

## Hepatitis—Cure and Prevention

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World Hepatitis Day has been celebrated annually on 28 July since 2008. This day was chosen as it was the birthday of Professor Baruch Blumberg who won a Nobel Prize in 1976 for his discovery of the hepatitis B virus (HBV). World Hepatitis Day is an official World Health Organisation (WHO) awareness day, one of only 4 official disease-specific world health days endorsed by WHO (the other 3 being World Tuberculosis Day, World Malaria Day and World AIDS Day). This year marks the 7<sup>th</sup> World Hepatitis Day.

Why a World Hepatitis Day? Hepatitis is a preventable chronic disease and yet it is the world's 8<sup>th</sup> biggest killer with the same mortality as the human immunodeficiency virus infection/acquired immunodeficiency syndrome (HIV/AIDS), but without the equivalent level of awareness and global political resolve to contain the disease unlike that for HIV/AIDS.<sup>1</sup> There are 240 million people in the world with chronic hepatitis B infection and 185 million with chronic hepatitis C infection.<sup>2,3</sup> World Hepatitis Day is pertinent in Singapore as chronic hepatitis B and C infections are significant diseases locally with important healthcare sequelae of liver cirrhosis, end-stage liver disease and hepatocellular carcinoma (HCC).

Besides the usual hepatitis B and C campaign staples regarding modes of acquisition and prevention, and the need for regular medical follow-up, when one discusses about hepatitis this year, the limelight will inevitably be on chronic hepatitis C, in particular the delicate issue of access to care. Sofosbuvir is a "miracle" oral drug for chronic hepatitis C infection belonging to the new class of oral hepatitis C direct-acting antivirals (DAAs). It has recently been approved by the drug authorities in the United States and Europe i.e. the Food and Drug Administration (FDA) and European Medicines Agency (EMA) respectively. This drug has revolutionised the landscape of chronic hepatitis C treatment from a 24 to 48 week regime of weekly pegylated interferon (Peg-IFN) injections and thrice-daily

oral medications with a cure rate of up to 75% in the most difficult to treat genotype 1 to current sofosbuvir once daily together with ribavirin twice daily and weekly Peg-IFN injections for just 12 weeks to yield an unprecedented superior cure rate of 89%.<sup>4,5</sup> There is more in the pipeline with an upcoming sofosbuvir-ledipasvir (another new DAA) once-daily monotherapy combination pill that gives a cure rate of 99% after 12 weeks of treatment.<sup>6</sup> It is difficult to imagine that we now have a once-daily all-oral monotherapy bereft of significant adverse effects that will give a near total cure rate in just 12 weeks of a disease that hitherto required weekly injections that had multiple side effects for up to 48 weeks in return for a cure rate of only up to 75%. This combination pill is on the threshold of approval by FDA which is expected in the fourth quarter of this year.

However, the cost of a course of treatment with sofosbuvir is USD 80,000 which works out to about SGD 1000 a tablet. Furthermore, we do not know the price of the superior sofosbuvir-ledipasvir combination pill which will obviously be higher than sofosbuvir alone. Paradoxically, nearly 90% of the approximately 185 million chronic hepatitis C sufferers worldwide reside in low- and middle-income countries that are unable to afford these new wonder drugs.<sup>3</sup> Thus the irony is that new superbly efficacious drugs for chronic hepatitis C will not be used in places that require them the most because of the high cost of the medications. This situation is reminiscent of the time when new effective drugs for HIV were first made available.

Unlike the situation with chronic hepatitis C, there is little significant recent treatment advancement in chronic hepatitis B. Satisfactory once-daily oral antiviral monotherapy treatment for chronic hepatitis B at a reasonable price has been around for some time. However, there are still targets to be achieved in the prevention of hepatitis B i.e. in hepatitis B vaccination programmes. Hepatitis B vaccination is highly efficacious and more importantly,

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it has been shown to reduce the incidence of HCC.<sup>7</sup> Hepatitis B vaccine is a true anticancer vaccine. In 2011, 180 countries have included hepatitis B vaccination in their routine vaccination schedules and achieved a coverage of about 80%.<sup>8</sup> However, the coverage is not uniform worldwide, with only 58% of the countries in the African region reporting the existence of a hepatitis B control and prevention (vaccination) programme. More needs to be done globally for the prevention of hepatitis B infection in view of the availability of a highly efficacious vaccine against hepatitis B. Cost of vaccine and poor infrastructure for delivery of vaccination are major obstacles to achieving better hepatitis B vaccination coverage.<sup>8</sup>

So, as we celebrate and commemorate this year's World Hepatitis Day on 28 July 2014, we should be mindful of the two basic pillars of any disease management – prevention and cure, and what needs to be done in the arena of hepatitis. We have the tools viz hepatitis B vaccine for prevention of hepatitis B infection and new super-efficacious DAA agents for cure of hepatitis C infection but the devil is in how to get them realised at the ground levels where they are most needed.

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