

Hepatitis

Improving the health of patients with viral hepatitis

Report by the Secretariat

1. The Executive Board at its 134th session noted an earlier version of this report,¹ and adopted resolution EB134.R18.² The version of the report below has been updated (particularly paragraphs 10, 14 and 15) to reflect new information concerning the price of, and access to, recently approved hepatitis C medicines.

2. Chronic hepatitis due to hepatitis B and C viruses affects large numbers of people and causes high morbidity and mortality. An estimated 240 million persons are chronically infected with hepatitis B virus and 150 million with hepatitis C virus. Chronic viral hepatitis is thus a serious but under-recognized global public health problem. Its diagnosis and management remain complex, and many countries lack the human resources and medical infrastructure to be able to provide treatment. New medicines are becoming available that cure or stop the progression of hepatitis C virus infection. Most people with chronic viral hepatitis, however, are not aware of their infection and do not receive appropriate treatment. Without appropriate diagnosis, referral for care and treatment, up to a third of individuals with chronic viral hepatitis will die of liver cancer or cirrhosis.

3. In 2010, the Health Assembly adopted resolution WHA63.18 on viral hepatitis, in which, inter alia, it urged Member States to support or enable an integrated and cost-effective approach to the prevention, control and management of viral hepatitis. To facilitate implementation of the resolution, the Secretariat established the global hepatitis programme. In 2012, the Secretariat issued a framework for global action to prevent and control viral hepatitis infection, which aligned actions along four strategic axes: (1) raising awareness, promoting partnerships and mobilizing resources; (2) evidence-based policy and data for action; (3) prevention of transmission; and (4) screening, care and treatment.³

¹ See the summary records of the Executive Board at its 134th session, fourth meeting, section 3, and thirteenth meeting, section 2.

² See document EB134/2014/REC/1 for the resolution, and for the financial and administrative implications for the Secretariat of the adoption of the resolution.

³ Prevention and control of viral hepatitis infection: framework for global action (document WHO/HSE/PED/HIP/GHP 2012.1).

THE EPIDEMIOLOGICAL SITUATION

4. Five distinct viruses (hepatitis A, B, C, D and E) are known to cause hepatitis, all of which have different routes of transmission and cause varying courses of disease, resulting in about 1.4 million deaths each year.¹ Of these deaths, nearly 800 000 are due to hepatitis B and nearly 500 000 due to hepatitis C, representing nearly 90% of all viral hepatitis-related deaths. Infections with hepatitis B and C viruses are not evenly distributed globally. The areas with highest prevalence of hepatitis B are western Africa, where in some countries more than 8% of the population is infected, and eastern and central Asia. A similar pattern is observed for hepatitis C, although the prevalence is extremely high in a few countries, most notably Egypt and Pakistan, where the incidence rates remain high largely due to transmission of the virus in health-care settings because of weak application of infection-control measures such as those to prevent reuse of syringes and needles.

5. The high death toll results because hepatitis B and C viruses cause chronic, life-long infection that can lead to cirrhosis and liver cancer. An estimated 78% of all cases of liver cancer and 57% of those of cirrhosis are caused by chronic hepatitis B or C virus infections. Mortality is very high in those people who develop these conditions. Because of the higher prevalence of hepatitis B and C in Asia and Africa, countries that are least able to deal with these conditions in these continents also experience the greatest number of deaths due to viral hepatitis. Even though liver cancer is the fifth most common cancer worldwide, in Africa it is the most common cancer among men and third most common in women.

CHALLENGES

6. **Diagnosis.** Chronic hepatitis B and C are diagnosed by detecting the presence of the virus in blood samples. A significant barrier to diagnosis is that most people with chronic hepatitis are asymptomatic, often for decades, and thus are unaware that they are infected. They often present to the health system only when they have symptoms related to cirrhosis or liver cancer. Health care workers often are not trained properly to counsel people presenting to the health system to be tested or to refer them for care if they are found to be infected.

7. **The medical care** of people diagnosed with chronic viral hepatitis is complicated. First, sophisticated molecular laboratory tests are needed in order to assess eligibility for and response to treatment. Other tests such as liver biopsy or ultrasonography are also important for assessing the degree of liver fibrosis in order to make treatment-related decisions. Liver biopsy is difficult to perform and specialized expertise is required in order to interpret the results, and adequate ultrasound machines can cost up to US\$ 100 000. Consequently, many countries have very limited access to these tests, which may be available only at tertiary-care facilities, if at all. Promising new techniques are being developed that allow point-of-care testing to measure viral load. As use of these tests would make treatment more available, it will be important for the Secretariat to promote their development and to evaluate and prequalify them as appropriate.

8. **Capacity-building.** Currently, patients with hepatitis B and C are treated by specialists (such as hepatologists, gastroenterologists and infectious-disease experts) but these specialists are in severely short supply in low- and middle-income countries. Administration of treatment on a larger scale would

¹ Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *The Lancet*. 2012;380(9859):2095–128 doi:10.1016/S0140-6736(12)61728-0.

need the expansion of the role of primary health care settings and primary health care workers, and the latter would need further training in the diagnosis, management and treatment of patients with chronic hepatitis B and C. Training materials aimed at primary care workers do not exist, and therefore need urgently to be developed.

9. An additional barrier to successful treatment is **access** to appropriate medicines. The currently recommended treatment for hepatitis C, pegylated interferon in combination with ribavirin, is expensive and inconvenient to take (with 24–48 weekly injections) and is associated with severe side effects. The cure rate is between 45% and 80%. Because of the cost, complexity and toxicity of existing regimens, there has not been strong advocacy to make these medicines available in low-income countries, and few national governments have plans to expand therapy for viral hepatitis.

10. This situation is about to change. Treatment experts predict that, in the next 2–5 years, 90% of hepatitis C infections will be curable with an all-oral, once-daily, 12-week regimen of safe medicines. These new medicines bring the promise of curing millions of people with chronic infection and thereby preventing deaths from cancer and cirrhosis. Some public health experts even talk of the eradication of hepatitis C. However, these treatments come at a **significant cost**. In December 2013, two new hepatitis C medicines, simeprevir and sofosbuvir, were approved in the United States of America. The price to treat one person with these medicines for a complete course of treatment in the United States of America is US\$ 66 000 and US\$ 84 000, respectively.

11. Therapy for chronic hepatitis B virus infection is also improving, with treatment regimens that are more potent, easier to administer and less likely to induce resistance. One of these medicines, tenofovir, which is also active against HIV, is available in generic form in some countries at a cost of US\$ 4 per month. Despite this relatively low cost, there has not been a noticeable increase in the number of persons with hepatitis B infection receiving this medicine. The reasons for this low level of uptake are the shortage of specialists and primary care expertise and capacity as described above, and because hepatitis B therapy is usually life-long, making the current medicines too costly for many people in low-income countries.

12. **Market shaping.** The market dynamics that drive the price of medicines are complicated. Prices, particularly of new medicines for use in low- and middle-income countries, depend on a combination of civil-society pressure on pharmaceutical companies, the strength and enforcement of patent laws, a solid medicines regulatory system for approving generics, and the assurance of a significant and reliable market. A combination of these factors has reduced the price of antiretroviral medicines for HIV infection by more than 100-fold in the past 15 years.

13. Many of these market-shaping forces are weak for viral hepatitis medicines. Civil society organizations are only now beginning to advocate more intensely for price reductions of medicines to treat hepatitis. None of the major global-health donors include hepatitis treatment in their programmes; as a result, the market demand for the medicines is weak. The International Drug Purchase Facility (UNITAID) has begun to tackle market barriers for hepatitis-related commodities, but the focus is limited to people who are co-infected with HIV and does not include the procurement of hepatitis medicines.

14. Regulatory approval of simeprevir and sofosbuvir in the United States of America has stimulated global discussion of access to hepatitis treatment, with a particular focus on reducing the prices of the new hepatitis medicines in low- and middle-income countries. A combination of approaches will need to be considered, such as voluntary licensing to generic manufacturers and tiered pricing of the branded medicine linked to a country's income level.

RESPONSES

15. Member States can undertake several activities to make progress. First, as most countries do not have accurate epidemiological estimates of the burden of chronic viral hepatitis, improved surveillance and serological surveys of hepatitis virus infections would provide decision-makers with more accurate information on the extent of the problem, geographical differences and risk groups affected. The Secretariat is drafting technical guidance to support Member States in strengthening their hepatitis surveillance programmes. Secondly, in order to increase coverage for testing for viral hepatitis, Member States should prepare recommendations for screening and testing that would identify appropriate test kits and testing algorithms. The Secretariat is updating its list of prequalified hepatitis B and C serological tests. Developing national treatment programmes for hepatitis B and C would help to define standardized approaches to treatment. The Secretariat is preparing treatment guidelines for hepatitis B and C for issue in 2014. As pegylated interferon, which is the mainstay of hepatitis C treatment, has been included in the 18th WHO Model List of Essential Medicines, Member States could work to include it in national formularies and, if possible, negotiate with manufacturers for lower prices. An example of the latter is in Egypt, where, in view of the large size of its programme and through concerted effort, the Government has negotiated a 10-fold reduction in the price of pegylated interferon. The Secretariat will provide support to Member States in developing national treatment strategies that take into consideration the emerging availability of new hepatitis medicines.

16. People with HIV infection who are co-infected with either hepatitis B or C virus need to be given priority attention. Of the 34 million people living with HIV, some 2–4 million and 4–5 million persons also have hepatitis B or C virus infection, respectively. Co-infection accelerates the progression of liver disease in these persons. In view of the significant investments made in HIV treatment programmes by the Global Fund to Fight AIDS, Tuberculosis and Malaria and other organizations, many countries have developed a strong medical infrastructure to provide chronic care for HIV-infected patients. Opportunities need to be sought to extend that platform to people with viral hepatitis, initially through the systematic screening of HIV-infected people already in care and the initiation of hepatitis treatment of those found to be co-infected. In June 2013, WHO published consolidated guidelines on the use of antiretroviral medicines for treating and preventing HIV infection,¹ a set of recommendations for a public health approach that includes guidance on HIV treatment for people co-infected with hepatitis B or C virus.

17. Finally, with all the focus on hepatitis treatment, it is vitally important that national hepatitis control efforts include a balanced approach that combines therapeutic and preventive interventions. Egypt's recent experience demonstrates this point. To tackle the very high rates of hepatitis C in the country, the Government of Egypt launched a hepatitis C treatment programme in 2008. Since its inception, the programme has treated more than 200 000 patients and enrolls about 50 000 new patients each year. This achievement is remarkable, but unfortunately this expansion in treatment was not matched by a similar effort in prevention. As a result, it is estimated that each year 150 000 people still become infected with hepatitis C virus. Thus, for each person treated, three persons become newly infected.

18. Effective hepatitis B prevention depends on vaccination. According to a WHO analysis, investment in hepatitis B vaccination could prevent an estimated 4.8 million hepatitis B-related deaths

¹ Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: Recommendations for a public health approach June 2013. Geneva: World Health Organization; 2013.

over a 10-year period in the 73 countries supported by the GAVI Alliance.¹ Hepatitis B vaccination coverage is one of the 25 indicators in the WHO global action plan for the prevention and control of noncommunicable diseases 2013–2020 and the vaccine is currently included in routine infant vaccination programmes in 180 countries.

19. Most new infections with hepatitis C virus occur as a result of unsafe injection practices or weak infection-control measures. The promotion of appropriate infection-control practices, including single-use syringes, is important. The Secretariat is working on a global campaign for safe injection that will promote reduction in unnecessary injections, the use of safety engineered injection devices and training of health care workers. Assuring the safety of blood transfusions also remains vitally important. Member States should continue to assure that all blood donations are screened for all relevant blood-borne pathogens, including hepatitis B and C viruses, in a quality-assured manner.

20. Prevention programmes also need to target those populations who are at high risk of hepatitis B and C virus infection through injecting drug use, unsafe tattooing and other skin-piercing practices, and unprotected sex. The main groups include people who inject drugs, prisoners, sex workers, men who have sex with men, and transgender people. Comprehensive hepatitis prevention programmes for the main target populations include vaccination against hepatitis A and B, sterile needle and syringe programmes, infection-control measures in tattooing establishments, provision of male and female condoms, and risk-reduction communication through outreach and peer programmes. In 2012, WHO published guidance on prevention of viral hepatitis B and C among people who inject drugs.² Additional WHO guidance on comprehensive HIV prevention and treatment services, including prevention of viral hepatitis, for target groups is scheduled to be launched in 2014.

ACTION BY THE HEALTH ASSEMBLY

21. The Health Assembly is invited to note the report, and consider the draft resolution as recommended by the Executive Board in resolution EB134.R18.

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¹ Lee LA, Franzel L, Atwell J, Datta SD, Friberg IK, Goldie SJ et al., 2013. The estimated mortality impact of vaccinations forecast to be administered during 2011–2020 in 73 countries supported by the GAVI Alliance. Vaccine 31(Supplement 2): B61-B72.

² Guidance on prevention of viral hepatitis B and C among people who inject drugs. Geneva: World Health Organization; 2012.