands of dollars, which leads both public and private insurers to limit coverage of DAAs in order to rein in costs.

Another obstacle to beating the HCV epidemic is reinfection—in other words, when someone cured of the virus contracts it again. Reinfection is particularly likely to occur among individuals who are currently engaging in the kind of high-risk practices that spread the virus. So this would not likely include the most significant bloc of people living with hep C in the United States: baby boomers (those born between 1945 and 1965), who likely contracted the virus in their youth, in theory through unsafe medical procedures. Instead, people who inject drugs (PWID) and men who have sex with men (MSM) are the two key demographics at notable risk of reinfection.

For PWID, reinfection risk is driven by sharing syringes, needles and other drug paraphernalia with others; among MSM, condomless anal intercourse is the major risk factor, especially when the men are HIV positive. (Researchers have found evidence that HIV causes biological changes that facilitate hep C acquisition through anal sex.)

Researchers have struggled to determine which sexual risk practices are most likely to transmit hep C among MSM. Studies have identified associations between such transmission and group sex, rough sex, having other sexually transmitted infections and using drugs such as crystal meth and GHB during sex. That said, simple condomless intercourse that does not involve any of those factors could indeed still transmit HCV between men.

Oluwaseun O. Falade-Nwulia, MBBS, MPH, an assistant professor of medicine in infectious diseases

at Johns Hopkins Medicine, is the lead author of a recent paper published in the Journal of Viral Hepatology that focused on the need to better understand and address the problem of hep C reinfection. As a clinician, she is a part of a team that saw great success in curing HCV among a large group of inner-city residents who were also living with HIV and who had many risk factors that might have compromised their chance of a hep C cure, including histories of drug use and psychiatric diagnoses.

Falade-Nwulia expresses worry that in the minds of some clinicians, "The thought is that these [HCV] treatments are pretty expensive, especially when treating populations of people who inject drugs, so [the clinicians'] concern is that if people continue to inject [drugs], then they'll just get reinfected. Then for those people, [treatment] is considered a waste."

For Falade-Nwuilia, such a mindset among clinicians is unfortunate. In her published paper, she and her coauthors write about how withholding HCV treatment from PWID in particular serves only to sustain the epidemic by allowing the infection to persist in people engaging in high-risk practices who may spread the virus to others.

"We spend so much time worrying about reinfection that there's been less done about understanding it and addressing it," Falade-Nwuilia says. "So far, from the data we have, it suggests that the rates of reinfection are actually pretty low."

A major caveat to this understanding of how common reinfection may be, however, is that most of the research into reinfection comes from the bygone era during which hepatitis C was treated with interferon, the dreaded injectable treatment that came with numerous onerous side effects. Given the arrival of DAAs, in particular Sovaldi (sofosbuvir) in 2013 and Harvoni (ledipasvir/sofosbuvir) in 2014, interferon has been phased out in recent years. The characteristics of those treated for hep C today may be different from those of individuals treated a decade ago in such a way as to skew reinfection rates one way or another.

One important study of hep C reinfection rates, which included the largest cohort to date of such a study, analyzed data on all those tested for HCV or HIV at the British Columbia Center for Disease Control Public Health Lab between 1990 and 2013. Among 5,915 people, 3,690 spontaneously cleared the virus without the need for treatment (this is a common phenomenon but apparently is much less common among those who also have HIV) and 2,225 people were cured of HCV through interferon-based treatment.

In the group as a whole, including those who spontaneously cleared the virus and those who were treated and cured, 452 people were reinfected during a cumulative 35,671 years of follow-up. This translated to a reinfection rate of 1.27 cases per cumulative 100 years of follow-up. That means that if 10,000 similar people lived for one year, an estimated 127 of them would become reinfected.

Just 50 of the 2,225 people who were cured of HCV through treatment were reinfected, for a very low reinfection rate of 0.48 cases per 100 cumulative years. The reinfection rate was higher, however, for PWID, at 1.14 cases, and HIV-positive individuals, at 2.56 cases per 100 cumulative

years.

Other studies have seen overall reinfection rates ranging between 1.21 and 4.9 cases per 100 cumulative years of follow-up. In research conducted during the interferon era among HIV-positive MSM, reinfection rates in this demographic ranged between 5.3 to 13.2 cases per 100 cumulative years. It is not uncommon for MSM to be reinfected multiple times.

“We really should be working harder to identify and treat populations of people who are transmitting hepatitis C to others,” says Falade-Nwuilia, “because that’s the only way that we are going to get the epidemic under control. If anything, we should be focusing on interventions, be it counseling, be it access to harm reduction, be it access to other services.”

Such harm reduction for PWID may include opioid substitution therapy and linkage to needle and syringe programs that can provide them with sterile injection equipment. Additionally, case management services can link individuals to various social service programs that can assist with housing and employment needs. Among MSM, counseling to encourage safer sex practices, including the use of condoms is important.

According to Falade-Nwuilia, for all those at high risk of HCV reinfection, the tracing of personal contacts, which has long been in practice for tackling the spread of STIs, such as syphilis, is a vitally important means of identifying the members of a network of people who have the virus. This would involve those who test positive for the virus referring others for testing, specifically MSM’s sexual partners and PWID’s fellow drug users. If testing can be done within such networks in a relatively short period of time, and if those who test positive are promptly treated, these interventions would result in a considerable reduction of virus circulating within a particular network of people and a lowering of the likelihood of reinfection among them.

“If everybody’s getting treated at the same time and everybody’s getting the same messaging,” Falade-Nwuilia adds, “then maybe it will actually change the norm in the whole network.”

In other words, if you take a group of socially connected individuals who engage in similar behaviors that are associated with various health risks and you engage them all with the health care and social services system at once, they may learn healthier behaviors that in turn could promote and maintain greater communal health going forward.

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