Viral hepatitis: a hidden killer gains visibility
As the epidemics of HIV, malaria and tuberculosis receded, viral hepatitis became more visible as a leading killer worldwide. Many hard-won lessons from the HIV experience provided a head start for a targeted approach to a disease situation that mirrors the early years of HIV. For example, while it took nearly a decade to get the price of antiretroviral therapy down, prices for the new hepatitis C cures plummeted within two years.

As huge gains were made in reducing the impact of HIV, another long-neglected epidemic became more visible: the devastating and complex health problems caused by viral hepatitis infections. No longer overshadowed, hepatitis moved into the spotlight as one of the leading killers worldwide. WHO estimates that, in 2015, infections with hepatitis B and C virus – the two out of five hepatitis viruses responsible for the greatest burden of disease – caused 1.34 million deaths worldwide, compared with 1.1 million deaths from HIV in that same year, 1.4 million deaths from tuberculosis, and 438,000 deaths from malaria. Whereas the HIV, TB, and malaria epidemics have peaked and are now in decline, morbidity and mortality from viral hepatitis are on the rise. WHO estimates that deaths from hepatitis have risen by 22% since 2000. Unless more people with chronic infections are diagnosed and treated, the number of deaths caused by viral hepatitis will continue to increase.

The burden of viral hepatitis

Hepatitis B and C are bloodborne infections, with significant transmission of hepatitis B occurring in early life and of hepatitis C occurring through unsafe injections, including injection drug use, and medical procedures. Transmission through sexual contact occurs, though less commonly. The resulting disease burden is enormous and felt worldwide. WHO estimates that, in 2015, 257 million people were living with chronic hepatitis B infection, and 71 million with chronic hepatitis C infection. The hepatitis B epidemic affects parts of Africa and the Western Pacific most severely, while the hepatitis C epidemic is more evenly distributed worldwide. An estimated 67% of people who inject drugs have been infected with the hepatitis C virus. The Eastern Mediterranean and European regions have the highest reported prevalence of hepatitis C infection. Among the 36.7 million people living with HIV in 2015, an estimated 2.7 million had chronic hepatitis B infection and 2.3 million had been infected with hepatitis C.

The burden of liver cancer is particularly heavy in the developing world.
Chronic infection from the viruses can severely damage the liver, leading to cirrhosis and hepatocellular cancer. The burden of liver cancer is particularly heavy in the developing world. In sub-Saharan Africa, for example, liver cancer is the most common cancer among men and the third most common cancer in women.

**Clinical management: the outlook is improving**

Although infections with both B and C hepatitis viruses can be prevented and treated, doing so encounters some challenges. Diagnosis is problematic. As chronic hepatitis infections can cause no symptoms and remain silent for decades, many people are unaware of their infection and do not seek treatment until the disease has progressed to severe – often irreversible – liver damage. Medical care is demanding. In wealthy countries, patients with hepatitis B and C infections are treated by highly trained specialists, such as hepatologists, gastroenterologists, and infectious-disease experts. Expanding care in countries with fewer resources calls for simplified and standardized protocols that extend clinical competence to non-specialized health professionals. WHO experiences with HIV show that such a transfer of competence is entirely feasible.

The recent development of highly effective medicines has revolutionized the treatment of chronic hepatitis C infections. The new oral direct-acting antivirals are well-tolerated and can achieve cure rates above 95%. However, with initial launch prices in the US of between $66,000 and $84,000 per patient per treatment course, the drugs were prohibitively expensive everywhere. Low-cost and effective medicines are available to treat hepatitis B infection, but most patients require lifelong treatment. The price of tenofovir, for example, has recently dropped to as little as $48 per person per year. However, costs mount for any drug that needs to be taken for a lifetime.

**The hepatitis B vaccine: an early win for prevention**

A safe and effective vaccine that prevents hepatitis B infection has been available since 1981. As mother-to-child transmission is an important route of infection, WHO recommends a three-dose immunization schedule with the first dose administered within 24 hours following birth. This is particularly important, as infection acquired at birth is more likely to result in chronic infection and subsequent liver disease. Introduction of the vaccine into routine childhood immunization programmes brought an early win in the hepatitis response. The world will reap major benefits from the current emergence of hepatitis B-free generations. WHO estimates that, in 2015, 84% of the world’s young children were reached with three doses of hepatitis B vaccine. The success achieved with the scaling up of immunization has helped to reduce hepatitis B infection in children, though more infants need to receive a first dose of the vaccine within 24 hours of birth. In Africa, for example, only 10% of newborns are covered with the birth dose.
Much more needs to be done to prevent hepatitis B and C infections in the general population. WHO recommends a comprehensive preventive approach that includes assurance of safe blood products, safe injection practices, preferably through the expanded use of self-destructing disposable syringes, comprehensive harm reduction services for people who inject drugs, and the promotion of safe sex. The political declaration agreed at the 2016 UN General Assembly Special Session on the World Drug Problem includes WHO recommendations for harm reduction as a way to protect the health of people who inject drugs. However, implementation of the WHO harm reduction package in countries remains patchy and insufficient.

Current challenges – like the early years of AIDS

In many ways, efforts to prevent and control viral hepatitis face challenges that mirror the early years of the AIDS epidemic, when public awareness and the determination to act were just beginning to build. Stigma and discrimination associated with hepatitis infection are high, as is the tendency of the disease to disproportionately affect marginalized populations. The groups at highest risk for hepatitis C infection are similar to those for HIV: men who have sex with men, sex workers, injecting drug users, and prisoners. As with HIV, viral hepatitis can be transmitted from mother to child. Both the HIV and the hepatitis epidemics require special attention to the safety of the blood supply.

The fact that chronic infection with viral hepatitis can remain silent for decades mimics the long incubation period for HIV infection, with all the challenges this means for early diagnosis and treatment as a strategy for preventing further spread. As with the early years of HIV, demanding requirements for diagnostic testing and clinical management raise questions about whether hepatitis can be effectively treated in resource-constrained settings. Finally, as was the case when the first antiretroviral medicines were licensed, the costs of hepatitis treatments are way too high, giving fair access to treatment a compelling moral imperative. People should not be denied access to life-saving interventions for unfair reasons, including those with economic or social causes.

Though hepatitis B and C are old diseases, they have been ignored for so long that the gaps in data and knowledge – like the paucity of reliable data from seroprevalence studies and the lack of country-specific data on the prevalence of liver cirrhosis and hepatocellular cancer – are what might be expected for a newly emerging disease. These gaps in knowledge make it difficult for health officials in high-burden countries to persuade their governments to make viral hepatitis a priority, in terms of policy and also for funding. At the same time, because the hepatitis epidemics are global in their impact, affecting rich countries as well as very poor ones, the incentives for the pharmaceutical industry to develop new products are high. A rich and promising set of new tools has been developed over the past few years. The job now, as in the early years with AIDS, is to push for lower prices and simplified diagnostics through a range of proven strategies that can shape market forces to serve the poor. Progress is being made. Over the past three years, WHO has prequalified three new diagnostic tests for hepatitis, including the first rapid test for detecting hepatitis C.
The similarities between the HIV and viral hepatitis epidemics are important in that they give efforts to control viral hepatitis a head start. Many hard-won lessons from the HIV experience provide a firm foundation for accelerated – and aggressive – action to get the hepatitis burden down. The pace of progress for hepatitis is indeed accelerated. While it took nearly a decade to get the price of antiretroviral treatments down, prices for hepatitis C treatments have plummeted in many countries over just the past two years.

95% of people with hepatitis do not know they are infected

Due to lack of awareness and poor access to hepatitis tests

Source: WHO

WHO reports: an eye-opener

Over the years, WHO governing bodies had addressed viral hepatitis, but nearly always as just one component of a much larger health problem. Beginning in 1992, hepatitis B was discussed at World Health Assemblies under agenda items on immunization, cancer prevention, and the protection of health care workers from the risk of infections. Some approaches to prevention were also discussed under agenda items on blood safety and safe injection practices.

Viral hepatitis first appeared as a stand-alone item on the agenda of the World Health Assembly in 2010. The WHO report for that session on the disease and its burden, and the many opportunities for prevention and control that were being missed, was an eye-opener for Member States. It led to the adoption of WHO’s first resolution on viral hepatitis, marking the dawning of a new era of awareness about the magnitude of the disease burden and the need for urgent action on multiple fronts. The resolution also led the WHO Director-General to establish the Organization’s first global viral hepatitis programme.
In response to growing concern and welcome pressure from active civil society groups, WHO issued a framework for hepatitis prevention and control in 2012. The framework aligned recommended actions around four strategic objectives: to raise awareness, promote partnerships, and mobilize resources, to gather data and evidence as policy support, to prevent transmission, and to improve screening, care, and treatment. Given several similar challenges facing the HIV and hepatitis epidemics and opportunities for synergistic responses, the Director-General placed management of the new programme under the WHO Department of HIV in late 2013.

Viral hepatitis returned to the agenda of the World Health Assembly in 2014, this time with a report that mapped out the many barriers to prevention and control. That report gave viral hepatitis the status of a serious but under-recognized global public health problem. Whereas hepatitis B vaccination programmes had expanded as primary prevention, diagnosis and management of existing cases were demanding, with most countries providing only limited clinical care to those who could afford it. Treatment and care needed a public health approach that could extend the benefits more equitably. Many countries lacked the human resources and sophisticated medical infrastructure needed to provide treatment. The road ahead would not be easy.

The 2030 Agenda for Sustainable Development, adopted in September 2015, included a target that called on the public health community to “combat hepatitis” but gave no endpoint for an expected result. Civil society organizations were instrumental in persuading WHO Member States to respond far more ambitiously, urging them to aim for elimination. Already in 2014, Member States asked WHO to explore the feasibility of eliminating the epidemic of viral hepatitis as a public health threat. In many ways, such a sweeping ambition made sense technically. Hepatitis C has no animal host or ecological reservoir of infection, and both diseases have proven tools for prevention and treatment. The ambition also looked appropriate for a disease that had moved out of obscurity to rank among the leading killers worldwide. Nonetheless, the obstacles to success were immense.

WHO’s first global strategy on viral hepatitis

In 2016, the World Health Assembly approved the Organization’s first-ever Global Health Sector Strategy on Viral Hepatitis, covering the five years from 2016 to 2021. As another first, the strategy set global targets for reducing hepatitis infections and deaths and expanding coverage with preventive, testing, and treatment services. As with the response to the HIV epidemic, the strategy adopted a public health approach that gives priority to the prevention of infection and disease, the promotion of health, and the prolongation of life among the population as a whole. It aims to ensure the widest possible access to high-quality services at the population level, based on simplified and standardized interventions and services that can be readily taken to scale and decentralized, including in resource-constrained settings.

As few high-burden countries have national hepatitis strategies, plans, and budgets, the strategy gives particular attention to the development of surveillance systems that can gather the data needed to leverage political commitment. Such data further allow the strategic targeting of high-impact interventions to match the distinct features of local epidemics. The strategy proposes a
set of six core interventions and services to end the epidemic: hepatitis B vaccination, prevention of mother-to-child transmission of hepatitis B, prevention in health care settings through injection and blood safety, harm reduction for people who inject drugs, hepatitis testing, and treatment and care for those with chronic infections.

In April 2017, WHO issued its first *Global Viral Hepatitis Report*, which sets out the first WHO-validated baseline data for monitoring progress and highlights examples of countries that have taken action to implement the strategy.

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**Making hepatitis C treatments affordable**

Work to reduce the prices of the new direct-acting antivirals that can cure hepatitis C is already bringing dramatic results for some populations in a number of countries. Mechanisms being used include licensing agreements that stimulate competition among generic manufacturers, local production, price negotiations with the originator company, and use of a game-changing Medicines Patent Pool. The Medicines Patent Pool, which relies on products prequalified by WHO, was set up in 2010 to improve access to antiretroviral therapy in low- and middle-income countries. Its remit was later expanded to include hepatitis C and tuberculosis treatments. It is sponsored and fully funded by UNITAID, a drug purchasing facility that draws substantial and sustainable funding from a levy on airline tickets.

In October 2016, WHO announced that more than one million people living in low- and middle-income countries had been treated with the revolutionary hepatitis C curative medicines since their introduction two years earlier. The announcement coincided with the release of a WHO report on *Access to Hepatitis C Treatment: Focus on Overcoming Barriers*. The report provides comprehensive data on levels of access, prices charged in different countries, and the situation with patents and registration of the medicines.

The report demonstrated the burden of unmet needs but also introduced transparency to the market, allowing price comparisons across countries. For example, costs per patient per treatment course range from $9,400 in Brazil to $79,900 in Romania. Egypt, which has the world’s largest hepatitis C burden, has also had the greatest success in getting prices down, from $900 in 2014 to less than $200 in 2016. Elsewhere, high costs have led to treatment rationing in some countries, including in the European Union, where price reductions are insufficient to allow national health budgets to cover all in need of treatment. However, several countries, including Australia, France, and Georgia, are now providing hepatitis C treatment through their public health budgets.

Inclusion of the new hepatitis C medicines in the 2015 WHO Model List of Essential Medicines is another step that is expected to further stimulate efforts to get prices down. To achieve the targets set out in the global health sector strategy for viral hepatitis, WHO estimates that 80% of patients with hepatitis C will need to be treated.
As happened with antiretroviral treatments for HIV, several civil society organizations, including Médecins Sans Frontières, have simultaneously filed patent challenges against the originator company in an effort to remove affordability barriers, improve access, and end the need to ration medicines. Opposition of this nature has already led to the revoking of patents in China and Ukraine; decisions are pending in other countries, including Argentina, Brazil, India, the Russian Federation, and Thailand.

Again, efforts to control viral hepatitis are benefitting from the hard-won lessons of the AIDS response. To date, the number of countries that have secured hepatitis C medicines at affordable prices is much too low for a disease that affects some 71 million people. The world needs to show more outrage over a situation in which the high price of medicines denies so many millions a cure for a disease that is highly stigmatized and so often fatal.