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Hepatitis Can't Wait: Teachings From COVID-19 To Combat Hepatitis B and C Viruses

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We are living in an era of overlapping pandemics. Like oceanic currents, some flow and spread discreetly under the surface. Others, like tsunamis, wreak havoc as they pass. Populations have been decimated by microscopic pathogens, but we have always come out on the other side, stronger and more knowledgeable. Unfortunately, the current COVID-19 pandemic reaffirms that we still have a lot to learn on how best to control pandemics and combat emerging pathogens. If we look under the surface, below the blaring crisis caused by SARS-CoV-2, more pandemics are ongoing. Silently, many viruses are circulating in the population and causing their slow but steady devastation. One such group of pathogens are hepatitis viruses.

Hepatitis B virus (HBV) and hepatitis C virus (HCV) are of particular concern, as they have established lifelong infection in over 300 million people worldwide. Chronic viral hepatitis is the leading cause of liver cancer and liver failure, which account for approximately 1.1 million deaths globally every year (1). The study of these viruses has led to many scientific advancements, such as an effective vaccine for HBV and curative treatments for HCV. These advancements prompted the World Health Organization's commitment to eliminate viral hepatitis as a public health threat by 2030 (2). Not only do these advancements bring hope to hepatitis elimination, but they have also been helping us cope with the ongoing COVID-19 pandemic. Despite these advancements, the road to eliminating HBV and HCV is paved with obstacles and we are not near the finish line yet.

In this letter, we discuss how the study of HBV and HCV has provided tools that are being used to tackle SARS-CoV-2 in the current pandemic, and in turn, how we can use lessons learned from this global crisis to improve care for viral hepatitis and accelerate progress towards elimination. Finally, we will mention some of the key elements needed to achieve the 2030 HBV and HCV elimination targets set by The World Health Organization, and why "hepatitis can't wait" (2).

How have HBV and HCV research provided useful tools to combat COVID-19?

Broad acting antivirals

Antivirals can be repurposed to target pathways that are conserved across several viruses. As such, the nucleoside analogs Remdesivir and Sofosbuvir, originally developed to target RNA viruses including Ebola virus and HCV (3), have been demonstrated to have some efficacy in combating COVID-19 infection (4, 5). RNA viruses often share similar features, such as the viral polymerase (an enzyme responsible for copying the viral genome and allow the virus to replicate), enabling us to target them with the same compounds. Other antivirals such as Daclatasvir, peginterferon-Lambda-1a, ribavirin, peginterferon-alpha-2b have been used to treat chronic HBV and HCV infection are also in phase II/III clinical trials for the treatment of SARS-CoV-2 (6-9).

Vaccine development platforms

Beyond antivirals, vaccines play a key role in eliminating any viral threat. The eradication of smallpox and the monumental progress towards eradicating polio has demonstrated the effectiveness of global vaccination efforts. Notably, the currently used HBV vaccine, approved in 1986, was the first approved vaccine to use recombinant DNA technology (10). This important milestone has paved the way for subsequent vaccines, including the COVID-19 vaccines (11). While no HCV vaccine has been approved yet, research is active in this area. The ChAdOx1 simian adenoviral vector was initially developed at the University of Oxford as a delivery vector for an HCV vaccine candidate. Although this platform was not successful at preventing chronic HCV infection, it was subsequently used in the Oxford-AstraZeneca COVID-19 vaccine with great success (12, 13). Finally, mRNA vaccines produced by Pfizer-BioNTech and Moderna may have reached approval for the first time, yet this technology was already being researched for the development of vaccines against several pathogens, including HCV (14, 15). Thus, vaccine development for both HBV and HCV infection has provided a steppingstone to accelerate COVID-19 vaccine development. In turn, the advancements in mRNA vaccine technologies can be applied in the future to produce an efficacious HCV vaccine.

Genotyping

Viruses that replicate using an RNA polymerase, like SARS-CoV-2, HBV, and HCV, are prone to changes in their genome called mutations. Many of these mutations can be harmful to the virus, while some provide increased fitness. Advantageous mutations can become prevalent in the viral population, leading to variants or even different genotypes and subtypes, as is the case for HBV and HCV. Effectively, different HBV or HCV genotypes are associated with various clinical outcomes such as disease severity and progression, or response to treatment (16). As such, genotyping is of great importance for providing optimal patient care and informed treatment. Previous knowledge about virus evolution has prompted surveillance of SARS-CoV-2 variants to identify mutations of concern and study their susceptibility to vaccines.

How can our response to the COVID-19 pandemic inform the future of HBV and HCV care?

Telemedicine

To reduce traveling and contacts, many activities were moved to a remote format during the COVID-19 pandemic — healthcare was no exception. Physician consultations were carried out remotely when possible, and this virtual approach has previously been shown to help lessen the stigma around various medical issues while making healthcare more accessible (17). This model comes with many benefits, such as reduced travel, clinic wait times, and anxiety related to HBV and HCV testing and treatment. Even in the post-COVID-19 era, we can look to implement telemedicine to simplify the viral hepatitis cascade of care.

Facilitated booking systems

Faced with the immense task of testing and vaccinating an entire population, provincial governments within Canada put in place an online system for individuals to book their appointments without any involvement of staff (18).

Historically, stigma and lack of access to testing have been some of the greatest barriers for the prevention, management, and treatment of infectious diseases (19). The testing system and government support currently in place are unable to rapidly screen individuals for bloodborne pathogens. The existing model requires individuals to first meet with their doctor, request screening, and then book an appointment with a clinic to get their blood drawn. To improve the standard of care, the online booking method should be expanded to include viral hepatitis testing and vaccination. Not only would this make people feel less stigmatized by not having to interact with an administrator for booking, but it would also save precious time and resources which can be put to good use to increase testing capacity.

Access to fast, easy, and widespread testing

To prevent the spread of infectious pathogens, the first and most important step is to get tested. The expansion of diagnostic laboratory services has been the main priority of many governments during the COVID-19 pandemic. The introduction of mobile high-capacity testing centers at diverse locations with specific guidelines for vulnerable populations such as people experiencing homelessness, drive-through testing, home testing kits, and fast turnaround times for results has provided the community with increased access to testing and has been the most important tool in tracking and managing the spread of SARS-CoV-2 within the population (20, 21).

There is now a vaccine available against HBV and a cure for HCV infection, but these pathogens continue to cause an ongoing pandemic due to the lack of sufficient widespread testing. Globally, we have diagnosed only about 10% of people living with hepatitis B and 21% of people living with hepatitis C (1). The implementation of large-scale testing platforms and the inclusion of mobile, community-based testing and vaccination sites could be used to reach underserved and marginalized populations. Scaling up testing capacity should also be supported with increased efforts to ensure and improve linkage to care, which could greatly improve hepatitis elimination efforts.

New point of care tests

To quickly detect infections and limit virus spread, rapid antigen and RNA tests were developed and administered in a community setting by non-specialized personnel. Such tests would be especially useful in the context of HBV and HCV for multiple reasons.

We must recognize that the blood draw process itself can also serve as a deterrent against testing for bloodborne pathogens such as HBV and HCV, especially among high-risk groups such as people who inject drugs (PWID). Additionally, among certain populations, such PWID, there is an increased risk of loss to follow-up due to many factors. For example, the many steps involved in the care cascade and the inability to contact individuals once test results are in. Among individuals who are at an increased risk of HBV and HCV infection, such as PWID, many do not have a contact phone number or stable housing.

To address these concerns and accommodate people who do not have access to clinics, newer, more innovative methods have been developed. One of these methods is dried blood spot testing (22). With a small finger prick, a few drops of blood are collected onto a filter paper. This filter paper can then be transported to a laboratory that can test the sample against a panel of bloodborne pathogens. Unfortunately, this practice is not yet widely used, but infrastructure put in place for rapid COVID-19 testing could be repurposed to address this issue. A widespread test and treat approach would increase the proportion of individuals diagnosed and linked to care.

Transparency and in-depth data tracking

Throughout the pandemic, the Canadian government has been extremely transparent by releasing daily counts of new infections, positive tests, hospital and intensive care unit (ICU) occupancies and deaths. COVID-19 regional hotspots and populations to be prioritized for vaccinations were also noted (23). This has improved disease awareness and democratized data such that targeted public health initiatives were implemented to further prevent virus spread. On the contrary, HBV and HCV surveillance reporting is not routine nor timely in many regions across Canada. This impedes our ability to address outbreaks with adequate localized prevention, testing, linkage to care and treatment offerings (24, 25). Viral hepatitis testing should be included as part of regular medical check-ups for key populations and one-time universal testing for the general population. Several studies suggest that this strategy would be cost-effective in high income countries, and it would improve the accuracy of viral hepatitis disease surveillance (26, 27). Applying similar dashboards used for COVID-19 surveillance to support the routine and transparent reporting of viral hepatitis data on incidence, test positivity, morbidity, and mortality trends could be a huge step towards normalizing hepatitis. This in turn would increase demand for HBV and HCV testing and treatment offerings and support public engagement in progress towards viral hepatitis elimination.

Concerted global efforts to accelerate evidence synthesis and support decision-making

Governments across the globe have been proactive during the COVID-19 pandemic to adopt public health measures, implement new models of testing and promote mass uptake of vaccination. Governments have thus relied upon access to the latest evidence to make informed decisions. Many international initiatives and networks have emerged during the pandemic to accelerate evidence synthesis and support decision-making. For example, the COVID-19 Evidence Network to support Decision-making (COVID-END) is a time-limited network of global evidence synthesis, guidance, and decision support organizations that aims to better coordinate the collective evidence response to the pandemic (28). Progress towards the global elimination of HBV and HCV is also contingent upon international coordination of efforts. Organizations like *Action Hepatitis Canada* and the *World Hepatitis Alliance* could draw upon the knowledge and experience acquired through such networks to engage with decision makers more effectively and, ultimately, optimize the global response to the HBV and HCV pandemics.

What has allowed us to respond so quickly to the COVID-19 pandemic?

The rapid spread of SARS-CoV-2 combined with a high fatality rate among certain populations called for a rapid global response from governments and The World Health Organization (29). This response provided financing to companies for vaccine development like never before. The investment into vaccine development allowed for the production of efficacious vaccines that became available for administration less than one year into the pandemic (30). Unlike COVID-19, chronic diseases like viral hepatitis take years to develop and lower an individual's quality of life slowly but steadily (31). Symptoms of HBV/HCV usually do not appear until late-stage liver disease, at which point the consequences are unlikely to be reversible. Because of the slow progression and lack of early signs, viral hepatitis does not receive a similar urgency-influenced response from the government, and the amount of funding and public attention that it does get limits research and elimination efforts.

The COVID-19 pandemic has demonstrated that strong political will, high public awareness, and a rapid and concerted response from scientists and pharmaceutical companies can lead to unprecedented breakthroughs. Using the lessons from COVID-19, we could formulate new guidelines for dealing with other ongoing pandemics and important epidemics. By applying similar strategies to increase disease awareness among the public, we can collectively work towards the elimination of several viral threats and prepare for future pandemics.

Concluding remarks

Learning as much as we can about pandemics and taking meaningful steps towards protection against infection and control of disease spread are key elements of an elimination strategy. Although we are beginning to see the light at the end of the tunnel for COVID-19, other pandemics are ongoing, and "hepatitis can't wait". Applying lessons from the COVID-19 pandemic could not only accelerate our progress towards the elimination of viral hepatitis but also help us limit the damage of the next pandemic. Similar to the study of oceanic currents and winds to determine where the next tsunami will hit, public health and research efforts directed at HBV and HCV can help build protective structures to break the waves before they even reach the shore.

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