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HIV AND HEPATITIS C AND B COINFECTIONS

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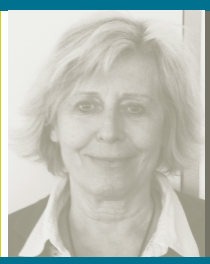


SCOR Global Life

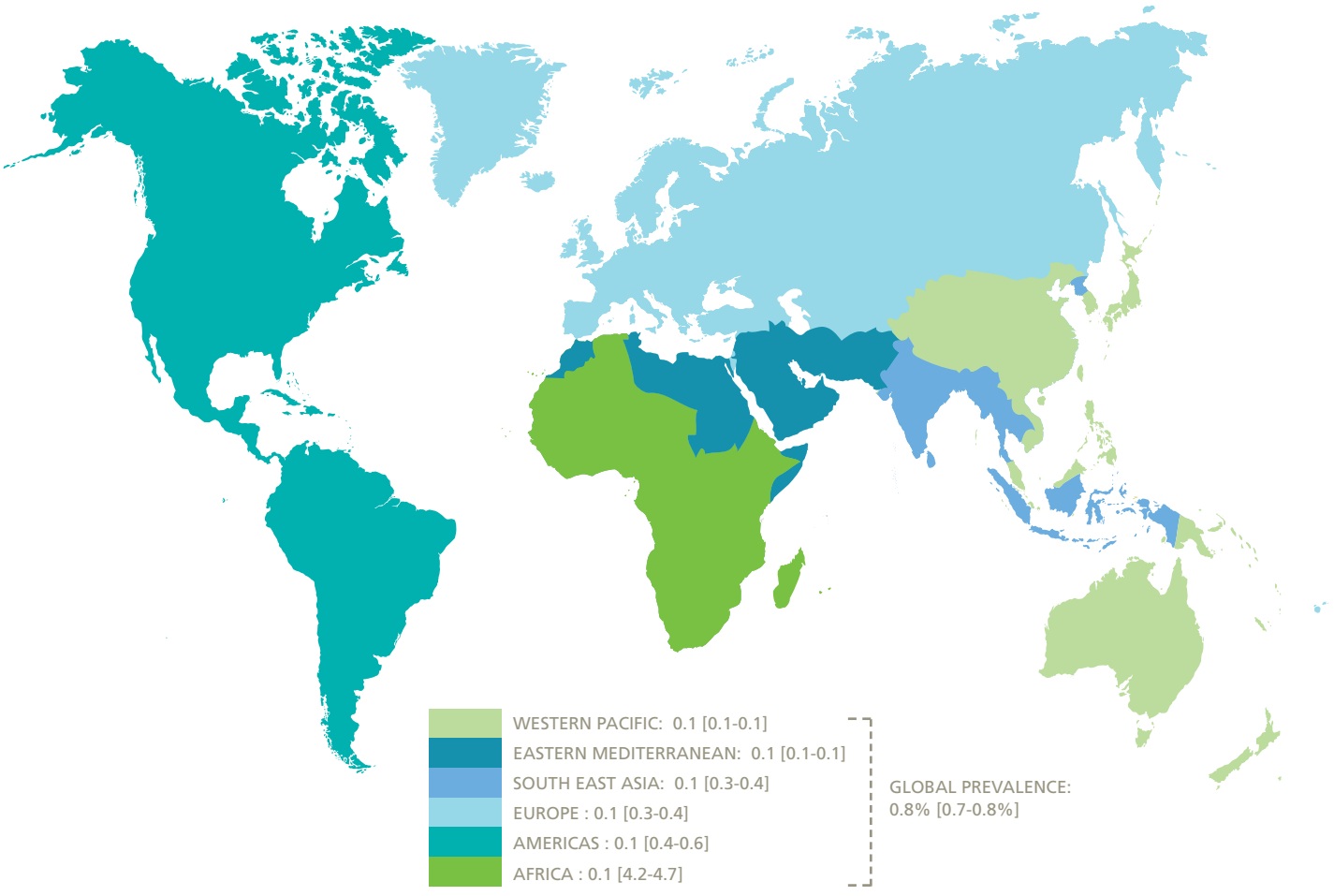
HIV and hepatitis C and B coinfections

Around 36 million people are living with HIV in the world today (LVWH). 5 million of them are also infected with the hepatitis C virus (HCV) and 4 million with hepatitis B virus (HBV). In both cases, HIV and the immunodeficiency it causes, accelerate the progression of hepatitis B or C, inducing increased morbidity and mortality for all three infections. .

Indeed, some coinfections with HCV or HBV have harmful effects on the progression of the HIV infection, increasing HIV replication and depletion of CD4 T-cells impacting all causes of mortality. Conversely, HIV infection and the immune deficiency that it induces diminish the immune defences and HBV and HCV clearance capacity, making hepatocytes more susceptible to inflammation and facilitating the development of hepatic fibrosis. Major progress has been made, however, in the treatment of these three infections, completely changing the prognosis and even providing a permanent cure for HCV infection. In this review, we will look in turn at the issues relating to HCV coinfection and HBV coinfection.

PREVALENCE OF HIV IN ADULTS (15-49), 2013 BY WHO REGION

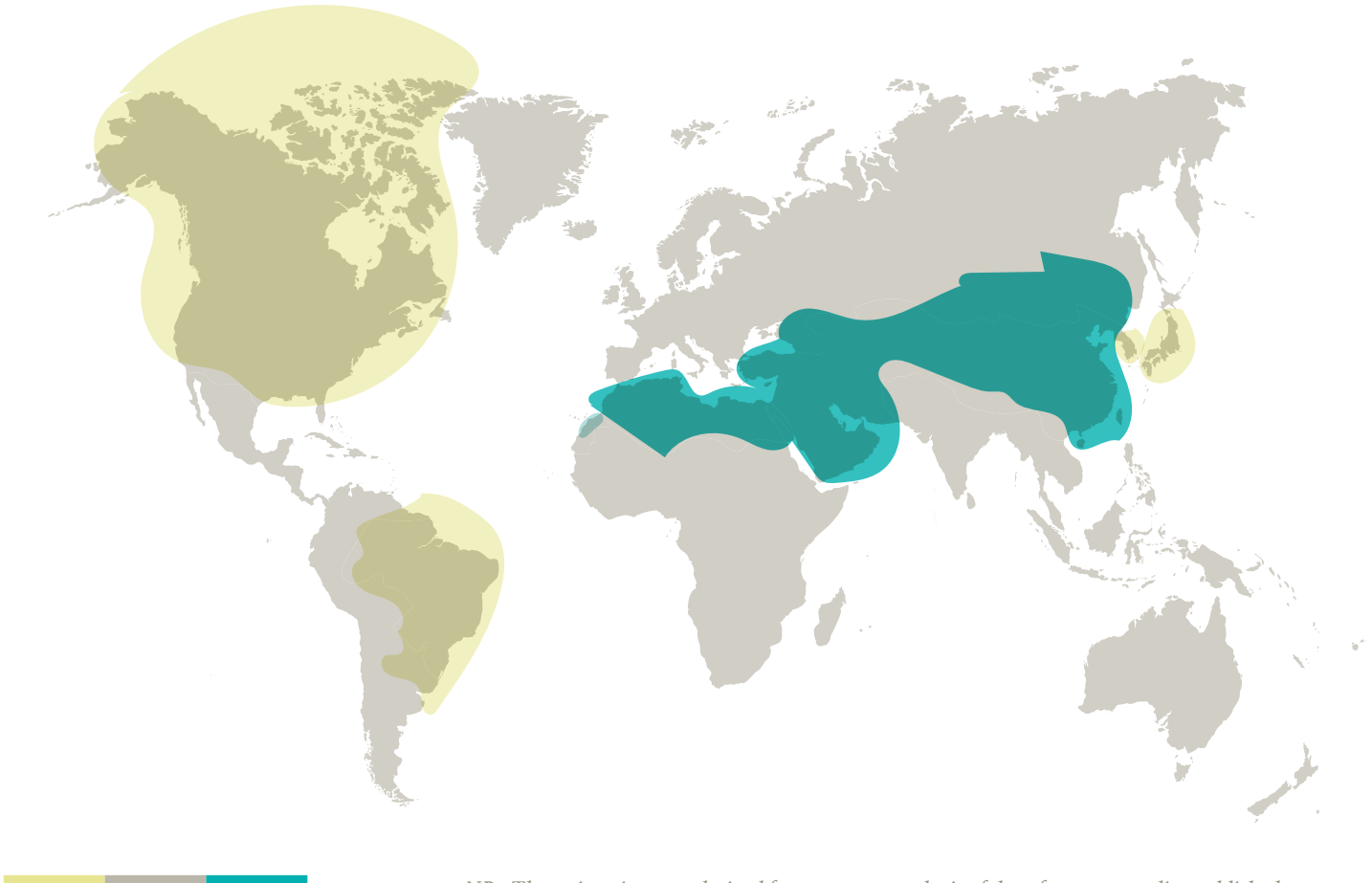
Source: World Health Organization



HCV coinfection

Equivalent modes of acquisition have led to a level of HIV-HCV coinfection of about 5 million people worldwide. This coinfection leads to an accelerated progression of hepatic fibrosis, the main cause of death despite the major advances on HIV achieved due to highly active antiretroviral therapies (HAART). The development of new direct-acting antiviral drugs against HCV has however led, spectacularly, to the curing of that disease, opening up an exciting new era to redefine the paradigms for treating this coinfection.

ANTI-HCV SEROPREVALENCE BY REGION, 2005



< 1,5%	1,5 – 3,5%	> 3,5%
Low	Moderate	High

NB : The estimations are derived from a meta-analysis of data from 232 studies published between 1997 and 2007, and NHANES data until 2010.

Source : Global Epidemiology of Hepatitis C Virus Infection : New Estimates of Age-Specific Antibody to HCV Seroprevalence. Khayriyyah Mohd Hanafiah, Justina Groeger, Abraham D. Flaxman, and Steven T. Wiersma HEPATOLOGY, Vol. 57, No. 4, 2013 1333-1342.

NATURAL HISTORY OF HIV-HCV COINFECTION

The HIV and HCV viruses share the same modes of transmission: often occurring by exposure to blood, sexual intercourse or by mother-to-child transmission, although HCV is 10 times more infectious than HIV. HIV-infected injection drug users represent the majority of HCV-HIV coinfections. Men who have sex with men (MSM) remain a minority, although there are micro-epidemics in urban centres in developed countries which highlights the importance of an annual HCV check for HIV-infected MSMs engaging in high-risk practices. HIV-HCV coinfection is not associated with an increase in the progression towards AIDS or HIV-related mortality, but could aggravate CD4 depletion.

On the other hand, HIV infection has had adverse effects on the natural history of HCV infection, facilitating the multiplication of the HCV, reducing by half the number of spontaneous recoveries following an acute infection with HCV (from 20% to 5-10%), and above all facilitating an accelerated progression towards fibrosis and liver cancer. One French study showed, before the HAART era, an increased rate of progression towards fibrosis in coinfected patients, HIV status and CD4 count being risks factors independent of progression. In addition, HIV-HCV coinfection is associated with higher rates of liver failure than in HCV monoinfection, with a 5-year survival rate of about 25 to 50% compared to 45 to 74% in HCV monoinfection.

Finally, coinfected subjects develop hepatocellular carcinoma more quickly than monoinfected patients. The introduction of HAART has made it possible to partially limit the progression towards fibrosis, as shown by a meta-analysis of 3,567 coinfected patients, confirming that under HAART the relative risk of cirrhosis fell from 2.9 to 2.1, whilst nevertheless remaining twice as high as in HCV monoinfection. Therefore, mortality remains 12 times higher under HAART (~4 for 100 patient-years), essentially due to end-stage liver failure. However, it is difficult to draw definitive conclusions from these studies due to their retrospective nature, the heterogeneity of the populations studied and missing data. Further studies are needed to better define the risks of fibrosis and morbidity and mortality of hepatic origin, particularly since the introduction of anti-HCV DAAs (direct-acting antiviral agents).

TREATMENT OF HCV INFECTION

The optimum treatment for HCV infection during HCV-HIV coinfection is still changing due to the multitude of direct-acting antiviral agents currently in development. Several new HCV DAAs already authorised, or in the course of being approved, make it possible to avoid treatments with alpha interferon, inducing high durable response rates, even at the cirrhosis stage or after the failure of an earlier treatment. If the classic treatments using IFN-a and ribavirin in coinfected patients induced lower rates of sustained virologic response (SVR) compared to HCV-monoinfected patients, this difference seems to disappear with DAAs.

It is recommended by the European consensus conference that all acute HCV infections be treated, even in HIV-coinfected patients. DAAs seem to allow a shorter treatment of the acute infection although further randomised studies are necessary to determine the efficacy and optimum duration of interferon-free regimens. Multiple studies have demonstrated significant advantages of treating chronic HCV in coinfected subjects, even at the fibrosis stage.

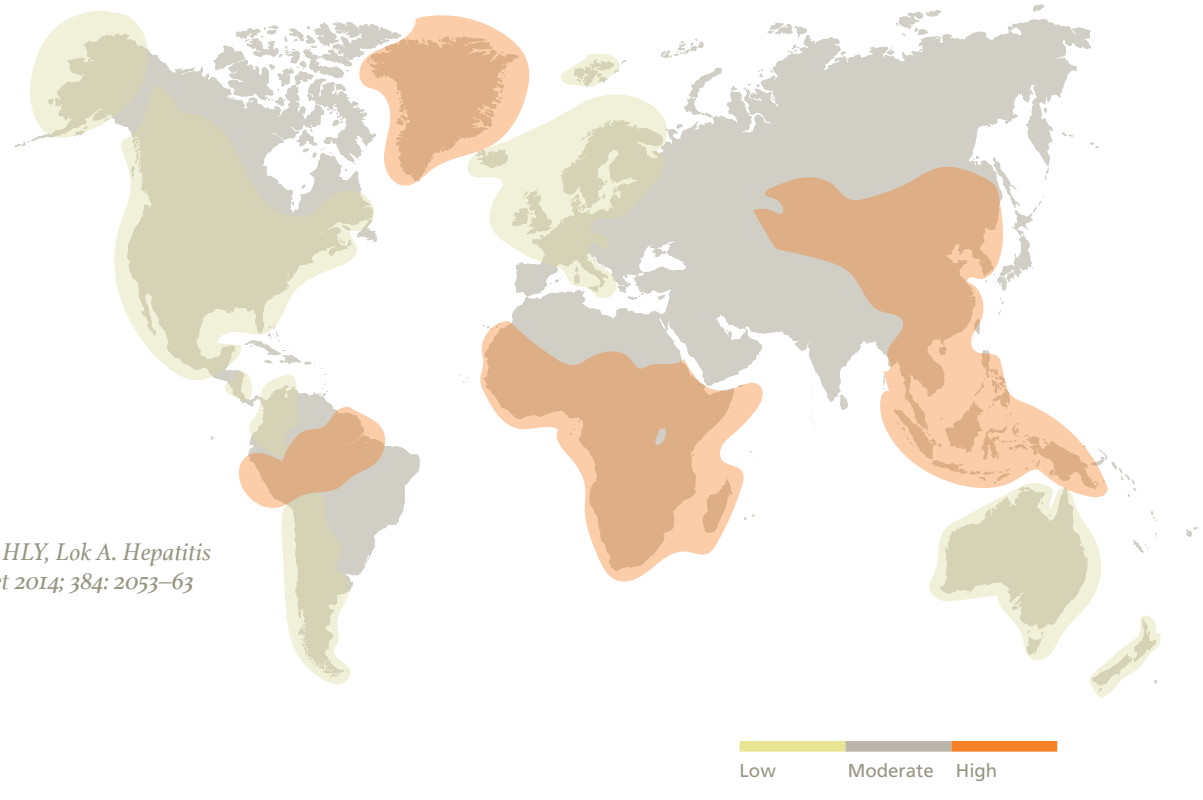
The side effects of the first generations of DAAs prevented their use, despite encouraging results. The second generation drugs are better tolerated. The protease inhibitor Simeprevir in combination with IFN-a and ribavirin has prompted a 74% SVR rate at 12 weeks in subjects coinfected by genotype 1. Nevertheless, the pharmacological interaction with HIV protease inhibitors and the non-nucleoside reverse-transcriptase inhibitor, efavirenz, force substitutions with integrase inhibitors. This obstacle has been removed with the more recent classes of DAAs such as Sofosbuvir, an HCV NS5B inhibitor with a powerful antiviral activity against all the C genotypes, a high barrier against resistance and better tolerance than interferon-based treatments, as well as metabolic independence with regards to cytochrome P450. Sofosbuvir has been associated with high rates of SVR, in several studies on chronic HCV monoinfection, equivalent to those obtained in HCV monoinfection. The PHOTON-1 study showed that 16 out of 17 HIV-positive patients coinfected with genotype 3 HCV reached a SVR after 24 weeks of sofosbuvir plus ribavirin. Combinations of DAAs induce high rates of permanent recovery from isolated HCV infection. Thus the combination of sofosbuvir and the NS5A inhibitor, ledipasvir, with or without ribavirin, induced 95% SVR rates at 12 weeks on genotype 1. The combination of sofosbuvir and simeprevir with or without ribavirin induced 96% SVR rates in the pre-cirrhosis stages with genotype 1 after failure of conventional treatments. Another study concerning 55 anti-HCV treatment-naive coinfected patients showed the induction of a sustained response after 12 weeks of treatment with a daily dose of ledipasvir and sofosbuvir in 98% of the participants. Other combinations of DAAs administered orally using ombitasvir, paritaprevir (associated with ritonavir), dasabuvir and ribavirin in patients co-infected a genotype 1 virus with or without cirrhosis were tested in the TURQUOISE-I randomised trial on 63 patients and a sustained response was obtained in 94% of the subjects after 12 weeks of treatment.

These excellent results prove that it is possible to obtain permanent recovery from the HCV infection associated with HIV infection without any severe side effects with the latest generations of DAAs. Since early 2014, the way is open for treatments using sofosbuvir plus ribavirin in coinfection, even at advanced stages of liver disease in France. The only limitation currently on sofosbuvir is its extremely high cost. The results of other phase III studies on HIV-HCV coinfection are anticipated with impatience.

HBV coinfection

Unlike hepatitis C, HBV coinfections mainly affect MSMs in Europe and the USA, 5 to 15% of them having markers of chronic HBV infection, while IV drug users only represent 7% to 10% of coinfections. Considerable therapeutic progress has also been made thanks to antiretrovirals acting on both HIV and HBV, but these do not lead to permanent recovery from the HBV infection. On the other hand, the frequency of new HBV infections has fallen thanks to increased anti-HBV vaccination coverage in these populations.

RATE OF CHRONIC HEPATITIS B VIRUS INFECTION



Source : Trépo C, Chan HLY, Lok A. Hepatitis B virus infection. Lancet 2014; 384: 2053–63

RELATIVE IMPACT OF HBV AND HIV COINFECTIONS

For primary HIV infection, HBV coinfection is a predictive factor independent of CD4 depletion (RR 3.46) and increases the relative risk of developing AIDS (RR 1.80) within 3 years of HIV infection. Coinfected patients have an all-cause mortality risk (excluding AIDS) increased by a factor of 3 compared to HIV infection alone, showing the need for regular monitoring of the coinfection and the severity of liver disease in this population. In fact, the rate of recovery from acute hepatitis with HBV is 5 times lower than in monoinfection, and the clearance rates of the HBe and HBs antigens depend heavily on the level of immunodeficiency and the ARVs.

Additionally, patients coinfected with HIV and HBV have an accelerated progression towards hepatic fibrosis, cirrhosis, end-stage liver failure and hepatocarcinoma (HCC). Superinfection by hepatitis D virus aggravates the complications of HIV-HBV coinfection.

OPTIMISED TREATMENT OF HBV

The aim of anti-HBV therapy is to suppress viral replication, reduce hepatic inflammation and prevent progression towards cirrhosis and HCC. The efficacy of anti-HBV therapies has increased considerably with the widespread use of antiretrovirals that act on HBV. Currently several agents can be used, including pegylated interferon (peg-IFN), lamivudine (LAM), emtricitabine (FTC), adefovir (ADV), entecavir (ETV) and tenofovir disoproxilfumarate (TDF). LAM, FTC and TDF are active on HBV and HIV. The main limitation on the use of lamivudine is the rapid appearance of mutations of the HBV polymerase gene (20% a year). It is therefore recommended that a dual anti-HBV therapy be used in any patient who is to begin ARVs. The use of tenofovir disoproxilfumarate (TDF), a very powerful reverse transcriptase inhibitor active against HBV has allowed major progress to be made in treatment-naive patients or patients pre-treated with lamivudine, thereby enabling end-stage liver failure due to HBV to be prevented. TDF administered with powerful combinations of ARVs currently represents the most effective therapeutic option in coinfected patients, achieving virologic control in over 95% of patients after 5 years of treatment. Clearance of the HBe antigen, however, only occurs in 35 to 45% of cases and that of HBs antigen in 3% to 12% of cases after 3 to 5 years of treatment. Significant improvements in histological status are also observed, even in patients with cirrhosis.

Important questions remain to be answered, such as when is the optimal moment for initiating TDF in the context of coinfection? European recommendations by the European AIDS Clinical Society (EACS) suggest beginning by assessing the degree of cirrhosis, the HBV-DNA levels (with a threshold of 2000 IU/ml) and the ALT levels. The best treatment option is early initiation of ARVs, including TDF, in combination with either lamivudine or emtricitabine. Where there is fibrosis, use of a dual anti-HBV therapy is recommended. In patients with HBV genotype A, high ALT levels and low HBV-DNA levels, it is suggested that a 1-year treatment with IFN-a be attempted. What strategy to follow with persistence of HBV replication under long-term TDF is another question in need of answering.

Intensification strategies are proposed, but have yet to be confirmed. The monitoring of the treatment of HBV infection rests on HBV-DNA level testing (every 6 months) and on annual HBV serology testing in order to identify patients with virologic control and clearance of HBe/HBs antigens, even though such results are the exception. HBV-DNA levels are poor predictors of HBe/HBs antigen clearance. The HBe level at 12 months predicts clearance at 36 months and HBs levels < 400 UI/ml at the time of initiating treatment are highly predictive of HBs clearance. However, the clinical relevance of these markers remains to be confirmed as it is not possible to anticipate interruption of treatment before clearance. The persistence of detectable levels of HBV-DNA reflects suboptimal treatment or therapeutic failure, and the need to look for viral drug resistances. Therapeutic efficacy must also be evaluated on the regression of the fibrosis on the basis of noninvasive markers. Finally, anti-HBV treatment reduces the risk of progression towards HCC.

INSURANCE INSERT

Since the arrival on the scene of triple therapy, the prognosis for people infected with HIV has improved substantially. People under treatment can access life insurance subject to certain conditions.

For patients co-infected with hepatitis B, the treatments as a general rule do not eradicate the hepatitis virus but simply reduce its replication. Therefore, hepatitis B cannot be cured in the strict sense of the word. For the time being, for insurance purposes, the long term prognosis of these patients remains difficult to evaluate which calls for careful analysis on a case-by-case basis.

However, for people coinfected with hepatitis C who do not respond to interferon-rivabirin, the prognosis remains poor in the medium term. The arrival of new treatments has changed the situation and there are now more and more treatment options. Recovery rates with the new treatments are as high in coinfected patients as in those with hepatitis C only.

The treatment is monitored and evaluated by measuring the hepatitis C viral load (HCV RNA). People under treatment who have a negative HCV RNA and a normal liver function test have an improved long-term prognosis with reduced mortality. Under these conditions, they too can access life insurance.

PREVENTION OF HBV INFECTION IN HIV-INFECTED SUBJECTS

Screening for HBV is recommended when HIV infection is diagnosed before initiating antiretrovirals, and, if there is coinfection with HBV, liver function should be assessed. The presence of anti-HBs antibodies at titers of > 10 IU/L is associated with seroprotection and titers of > 100 IU/L are associated with long-term protection. In the event of negative results for HBs antigen, anti-HBs and anti-HBc antibodies, HBV vaccination is recommended, but its efficacy is limited by the immune deficiency related to HIV infection. Improving the efficacy of HBV vaccination by administering an additional dose of the vaccine has enabled better prevention of the transmission of HBV in HIV-infected patients.

LIVER TRANSPLANT AND HBV-RELATED LIVER FAILURE

The progress with anti-HIV therapies has increased the need to treat chronic hepatitis B. In most cases of end-stage liver failure, a liver transplant is the best option, with survival rates similar to those observed in HBV monoinfection. It must be considered quickly, as soon as signs of liver failure appear.

CONCLUSION

Remarkable progress has been achieved in the treatment of these types of hepatitis associated with HIV infection and it has considerably modified the prognosis for these infections. It is still too early to predict the efficacy of anti-HCV treatments in the prevention of cirrhosis and hepatocarcinoma, but studies currently in progress are expected to soon give long-awaited results. The outcomes of these studies could again radically change the indications of these treatments, which are still limited by their extremely high cost. The efficacy of certain antiretrovirals on hepatitis B has led to more modest progress since recovery remains the exception rather than the rule for these cases. It has however encouraged some innovative strategies in the treatment and prevention of this infection that are remarkably effective. The new challenge remains that of finding treatments that truly eradicate the hepatitis B virus in the context of HIV coinfection.

References

Chen, J. Y. et al. Nat. Rev. Gastroenterol. Hepatol. 11, 362–371 (2014); published online 18 February 2014; doi:10.1038/nrgastro.2014.

Hsin-Yun Sun, Wang-Huei Sheng, Mao-Song Tsai, Kuan-Yeh Lee, Sui-Yuan Chang, Chien-Ching Hung Hepatitis B virus coinfection in human immunodeficiency virus-infected patients: A review World J Gastroenterol 2014 October 28; 20(40): 14598-14614. ISSN 1007-9327 (print) ISSN 2219-2840 (online).

Kim, A. Y. & Chung, R. T. Coinfection with HIV 1 and VHC—a one-two punch. Gastroenterology 137, 795–814 (2009).

Smith, C. et al. Factors associated with specific causes of death amongst HIV-positive individuals in the D:A:D Study. AIDS 24, 1537–1548 (2010).

Quan, V. M. et al. Risks for HIV, VHB, and VHC infections among male injection drug users in northern Vietnam: a case–control study. AIDS Care 21, 7–16 (2009).

Van de Laar, T. et al. Evidence of a large, international network of VHC transmission in HIV-positive men who have sex with men. Gastroenterology 136, 1609–1617 (2009).

Vogel M, Dominguez S, Bhagani S, Azwa A, Page E, Guiguet M, Valantin MA, Katlama C, Rockstroh JK, Nelson M. Treatment of acute VHC infection in HIV-positive patients: experience from a multicentre European cohort. Antivir Ther. 2010;15(2):267-79. doi: 10.3851/IMP150.

Rockstroh, J. K. et al. European AIDS Clinical Society (EACS) guidelines for the clinical management and treatment of chronic hepatitis B and C coinfection in HIV-infected adults. HIV Med. 9, 82–88 (2008).

European AIDS Treatment Network (NEAT) Acute Hepatitis C Infection Consensus Panel. Acute hepatitis C in HIV-infected individuals: recommendations from the European AIDS Treatment Network (NEAT) consensus conference. AIDS 25, 399–409 (2011).

Hernando, V. et al. All-cause and liver-related mortality in HIV positive subjects compared to the general population: differences by VHC co infection. J. Hepatol. 57, 743–751 (2012).

Chen, T. Y. et al. Meta-analysis: increased mortality associated with hepatitis C in HIV-infected persons is unrelated to HIV disease progression. Clin. Infect. Dis. 49, 1605–1615 (2009).

Benhamou, Y. et al. Liver fibrosis progression in human immunodeficiency virus and hepatitis C virus coinfected patients. The Multivirc Group. Hepatology 30, 1054–1058 (1999).

Pineda, J. A. et al. Natural history of compensated hepatitis C virus-related cirrhosis in HIV-infected patients. Clin. Infect. Dis. 49, 1274–1282 (2009).

Giron-Gonzalez, J. A. et al. Natural history of compensated and decompensated VHC-related cirrhosis in HIV-infected patients: a prospective multicentre study. Antivir. Ther. 12, 899–907 (2007)

Thein, H. H. et al. Natural history of hepatitis C virus infection in HIV-infected individuals and the impact of HIV in the era of highly active antiretroviral therapy: a meta-analysis. AIDS 22, 1979–1991 (2008).

Klein MB, Rollet-Kurhajec KC, Moodie EE, Yaphe S, Tyndall M, Walmsley S, et al. Mortality in HIV-hepatitis C co-infected patients in Canada compared to the general Canadian population (2003-2013). AIDS 2014; 28:1957-1965.

Van der Meer, A. J. et al. Association between sustained virological response and all-cause mortality among patients with chronic hepatitis C and advanced hepatic fibrosis. JAMA 308, 2584–2593 (2012).

Berenguer, J. et al. Sustained virological response to interferon plus ribavirin reduces liver-related complications and mortality in patients coinfected with human immunodeficiency virus and hepatitis C virus. Hepatology 50, 407–413 (2009).

Lawitz, E. et al. Sofosbuvir in combination with peginterferon α2a and ribavirin for non-cirrhotic, treatment-naive patients with genotypes 1, 2, and 3 hepatitis C infection: a randomised, double-blind, phase 2 trial. Lancet Infect. Dis. 13, 401–408 (2013).

Lawitz, E. & Gane, E. J. Sofosbuvir for previously untreated chronic hepatitis C infection. N. Engl. J. Med. 369, 678–679 (2013).

Sulkowski MS, Naggie S, Lalezari J, Fessel WJ, Mounzer K, Shuhart M, et al. Sofosbuvir and Ribavirin for Hepatitis C in Patients With HIV Coinfection. JAMA 2014; 312:353-361.

Lawitz, E. et al. Sofosbuvir and ledipasvir fixed-dose combination with and without ribavirin in treatment-naive and previously treated patients with genotype 1 hepatitis C virus infection (LONESTAR): an open-label, randomised, phase 2 trial. Lancet http://dx.doi.org/10.1016/S0140-6737(13)62121-2.

Jacobson, I. M. et al. SVR results of a once-daily regimen of simeprevir (SMV, TMC435) plus sofosbuvir (SOF, GS 7977) with or without ribavirin in cirrhotic and non-cirrhotic VHC genotype 1 treatment-naïve and prior null responder patients: the COSMOS study [abstract LB-3]. Presented at the 64th Annual Meeting of the American Association for the Study of Liver Diseases, Washington, DC (2013).

Sulkowski MS, Eron JJ, Wyles D, Trinh R, Lalezari J, Wang C, et al. Ombitasvir, paritaprevir co-dosed with ritonavir, dasabuvir, and ribavirin for hepatitis C in patients co-infected with HIV-1: a randomized trial. JAMA. 2015 Mar 24-31;313(12):1223-31. doi: 10.1001/jama.2015.1328.

Osinusi A, Townsend K, Kohli A, Nelson A, Seamon C, Meissner EG, et al. Virologic response following combined ledipasvir and sofosbuvir administration in patients with HCV genotype 1 and HIV co-infection. JAMA. 2015 Mar 24-31;313(12):1232-9. doi: 10.1001/jama.2015.1373.

Kourtis AP, Bulterys M, Hu DJ, Jamieson DJ. HIV-VHB coinfection-- a global challenge. N Engl J Med 2012; 366: 1749-1752 [PMID: 22571198 DOI: 10.1056/NEJMp1201796].

Lacombe K, Rockstroh. HIV and viral hepatitis coinfections: advanced and challenges. Guy 2012;61(Supp 1):i47ei58. doi:10.1136/gutjnl-2012-302062.

Chun HM, Roediger MP, Hullsiek KH, Thio CL, Agan BK, Bradley WP, Peel SA, Jagodzinski LL, Weintrob AC, Ganesan A, Wortmann G, Crum-Cianflone NF, Maguire JD, Landrum ML. Hepatitis B virus coinfection negatively impacts HIV outcomes in HIV seroconverters. J Infect Dis 2012; 205:
185-193 MID: 22147794 DOI: 10.1093/infdis/jir720].

Wandeler G, Gsponer T, Bihl F, Bernasconi E, Cavassini M, Kovari H, Schmid P, Battegay M, Calmy A, Egger M, Furrer H, Rauch A. Hepatitis B virus infection is associated with impaired immunological recovery during antiretroviral therapy in the Swiss HIV cohort study. J Infect Dis 2013; 208:1454-1458.

Hung CC, Wu SM, Lin PH, Sheng WH, Yang ZY, Sun HY, Tsai MS, Lee KY, Huang MS, Chang SF, Su YC, Liu WC, Chang SY. Increasing incidence of recent hepatitis D virus infection in HIV-infected patients in an area hyperendemic for hepatitis B virus infection. Clin Infect Dis 2014; 58: 1625-1633

European Association For The Study Of The Liver. EASL clinical practice guidelines: Management of chronic hepatitis B virus infection. J Hepatol 2012; 57: 167-185.

Lopes VB, Hassing RJ, de Vries-Sluijs TE, El Barzouhi A, Hansen BE, Schutten M, de Man RA, van der Ende ME. Long-term response rates of successful hepatitis B vaccination in HIV-infected patients. Vaccine 2013; 31: 1040-1044.

De Vries-Sluijs TE, Hansen BE, van Doornum GJ, Kauffmann RH, Leyten EM, Mudrikova T, Brinkman K, den Hollander JG, Kroon FP, Janssen HL, van der Ende ME, de Man RA. A randomized controlled study of accelerated versus standard hepatitis B vaccination in HIV-positive patients. J Infect Dis 2011; 203: 984-991.

Potsch DV, Camacho LA, Tuboi S, Villar LM, Miguel JC, Ginuíno C, Silva EF, Mendonça RM, Moreira RB, Barroso PF. Vaccination against hepatitis B with 4-double doses increases response rates and antibodies titers in HIV-infected adults. Vaccine 2012; 30: 5973-5977.

Launay O, van der Vliet D, Rosenberg AR, et al; ANRS HB03 VIHVAC-B Trial. Safety and immunogenicity of 4 intramuscular double doses and 4 intradermal low doses vs standard hepatitis B vaccine regimen in adults with HIV-1: a randomized controlled trial. JAMA 2011;305:1432e40.

(OARAC) OoARAC. DHHS Guidelines for the Use of Antiretroviral Agents in HIV-1-infected Adults and Adolescents. AIDS info website 2013. Available from: URL: http://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.

EACS European AIDS Clinical Society. EACS Guidelines Version 7.0. 2013 Available from: URL: http://www.eacsociety. org/Portals/0/Guidelines_Online_131014.pdf.

Schildgen O, Schewe CK, Vogel M, et al. Successful therapy of hepatitis B with tenofovir in HIV-infected patients failing previous adefovir and lamivudine treatment. AIDS 2004;18:2325e7.

De Vries-Sluijs TE, Reijnders JG, Hansen BE, et al. Long-term therapy with tenofovir is effective for patients co-infected with human immunodeficiency virus and hepatitis B virus.Gastroenterology 2010;139:1934e41.

Boyd A, Lasnier E, Molina JM, et al. Liver fibrosis changes in HIV-VHB-coinfected patients: clinical, biochemical and histological effect of long-term tenofovir disoproxil fumarate use. Antivir Ther 2010;15:963e74.

Maylin S, Boyd A, Lavocat F, et al. Kinetics of HBs and HBe antigen and prediction of treatment response to tenofovir in antiretroviral-experienced HIV-VHB infected patients. AIDS 13 February 2012. doi:10.1097/QAD.0b013e328352224d.

Papatheodoridis GV, Lampertico P, Manolakopoulos S, Lok A. Incidence of hepatocellular carcinoma in chronic hepatitis B patients receiving nucleos(t)ide therapy: a systematic review. J Hepatol 2010; 53: 348-356 [PMID: 20483498 DOI: 10.1016/j.jhep.2010.02.035].

Tateo M, Roque-Afonso AM, Antonini TM, Medja F, Lombes A, Jardel C, Teicher E, Sebagh M, Roche B, Castaing D, Samuel D, Duclos-Vallee JC. Long-term follow-up of liver transplanted HIV/hepatitis B virus coinfected patients: perfect control of hepatitis B virus replication and absence of mitochondrial toxicity. AIDS 2009; 23: 1069-1076.

Coffin CS, Stock PG, Dove LM, Berg CL, Nissen NN, Curry MP, Ragni M, Regenstein FG, Sherman KE, Roland ME, Terrault NA. Virologic and clinical outcomes of hepatitis B virus infection in HIV-VHB coinfected transplant recipients. Am J Transplant 2010; 10: 1268-1275.

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