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REVIEW

HIV, HCV and HBV: A Review of Parallels and Differences

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ABSTRACT

Elimination of the three blood-borne viruses—human immunodeficiency virus (HIV), hepatitis B (HBV) and hepatitis C (HCV)—as public health issues may be plausible in the near future. Spectacular advances have been made with the introduction of highly effective antiviral agents into clinical practice, and prevention strategies are available for all three infections. Effective disease control, laid out by WHO global strategies, is currently feasible for all three viruses. However, for worldwide elimination of these viruses, effective vaccines are required that are currently only available for HBV. In this review differences and parallels among HIV, HCV and HBV will be discussed with a focus on virologic and therapeutic issues, and prospects for the future of HBV will be presented.

Keywords: Antiviral therapy; Elimination; Hepatitis B virus; Hepatitis C virus; HIV virus; Vaccination

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INTRODUCTION

Twenty-five years after the discovery of the human immunodeficiency virus (HIV), it is apparent that tremendous progress has been made [1]. From a poorly understood, largely fatal disease, it has become a treatable chronic condition with, at least in the Western world, a potential for a normal life expectancy [2]. As a result, patients and clinicians are encountering an increasing prevalence of comorbidities such as cardiovascular diseases and non-AIDS malignancies [3, 4]. A similar change has taken place in the treatment of patients chronically infected with the hepatitis C virus (HCV) [5]. The introduction of direct-acting antiviral agents (DAAs) has revolutionized HCV treatment with cure rates (sustained virologic response, SVR) above 95% [6] and an associated significant reduction in the risk of hepatocellular

carcinoma (HCC) and the de-listing of cirrhotic HCV-infected patients from liver-transplant lists [7, 8]. For chronic hepatitis B virus (HBV) the current pipeline of drug development is promising [9]. The question is whether we could expect the same spectacular advancements for HBV in the near future.

HIV, HCV and HBV are three distinct viruses (retro-virus, RNA virus and DNA virus, respectively) with distinct differences—including affected organ systems, life cycles and host cell integration. There are also several similarities however—such as their main modes of transmission and favorable treatment outcomes with antiviral drugs. It is therefore of interest, and perhaps utility, to study, compare and contrast these three viruses.

In this review, differences and parallels among HIV, HCV and HBV will be discussed with a focus on virologic and therapeutic issues.

Compliance with Ethics Guidelines

This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

PARAMETERS AND END POINTS

HBV Categorization

In the clinical care of individuals with HBV there are multiple results/readouts that have been used in combination to loosely categorize patients—to determine whether treatment is indicated and its effectiveness when used.

Individuals are considered to have acute infection if they have been positive for surface antigen (HBsAg) for < 6 months and chronically infected if they remain HBsAg positive subsequent to this. The main further categorization has been based on the presence or absence of e antigen (eAg), the presence or absence of e antibody (eAb), elevations in markers of liver injury (principally transaminitis) and viral load quantification in plasma. The European Association for the Study of the Liver (EASL) and the American Association for the Study of Liver Diseases (AASLD) had categorized chronic HBV infection into four phases (see Table 1). Both associations acknowledged that throughout the four phases, HBV DNA, HBeAg, HBeAb and ALT levels may fluctuate and can be possibly negative/normal depending on the phase.

These classifications have been used to determine which individuals should be treated—with treatment not normally having been advocated for those classified as immune-tolerant or in the inactive phase.

Such treatment decisions can be complex, and there may be some disagreement between different specialist organizations and also (within the use of a single guideline) between different clinicians. This has been compounded by the fact that a significant proportion of individuals was not easily classifiable within these definitions (e.g., had an ALT > 2 times the upper limit of normal (ULN) but an HBV-DNA level $<$ 2000 IU/ml or an HBV-DNA 20,000–100,000 IU/ml but persistently normal ALT levels) or had variations in assay results over time that shifted them repeatedly from one category to another. The complex classifications in HBV arose secondary to the observations that many individuals had a seemingly good prognosis. Those with a very high viral load but persistently normal transaminases appeared to have a good outcome while they remained with such results. They were classified as 'immune tolerant' in recognition of the belief that the pathogenesis of HBV was immune mediated and if there was no significant immune activation, even with very high viral load, no significant damage or impairment of health was resulting [10]. Similarly, those with immune activation and consequent viral control, but without pathologic inflammation of the liver, also appeared to have a good prognosis [11, 12].

HCV and HIV

The above is in contrast to the current situation in those patients with HIV or hepatitis C infection. Here the sole virologic readout routinely required for patient categorization is the

Table 1 Phases of HBV infection adapted from previous EASL [11] and AASLD Guidelines [12]

Phase	ALT		HBV DNA		HBeAg		Liver histology	
	EASL	AASLD	EASL	AASLD	EASL	AASLD	EASL	AASLD
Immune-tolerant	Normal	Normal	> 2000 < 20,000 IU/ml	> 1 million IU/ml	Positive	Positive	Nil-minimal liver parenchymal damage	Minimal inflammation or fibrosis
Immune active	Elevated	Elevated	> 20,000 IU/ml	≥ 20,000 IU/ml	Positive ± anti-Hbe	Positive	Active liver parenchymal damage	Moderate to severe inflammation or fibrosis
Inactive CHB	Normal	Normal	< 2000 IU/ml	< 2000 IU/ml	Positive ± anti-Hbe	Negative	Nil-minimal liver parenchymal damage	Minimal necroinflammation but variable fibrosis
Late reactivation	Elevated	Elevated	High	≥ 2000 IU/ml	Negative + anti-Hbe	Negative	Active liver parenchymal damage	Moderate to severe inflammation or fibrosis

viral load in plasma. Until recent years treatment decisions in both HIV and HCV also depended on markers of end-organ damage (a CD4 count and assessments of liver fibrosis, respectively); however, more recently guidelines have altered to promote treatment of all—regardless of these results. Supportive information may still be required to determine which specific treatment was most suitable—predominately resistance assays and genotypes—but not for categorization.

This has not always been the situation in HIV and HCV. The development of polymerase chain reaction (PCR) viral quantification was vital to the battle against HIV as the ability to adequately measure the HIV-RNA viral load became a useful accepted end point of successful therapy—though was initially not without controversy [13–19]. Prior to this, study of newer agents was protracted and required the determination of clinical end points such as death and development of AIDS. In the pre-DAA era of HCV treatment, definitions of virologic success such as partial early viral response (i.e., a > 2 log10 drop in HCV-RNA at week 12 of therapy) took months to be reached and had suboptimal predictive value for eventual cure. In addition, based on such a virologic criteria, treatment durations of 48 to even 72 weeks were decided upon [20]. Together with a further 6 months waiting after treatment discontinuation to determine success and failure, such a cycle took about 1.5–2 years. The introduction of DAAs to the market resulted in shortened treatment durations of 8–12 weeks without virologic kinetic decisions about prolongation of therapy [21]. Also, SVR was validated at the 12-week post-treatment time point resulting in much shorter treatment cycles and thus quicker phase-2/3 trial turnover. The use of viral load clearance and SVR12 time points however has not been universally accepted [22], but is accepted as an end point for clinical studies and therefore drug development.

FUTURE PROSPECTS FOR HBV

Are we progressing to a similar situation for HBV where categorization and treatment

decisions are more simple, rapid and clear cut? Or to a situation where treatment is advocated for all?

Assessments of immune responsiveness and exhaustion have allowed classification and monitoring to be revisited, and data on outcomes in those previously defined as immune tolerant have directed a re-appraisal of patient categorization. For example, studies have demonstrated that the previously labeled 'immune-tolerant' phenotype is actually associated with immune activation and increased expression of immune check point inhibitors such as PD-1 [23, 24]. These factors, and a general better understanding of outcomes, have allowed a reassessment of classification of patients with HBV infection.

In 2017, the European Association for the Study of Liver (EASL) introduced a new nomenclature based on five phases of hepatitis B infection (see Table 2). Although this is an advance, it is still complex compared with HIV and HCV. There are however potential advances that may further simplify these classifications in the future. The ability to relatively easily quantify surface antigen (sAg) levels in plasma has the potential to further adapt our algorithms on monitoring or determining treatment [25, 26]. Until such assays and newer laboratory end points become established, the current assessment of regimen effectiveness in HBV remains predominately HBV-DNA viral load. HBsAg seroconversion is perhaps the ultimate goal of therapy; however, this is only reached in a minority of patients and can take years to develop. An important future end point would be the elimination of covalently closed circular DNA (cccDNA)—the long-lived nucleic acid moiety in hepatocytes that prevents true virologic clearance of HBV with currently available treatments (that do not adequately target this reservoir). At the moment there are several classes of drugs in pre-clinical and early clinical stages of development such as zinc-finger nucleases, disubstituted sulfonamide compounds, APOBEC proteins and RNA interference molecules that target cccDNA or similar pathways [27]. The challenge is that even when these drugs are able to silence or disrupt the cccDNA intra-hepatically, there is currently no easy way to quantify hepatic cccDNA in the liver except by performing liver biopsy. In most situations a liver biopsy solely for research purposes would be deemed unethical. On-treatment and then early off-treatment sAg kinetics are being utilized but do not, as yet, have good correlation with longer-term responses or cures. Plasma HBV RNA has been investigated as has core-related antigen [28, 29]. However, none have yet been shown to have sufficiently robust correlation as a surrogate for efficacy, and the assessment of long-term off-treatment responses, though possible, results in long studies and significant delays in determining efficacy that inhibit the progression of science in this regard. Therefore, progression of promising agents to phase 3 and thence to the clinic is currently significantly delayed [9]. A robust non-invasive surrogate marker of cccDNA loss or inhibition is therefore urgently required in HBV.

This delay in progression of promising agents to general use also means that we remain in a situation where not all patients meet criteria for treatment. If we develop an agent, or combination, that has a significant impact on ccc-DNA, then it is possible that we move to a

Table 2 Current EASL Guidelines (2017) [76]

Phase	sAg	eAg	HBV DNA	ALT	Liver disease
eAg-positive chronic infection	High	Positive	$> 10^7$ IU/ml	Normal	None/minimal
eAg-positive chronic hepatitis	High/intermediate	Positive	10^4–10^7 IU/ml	Elevated	Moderate/severe
eAg-negative chronic infection	Low	Negative	< 2000 IU/ml	Normal	None
eAg-negative chronic infection	Intermediate	Negative	> 2000 IU/ml	Elevated	Moderate/severe

situation in HBV analogous to that currently in HIV and HCV—treatment for all and not dependent on sub-classification.

In the near future, we may move to simpler classification as we get more experience of the utility of sAg or from quantification of other viral factors currently being investigated (e.g., core-related antigen), and monitoring and assessment of HBV may become more aligned to that of HCV and HIV. There may be similar improvements resulting in study end points that will permit a more rapid progression of promising agents toward clinical use and potentially a future where all those with evidence of HBV infection will be treated with efficacious therapies.

IS ELIMINATION FOR HIV, HCV AND HBV ON THE HORIZON?

Where We Are Now

UNAIDS and WHO have approved different global strategies to achieve elimination of HIV, HBV and HCV as public health issues by 2030. The burden of the three infections is still high worldwide with approximately 257 million people with chronic HBV infection, 71 million people chronically infected with hepatitis C (HCV) and an estimated 36.7 million people living with HIV. There are important differences between the viruses with respect to geographical distribution and routes of transmission that influence plans and strategies for worldwide elimination. The principal targets of the eliminations programs (Tables 3, 4) are based on implementing current available preventive strategies and treatment options (Table 5). Applying for all three viruses is that the availability of effective (generic) antivirals is mandatory for worldwide elimination. In addition, easy-to-use point-of-care testing already available for HIV and HCV should routinely be used to lower the barriers of diagnosis and linkage to care.

HIV: On Our Way to Global Control

Considering its high effectiveness, the WHO and UNAIDS have recommended Treatment as Prevention (TasP) for HIV to be widely implemented [30]. It has been demonstrated that effective treatment suppresses the viral load, and this correlates with a significantly decreased chance of transmission to uninfected individuals [i.e., the Undetectable is Untransmittable (U = U) paradigm] [31]. The landmark HIV Prevention Trials Network published a landmark trial in 2011, showing that treating HIV-infected individuals from a discordant couple was 96% effective in preventing HIV infection of their partner [32]. In addition, no linked infections were observed when HIV was successfully undetectable by ART [33]. A more recent study conducted within Danish men who have sex with men (MSM) demonstrated that TasP could contribute to HIV epidemic elimination when the treatment coverage and viral load suppression rate are high [31]. Finally, these observations were confirmed by the large Partner-1 (in sero-discordant couples) and -2 (in MSM) studies [34, 35] again clearly demonstrating no HIV transmissions when there is an undetectable viral load after nearly 77,000 acts of condomless sex.

Furthermore, a modeling study from South Africa has demonstrated that in the 10 years between 1996 and 2016 there was a reduction of 72% in incidence of new HIV cases and a drop of 74% in AIDS-related mortality as a result of expanded testing and treatment. In addition, if South Africa continues to extend testing, offers treatment to every infected person and improves access to prevention for people at high risk of HIV infection then both incidence and mortality will be less than 1 event per 1000 people by 2030. That will also be a very cost-effective strategy [36].

Another important step toward HIV control is targeted provision of pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP). It has been demonstrated that taking tenofovir disoproxil fumarate/emtricitabine every day or “on demand” (shown to be effective only in the case of MSM) before high-risk exposure is effective in preventing HIV

Table 3 UNAIDS strategy 2016–2021 and WHO targets 2030 based on the total number of 36.7 million people living with HIV worldwide in 2016 according to WHO

	Indicators	Global burden	Target 2020	Target 2030
PMTCT	Mother treatment	76% Pregnant women on ARV	No infection among children	
Incidence	No. of new infection/year	1.8 million (2016)	< 500,000	< 200,000
Mortality	No. of people dying from HIV	1 million	< 500.000	< 400.000
Testing service	No. of people aware of HIV status	25.5 million	90%	
Treatment	HIV diagnosed on treatment	19.5 million	Ca 30 million (90%)	Ca 33 million
Efficacy of treatment	HIV viral load undetectable	16 million	90%	

PMTC prevention mother-to-child transmission

Table 4 Hepatitis B and C WHO targets for elimination

Intervention	Indicators	Global	Targets	
		2015	2020	2030
HBV vaccination	HepB3 coverage	84%	90%	90%
HBV PMTCT	Hep vaccine birth dose coverage	39%	50%	90%
Blood safety	Donation screening	97%	95%	100%
Injection safety	Proportion of unsafe injection	5%	0	0
Harm reduction	Syringes/needles distributed/PWID/year	27	200	300
Testing	People aware of HBV status	9%	30%	90%
	People aware of HCV status	20%	30%	90%
Treatment	Diagnoses with HBV on treatment	8%		80%
	Diagnosed with HCV started on treatment	7%		80%

HBV hepatitis B virus, *HepB3* hepatitis B 3 doses vaccine, *PWID* people who inject drugs, *HCV* hepatitis C virus, *PMTCT* prevention mother-to-child transmission

infection in people who have high-risk sexual contacts (partner with HIV, partners with unknown HIV status) or in people who inject drugs (PWID) who share needles [37–39]. PEP is already included in all guidelines for both occupational and non-occupational exposure. Mother-to-child transmission (MTCT) is another crucial aspect as it can be nearly fully prevented if both the mother and infant are provided with antiretroviral drugs (ARVs) as early as possible in pregnancy and during the period of breastfeeding. Over the years, a growing number of countries have been achieving very low rates of MTCT, and some

Table 5 Current available tools for prevention and treatment of HIV, HBV HCV

	Vaccination	Preventive strategies	Antiviral treatment
HIV	No	Safe sex	Lifelong and chronic treatment
		Screening and treat pregnant woman (PMTCT)	
		PreP, PEP	
		Early treatment	
HBV	Effective vaccine	Screening blood	Lifelong and chronic treatment
		Safe sex	
		Active and passive immunization at birth	
		Vaccination	
HCV	No	Harm reduction[a]	Short-term and curative treatment
		Safe sex for MSM	
		Treat acute infection	

PreP pre-exposure prophylaxis, *PEP* post-exposure prophylaxis, *PMTCT* prevent mother-to-child transmission
[a] Needle and syringe programs (NSP) and opiate substitution treatment (OST)

(Armenia, Belarus, Cuba and Thailand) have been formally validated as having achieved elimination of MTCT of HIV as a public health problem.

Although such non-vaccine approaches to HIV prevention appear very promising and will probably markedly diminish new infections, it has been demonstrated that a safe and at least moderately effective vaccine (together with vigorous implementation of non-vaccine prevention tools) would achieve a more rapid and sustained end of the HIV/AIDS pandemic [40]. In combination with the influence of ART, this would have a substantial long-term impact on the HIV epidemic in southern Africa. The first HIV vaccine trial (termed RV 144) that showed a positive protective signal came from Thailand in 2009. The group receiving the vaccine had an infection rate of 31.2% lower than the group that received placebo [41]. Although this result was not enough to qualify the vaccine for licensure, RV144 has provided very useful pointers for a way forward. More recently, new promising targets for vaccination such as novel B- or T-cell approaches were identified [42]. Several phase 1/2 clinical trials are currently ongoing with the APPROACH study recently showing robust and protective immune responses in humans and rhesus monkeys [43].

HCV: On the Path Toward Elimination

Since the isolation of hepatitis C virus in 1989, strategies to eradicate the virus have evolved rapidly. Interferon was the first drug used to treat the infection and, with addition of ribavirin, SVR rates around 54–56% were achieved [44]. The real revolution came with the advent of DAAs: treatments of shorter duration achieved SVR rates above 95% for nearly all patient groups. However problems come from reinfection that can occur even after a successful treatment (as treatment does not result in any protective HCV-specific immunity). Reinfection among PWID and MSM due to ongoing risk behaviour (sharing needle/syringes/other injecting equipment or unsafe sexual practices) could compromise both individual and population treatment benefit [45]. Modeling studies conducted in North America among PWID showed that treatment with DAAs offered a high chance for HCV elimination at an attainable cost if implemented in combination with increased access to HCV testing and harm

reduction [46, 47]. Another study based on theoretical model projections showed that in Greece chronic hepatitis C could be eliminated in the next 4–5 years by increasing treatment to more than 16% of PWID per year in combination with moderate increases in harm reduction coverage [48].

At this time, no effective vaccination is available for hepatitis C. It has been proposed that vaccinating after treatment would be an effective and practical method of administration and in settings with high chronic HCV prevalence among PWID, even modest coverage with a low-effectiveness vaccine could provide significant additional prevalence reduction beyond treatment alone and would likely reduce the cost of achieving prevalence reduction targets [49]. This, in addition to current high treatment costs, ensures that vaccination could still be an important intervention on the way toward the elimination of HCV infection [50]. The ability to produce a vaccine is hampered by the huge diversity of HCV and its capacity to escape and downregulate T cell immunity. There have been promising advances such as the studies by Branes et al. that demonstrated that it is possible to generate very strong, broad, long-lasting and functional T-cell responses against HCV in healthy donors using an adenovirus-based approach [51]. However, it has been disappointing that, to date, early phase-II studies in chronic HCV-infected patients have resulted in only poor HCV-specific T cell responses and thus development of these types of vaccine has been discontinued [52].

HBV Infection: Chronic but Preventable Disease

Current treatment strategies do not allow complete viral eradication in HBV infection. Peg-IFN has significant side effects, but it is able to achieve a functional cure in a number of patients and remains a possible therapeutic option [53]. Lifelong nucleos(t)ide analog (NUC) therapy, on the other hand, has few side effects but achieves functional cure only in a small minority of patients [54].

What makes hepatitis B infection really different from HIV and HCV is the availability of an effective vaccination since the early 1980s. A long-term study of 14 years conducted in The Gambia showed a high effectiveness of vaccination against chronic carriage (94%) and new infection (80%) among children and young people at different ages [55]. To date, 183 (94%) of the 193 WHO member states have initiated an hepatitis B vaccination program [56]. Approximately 84% of children worldwide (92% in the Asian region) received three doses of hepatitis B vaccine and are thus probably protected from HBV infection for life. The additional administration of hepatitis B immune globulin at birth can further reduce the risk of MTCT in high-risk deliveries [57].

There is also evidence of the effectiveness of maternal NUC therapy. A study conducted in Thailand demonstrated that, in the context of a low rate of HBV transmission, maternal use of TDF in addition to the administration of hepatitis B immune globulin and the HBV vaccine to infants resulted in a lower rate of mother-to-child HBV transmission than placebo [58]. It has subsequently been accepted in all international guidelines that antiviral therapy with TDF (or possibly lamivudine or telbivudine) may be indicated to reduce levels of maternal HBV DNA to below 10E6 IU/ml before delivery. A modeling study published in 2016 estimated that a 90% reduction in new chronic infections and 65% reduction in mortality could be achieved by scaling up the coverage of infant vaccination (to 90% of infants), birth-dose vaccination (to 80% of neonates), use of peripartum antivirals (to 80% of HBeAg-positive mothers) and population-wide testing and treatment (to 80% of eligible people). These interventions would prevent 7.3 million deaths between 2015 and 2030. An elimination threshold for incidence of new chronic infections would be reached by 2090 worldwide [59].

FUTURE PERSPECTIVE

The major obstacle to the worldwide elimination of HBV and HIV infection is their persistence in the host. For HIV there is an integrated

viral reservoir in different cells and several tissue compartments [60], whereas for HBV definitive cure requires elimination of the persistent intrahepatic replication-competent cccDNA from every infected hepatocyte [61]. Since HCV does not persist in cells, definitive cure can currently be achieved. There are significant ongoing research efforts with the goals of achieving functional cure regimens in HBV and HIV, essentially referring to the absence of viral replication after treatment even if viral replication components persist in the body [62, 63]. If achieved, these would be very significant advances.

For HIV, new therapeutic approaches mainly try to induce virus expression from latently infected cells and thence to stimulate clearance of these cells. This "shock and kill" therapeutic strategy involves drugs that activate viral replication in latent infected cells by, for example, inhibiting the target enzyme histone deacetylase (HDAC) while under cART therapy (to prevent infection of uninfected T cells) [64, 65]. Although regarded as promising, no studies have yet shown a consistent decrease in the size of the HIV reservoir by using these interventions, and the potential of adding in strategies that facilitate concurrent immune-mediated clearance of infected cells is being pursued [66]. Toll-like receptor (TLR) activation could be another possible target for new therapy. A first promising example of this was shown in simian immunodeficiency virus (SIV)-infected rhesus macaques of whom a subset achieved a reduction of the viral reservoir after treatment with TLR agonists GS-986 and GS-9620. The TLR7 agonists activated multiple innate and adaptive immune cell populations in addition to inducing expression of SIV RNA. Moreover, after stopping cART, two of nine treated animals remained aviremic for more than 2 years, even after in vivo CD8 + T cell depletion, and adoptive transfer of cells from aviremic animals could not induce de novo infection in naïve recipient macaques [67]. Further ex vivo development in humans demonstrated that the selective TLR7 agonist GS-9620 induced expression of HIV in peripheral blood mononuclear cells from HIV-infected individuals on suppressive antiretroviral therapy and also activated HIV-specific T cells and enhanced antibody-mediated clearance of HIV-infected cells, suggesting a possible utility of this approach [68].

For hepatitis B there are multiple new promising therapies with differing targets in the virus life cycle. The hepatocyte surface receptor utilized by the virus has been identified and opened up the potential to develop drugs that block viral entry. Myrcludex B (synthetic 47-amino-acid N-myristoylated lipopeptide, derived from the preS region of hepatitis B virus) is one such potential therapy—a first-in-class entry inhibitor for treatment of hepatitis B (HBV) and hepatitis delta (HDV) infection [69–72]. Several other new antiviral and immunomodulatory compounds have reached preclinical and/or early clinical evaluation for HBV infection, many with the aim of silencing cccDNA and/or reducing the size of the cccDNA pool [27].

However, history has shown that for a disease to become truly controlled, or even eradicated worldwide, effective medications alone are not sufficient, and robust preventive measures such as effective vaccination, in combination with prevention of mother-to-child transmission, safe medical procedures, safe sexual practices and other harm reduction procedures, are required and need to be widely implemented and available. When reviewing the three blood-borne viruses discussed, for HBV all the latter measures are already established in most countries, and it is the lack of an effective vaccination that is largely hampering worldwide elimination strategies for HCV and HIV [73].

Finally, for all three viruses a key point is to facilitate all those in need to have access to treatment. Tenofovir disoproxil fumarate has recently become available as a generic with a cost of as little as $48 per year in many low- and middle-income countries. Using Europe as an example, it has been suggested that, among low HBV prevalence countries, there are no significant restrictions in diagnostic or drug availability if they are upper-middle- or high-income countries [74]. In contrast, some upper-middle-income countries with moderate to high prevalence rates, such as Albania and Iran, have

restrictions on diagnostics and/or management [74]. Throughout Europe (and other regions), limited access to treatment of HBV and HCV infections occurs among vulnerable populations such as undocumented migrants, asylum seekers and people without insurance [75]. In 2015, only 7% of the 71 million people with chronic hepatitis C had access to treatment. WHO is working to ensure that DAAs are affordable and accessible to those who need them, and prices have dropped dramatically in some areas (primarily in some high-burden, low- and lower-middle-income countries) facilitated by the introduction of generics.

CONCLUSION

Elimination of HIV, HBV and HCV infections as public health issues seems to be plausible in a not so far future—largely as a result of implementing preventive strategies and the development of new drugs or vaccines. Each of the infections has its own issues and needs. It is currently unclear which will win the race to be the first to achieve elimination as a public health issue—each should aim to be the first, and such competition can only be useful to ultimately end the burden of blood-borne viruses. Ultimate eradication worldwide requires an effective vaccination, and here HBV remains the current front runner. Since vaccination appears to be an essential tool to reach this goal together with new effective drugs and reliable end points, hepatitis B could be the first of the three infections to be eliminated.

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