World Journal of Gastroenterology

Submit a Manuscript: http://www.wjgnet.com/esps/
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
DOI: 10.3748/wjg.v22.i22.5137

World J Gastroenterol 2016 June 14; 22(22): 5137-5142
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

EDITORIAL

Need of righteous attitudes towards eradication of hepatitis C virus infection in Latin America

Arturo Panduro, Sonia Roman

Arturo Panduro, Sonia Roman, Department of Molecular Biology in Medicine, Civil Hospital of Guadalajara, "Fray Antonio Alcalde", Guadalajara, 44280 Jalisco, Mexico

Arturo Panduro, Sonia Roman, Health Sciences Center, University of Guadalajara, Guadalajara, 44340 Jalisco, Mexico

Author contributions: Panduro A and Roman S contributed equally to this work.

Conflict-of-interest statement: There is no conflict of interests in this study.

Correspondence to: Arturo Panduro, MD, PhD, FAASLD, Department of Molecular Biology in Medicine, Civil Hospital of Guadalajara, "Fray Antonio Alcalde", Hospital No. 278, Col. El Retiro, Guadalajara, 44280 Jalisco, Mexico. apanduro@prodigy.net.mx
Telephone: +52-33-36147743
Fax: +52-33-36147743

Received: March 25, 2016
Peer-review started: March 25, 2016
First decision: April 14, 2016
Revised: April 22, 2016
Accepted: May 4, 2016
Article in press: May 4, 2016
Published online: June 14, 2016

Abstract

Over the last few years, we have expanded our knowledge on numerous facets of the hepatitis C virus (HCV). Beginning with its discovery and viral life cycle, its impact on health, the development of liver disease and currently, effective antiviral treatments. The latter point has become of great interest throughout the developed world, where the possible eradication of HCV through specific strategies to reach all HCV-infected people has been announced. However, this scenario is very different in the countries of Latin America (LA), in which < 2% of infected patients requiring treatment have access to HCV medications. It has been estimated that at least ten million Latin Americans may be infected with HCV. Despite the numbers, viral hepatitis does not seem to be considered a health problem in this region of the world. This reality poses a challenge for politicians and governments of these countries, as well as to the pharmaceutical industry, the medical practitioners, and academics in LA. In this editorial, we state the need for alterations in the attitudes of the integral players involved in this situation. A recognition shift could help to create preventive strategies of viral hepatitis and to advocate for accessibility to new HCV treatments.

Key words: Low-income; Antiviral agents; Public health; Medical societies; Drug industry

Core tip: Global eradication of hepatitis C virus (HCV) infection is causing considerable interest, especially in the developed world. However, the accessibility to the new direct-acting antiviral regimens in low- and middle- income countries is an unmet need. At least ten million HCV-infected persons in Latin America (LA) are confronted by multiple barriers to HCV treatment. Moreover, for the LA countries, paradoxically at it seems, money may not be the only issue. The health authorities, the medical community, and the pharmaceutical industry are the key players that need to alter their attitude towards the delivery of HCV treatments to all patients irrespective of their socio-

economic status.

Panduro A, Roman S. Need of righteous attitudes towards eradication of hepatitis C virus infection in Latin America. *World J Gastroenterol* 2016; 22(22): 5137-5142 Available from: URL: http://www.wjgnet.com/1007-9327/full/v22/i22/5137.htm DOI: http://dx.doi.org/10.3748/wjg.v22.i22.5137

INTRODUCTION

Early years of hepatitis C virus infection

The history of the hepatitis C virus (HCV) is a strong example of a bench-to-bedside approach illustrating how basic scientific knowledge is applied to patient care.

Following the discovery of hepatitis B virus (HBV) in 1965[1], and hepatitis A virus (HAV) in 1973[2], a clinical entity known as post-transfusion non-A non-B (NANB) hepatitis became more evident[3]. This was regardless of the banning of commercial blood donations systems, and the implementation of HAV and HBV blood testing in 1975[3,4]. Furthermore in 1989, after years of intensive research[5], a scientific breakthrough discovered another virus consisting of a single positive strand of RNA, the HCV, classified in the *Flaviridae* family[6]. HCV was determined to be the causing agent of the post-transfusion NANB hepatitis[4,5].

In 1992, following the cloning of HCV, an evolving series of sensitive and specific anti-HCV antibody immunoassays were developed which allowed for the mandatory testing of blood collections in the United States[3]. Subsequently, third-generation immunoassays and RNA-HCV nucleic acid amplification tests improved the diagnostics of HCV for blood transfusion safety[7]. During the 90's, the HCV genotypes and subtypes, as well as their heterogeneous geographic distribution became apparent through basic research and molecular epidemiology[8]. Additionally in the United States, blood transfusions, injection drug use (IDU) and several medical procedures were identified as high-risk factors[3].

During the 90's but before 2011, the first antivirals to be marketed were standard interferon, followed by pegylated-interferon which was later combined with ribavirin[9]. Unfortunately, these antivirals achieved a low-level of sustained viral response (SVR) among patients with HCV genotype 1 compared to other genotypes[10]. However after 2011, the first and second generation direct-acting antivirals based on targeting the specific molecules of the HCV life cycle have proven more efficient regardless of genotype reaching an SVR in more than 90% or 95% of the patients who receive treatment[10].

In recent years, DNA sequencing and bioinformatics of HCV strains worldwide have allowed the evolutionary analysis and molecular tracing of the HCV epidemic across countries, mainly focusing on genotype 1a and 1b[11]. These studies have documented the prevalence of HCV in Japan since 1920, in Europe since 1940 and the United States since 1960[11,12]. Further studies have confirmed that the introduction of HCV in the United States may have occurred even earlier (in the 1950's) and is related to the use of contaminated blood obtained from commercial blood donors and the return of World War Ⅱ soldiers[13]. These reasons, along with the fact that hepatitis C is a stealthy virus causing injury to the liver in a silent manner, people who were born from 1945-1965 are currently in the target population of the "baby boomers" screening campaign for HCV in the United States[14].

Transmission of HCV infection in Latin America

Mexico's geographic location serves as a common pathway of intracontinental migration between the United States and other countries of LA. Thus, HCV could have spread from the United States to this region. However in LA, awareness of an NANB hepatitis did not intensify until the late 1970s and early 1980s[15]. During this period, the United States veterans returning from Vietnam, as well as the migration of Latin Americans to their homeland as retirees or by multiple processes of deportation and migration between countries became a major social-demographic phenomenon.

The first HCV epidemic outbreak was associated with the emergence of HIV in the mid-1980s, at a time where the presence of paid blood donors was a common situation[16]. This parenteral route of transmission may have been the primary source of dispersion in Central and South America since IDU, during those decades, was very rare in LA[17]. Furthermore, even though in the United States mandatory screening of blood-borne viruses had been implemented in 1992, it was not fully established in Mexico and LA until 1996[18,19]. This information indicates that even before 2000, blood donations contaminated with HCV were still a relevant risk factor[20]. Moreover, an additional route of HCV infection in the LA may have been the indiscriminate use of caesarean births and other medical procedures that took place during the same period[21]. Brazil and Mexico[22] are the two countries with the highest rates of cesarean sections within the Americas[23]. This could explain why Mexico has a female-to-male ratio of 2:1 of HCV infection[21].

Although partial reports were stating the frequency of HCV in countries of LA during the 1990s, it was not until after 2000 that HCV-related liver cirrhosis began to rise. In Mexico, this disease entity represents over 12 deaths per 100000 inhabitants and the estimated number of people infected with HCV may range from 1.5 to 2 million[24-26], and at least ten million in LA[26-28]. In this region the route of transmission of HCV may have been similar as it was in Mexico, taking into account that as of 2000 the use of IDU, as well as tattooing and piercing, had increased from that year

forward[17].

HCV TREATMENT IN LATIN AMERICA

HCV infection can only be prevented by evading or eradicating the virus. To achieve eradication, treatment with highly effective drugs to all who are infected is required. Currently with the introduction of the new, but very costly, direct-acting antivirals (DAAs) an enormous feeling of success is felt. This elation may be comprehensible for the developed countries, but it may not be true for many developing countries worldwide[29-32], including those in LA[33-37].

However, there are two sides to this story. On one hand, the feasibility of eradicating HCV is closer than ever due to new treatments[38]; yet, on the other hand, neither the authorities nor the physicians, recognize that many infected patients are the result of an iatrogenic spread of HCV. More than 95% of patients infected with viral hepatitis belong to a lower social class in their respective countries, and they can not afford to pay the current market prices of these new antiviral drugs[39].

Additionally, a significant challenge for the eradication of HCV is that there is more than one genotype of the human virus. There are seven genotypes and multiple subtypes[40], which have infected populations with heterogeneous genetic makeups worldwide. This point indicates that research data on HCV needs to be population-based, especially in LA. Further studies are required to identify the genotypes that circulate[41,42], the main risk factors[17,20,21] and the immunogenetic background of the population[43-45].

To date, less than 2% of the people infected with HCV have been treated with the standard pegylated-interferon/ribavirin therapy. The new DAAs, such as boceprevir, telaprevir, simeprevir, and sofosbuvir have been slowly licensed in a limited number of countries in LA. Moreover, HCV treatments are based on the United States and European guidelines which provide evidence of the SVR obtained in clinical trials carried out in populations other than LA.

Thus, under these circumstances who will have access to treatment in Latin America? A substantial body of literature has documented the multiple barriers to health care in HCV-infected patients[46-49]. Although crucial, they are not within the scope of this editorial. Alternatively, we address several issues regarding the health authorities, the medical community, and the pharmaceutical industry. These are key players involved in the prevention, diagnosis, and treatment of this disease.

KEY PLAYERS

Health authorities

The health officials have not considered viral hepatitis to be a severe health problem, which in turn has manifested ignorance or reluctance towards a state program of detection or treatment of this disease. Consequently, there are a limited number of up-to-date population-based epidemiological studies of viral hepatitis in most LA countries[35,36] sponsored by the government. The few that do exist are accomplished by the attention and personal interest of researchers, rather than the concern of the health authorities. This lack of concern from the health authorities translates into key factors and information being overlooked. Some of these factors include; lack of precision of who and how many people are infected, primary risk factors involved[50], transition in genotypes[17] and co-morbidities (obesity, diabetes, alcoholism, co-infection with HVB and HIV)[51]. Furthermore, these epidemiological studies need to be documented in the population of LA because most clinicians assume that the same SVR achieved in Caucasians will replicate in people from this region.

Medical community

In LA, including Mexico, most medical societies involved in the study of the liver have a limited number of members with a solid scientific career, based on their poor scientific productivity in indexed and high impact factor journals in their dedicated fields[52,53]. These society members are hosted by the pharmaceutical companies to attend international forums. In turn, they are the only speakers that echo their experience at the liver meetings to their fellows but do not contribute with scientific data or share their clinical experience. This circumstance has led to the situation that some members only intend to be their society's President (or Chairperson) without the actual contribution of new knowledge in their field of expertise. Moreover, it is precisely these "leaders of the field" who take part, on multiple occasions, as representatives of the health authority, sometimes playing a dual role as clinician and politician.

Therefore, when the support of the medical community is required to establish health policies that have an impact on vulnerable social groups, the members are left without a voice, and vote, on these issues. Consequently, the decisions are made in an unipersonal manner. Furthermore, if the clinician-politician now has a position within the health institutions or the government, he/she may now have a conflict of interest with his/her private practice.

Unfortunately, the lack of an official standpoint in many educational or health institutions to promote a high standard of scientific and academic quality is a serious weakness. This challenge, paired together with a high level of corruption and preferential treatment that prevails among some government authorities, makes it tough to provide treatment for this virus. This situation has created elitist groups of treating physicians being sponsored by the pharmaceutical industry. These doctors may be knowledgeable, however, in some cases, this information does not

necessarily apply to their respective countries or communities.

Furthermore, many of these physicians focus on his/her private practice and have negligible interest in understanding the reality of the disease in their community or country of origin. A reminder of the Hippocratic Oath is "We as doctors should seek the best benefit for the patients, including those who do not have access to treatment".

Likewise, in the majority of LA countries, there are no specialists in hepatology. Patients living with liver diseases are treated mainly by a gastroenterologist or internist[54]. However, with the introduction of the new effective antivirals, and the possibility of the pharmaceutical industry involvement, medical specialists from different fields now claim the liver-diseased patient. Thus, a specialty or subspecialty in hepatology supported by academic institutions should be established as soon as possible.

Pharmaceutical industry

The pharmaceutical industry has declared a responsibility to eradicate HCV by creating agreements based on the economy of each country for the marketing of the antiviral drugs. In general, the standard procedure for the pricing of these drugs is to achieve a full refund of the R and D investment in the developed countries, intermediate reimbursement in the middle-income countries, and the possibility to offer a generic product at a lower and accessible cost for the low-income countries (defined as a win-win situation).

Unfortunately, there are still some well-known challenges to overcome in many developing countries, such as corruption and slow bureaucracy to introduce these drugs[55]. Additionally, the lack of precise epidemiological information about HCV infection is an ongoing difficulty.

Another obstacle is performing the diagnostic tests. Each patient should be evaluated before treatment because not all patients that are positive for anti-HCV antibodies have detectable viral loads or have a similar grade of liver damage. Thus, a pretreatment algorithm including initial and follow-up viral loads, genotyping and identification of possible resistance mutations, and staging of liver damage (fibrosis/cirrhosis) should be considered. A conservative estimate of the costs of these tests may exceed up to $2000 to $4000 United States dollars before paying at least $10000 to $80000 United States dollars for a three-month period of treatment[56]. If the patient is a potential non-responder or present with advanced liver damage, this cost may rise even higher.

Considering these conditions several options have been proposed, such as the establishment of non-profit societies that aid in the funding of these high costs for the poor. This creates a risky situation, given the lack of transparency and poor attitudes of some key players previously mentioned, there is a chance that these "non-profit" organizations may end up as personal or family businesses, or in the hand of small groups who are in power.

Nevertheless, with the justification of "supporting updated scientific medical education", the pharmaceutical companies focus mainly on the treating physicians (clinicians) by selecting medical "leaders", doctors who have influence among the medical groups or societies, or are representatives of health institutions. Whereas, the few scholars or scientists who are knowledgeable in the field of viral hepatitis are not considered under the argument that they are not clinicians or do not treat patients.

This situation leads to the lost opportunity to be supported by the pharmaceutical industry. Thus, in the absence of proposals and sanitary laws, the pharmaceutical industry is interested in selling their drug; but the academic or research sector in the developing countries do not fall within their scope.

RECOMMENDATIONS

HCV infection imposes a large challenge in the world, and it certainly will be eradicated faster in some regions than others. In low- and medium-income countries of LA the health problem of HCV may not depend entirely on money, other nations with fewer resources are proactively establishing public-private partnerships to lower the cost of the DDAs (*e.g.*, Egypt). Hopefully, these strategies will close the gap between the number of patients who are infected (diagnosed) versus those who are treated.

The advancement of scientific knowledge and its impact on health are correlated with the progressive changes in the attitude and behavior of key players and others responsible. The increase in knowledge should benefit all people irrespective of their socio-economic status. To achieve such impact, and to reach all those who need an efficient antiviral therapy, this change in attitude needs to become a reality.

Where and how to start to face this critical situation in Latin America? One recommendation is that both politicians and authorities must consider viral hepatitis as a health problem in their respective region, and establish support strategies to investigate the burden of HCV infection. It is no longer safe to assume that any health issue can be resolved without recognizing the magnitude of the situation.

In the medical communities, a good start would be to establish a partnership between the academic sector, researchers, and physicians, instead of independently acting on their own. This collaborative shift could strengthen the figure of the MD/PhD in each medical society. This may be achieved if alongside, the academic institutions in LA make every effort towards higher standards of education and professionalism. This would greatly strengthen the quality of the medical associations with academic leaders that contribute with knowledge publishable in indexed

international journals. In countries such as Spain and Brasil, the use of the h-index (Hirsch-index) has been considered to grant membership to their respective National Academy of Medicine.

Another important change would be to educate the younger generations that the purpose of belonging to a medical society is not only to be their president or chairperson. As mentioned above, the ultimate goals are to provide prestige and effectiveness by contributing to new knowledge about their country or city in matters of health. The higher income groups require treatments, however, so does the general population. If we reconsider and always remember the Hippocratic Oath, this will help to reflect and advance the field quickly to achieve these goals.

To conclude, the disclosure of the clinicians (speakers), in regards to their sponsorship by the pharmaceutical industry, should be regulated by law and enforced by an ethical practice. Likewise, academics, scientists, medical practitioners and the pharmaceutical companies should equally engage and commit to solving the problem of HCV infection in this region of the world. Moreover, grants given by the pharmaceutical industry in LA to support research in liver disease would be extremely beneficial. These are recommendations that need to be heavily considered by all key players.

REFERENCES

1 **Blumberg BS**, Alter HJ, Visnich S. A "new" antigen in leukemia sera. *JAMA* 1965; **191**: 541-546 [PMID: 14239025 DOI: 10.1001/jama.1965.03080070025007]

2 **Feinstone SM**, Kapikian AZ, Purceli RH. Hepatitis A: detection by immune electron microscopy of a viruslike antigen associated with acute illness. *Science* 1973; **182**: 1026-1028 [PMID: 4356028 DOI: 10.1126/science.182.4116.1026]

3 Institute of Medicine (US) Committee to study HIV transmission through blood and blood products. HIV and the Blood Supply: An analysis of crisis decisionmaking. 2nd ed. Leveton LB, Sox HC Jr, Stoto MA, editors. Washington (DC): National Academies Press (US), 1995. Available from: URL: http: //www.ncbi.nlm.nih.gov/books/NBK232409/

4 **Alter HJ**, Houghton M. Clinical Medical Research Award. Hepatitis C virus and eliminating post-transfusion hepatitis. *Nat Med* 2000; **6**: 1082-1086 [PMID: 11017126 DOI: 10.1038/80394]

5 **Houghton M**. Discovery of the hepatitis C virus. *Liver Int* 2009; **29** Suppl 1: 82-88 [PMID: 19207970 DOI: 10.1111/j.1478-3231.2008.01925.x]

6 **Choo QL**, Kuo G, Weiner AJ, Overby LR, Bradley DW, Houghton M. Isolation of a cDNA clone derived from a blood-borne non-A, non-B viral hepatitis genome. *Science* 1989; **244**: 359-362 [PMID: 2523562 DOI: 10.1126/science.2523562]

7 **Busch MP**, Kleinman SH, Jackson B, Stramer SL, Hewlett I, Preston S. Committee report. Nucleic acid amplification testing of blood donors for transfusion-transmitted infectious diseases: Report of the Interorganizational Task Force on Nucleic Acid Amplification Testing of Blood Donors. *Transfusion* 2000; **40**: 143-159 [PMID: 10685998 DOI: 10.1046/j.1537-2995.2000.40020143.x]

8 **Zein NN**. Clinical significance of hepatitis C virus genotypes. *Clin Microbiol Rev* 2000; **13**: 223-235 [PMID: 10755999 DOI: 10.1128/CMR.13.2.223-235.2000]

9 **Littler E**, Oberg B. Achievements and challenges in antiviral drug discovery. *Antivir Chem Chemother* 2005; **16**: 155-168 [PMID: 16004079 DOI: 10.1177/095632020501600302]

10 **Nakamoto S**, Kanda T, Shirasawa H, Yokosuka O. Antiviral therapies for chronic hepatitis C virus infection with cirrhosis. *World J Hepatol* 2015; **7**: 1133-1141 [PMID: 26052402 DOI: 10.4254/wjh.v7.i8.1133]

11 **Mizokami M**, Tanaka Y. Tracing the evolution of hepatitis C virus in the United States, Japan, and Egypt by using the molecular clock. *Clin Gastroenterol Hepatol* 2005; **3**: S82-S85 [PMID: 16234067 DOI: 10.1016/S1542-3565(05)00705-6]

12 **Magiorkinis G**, Magiorkinis E, Paraskevis D, Ho SY, Shapiro B, Pybus OG, Allain JP, Hatzakis A. The global spread of hepatitis C virus 1a and 1b: a phylodynamic and phylogeographic analysis. *PLoS Med* 2009; **6**: e1000198 [PMID: 20041120 DOI: 10.1371/journal.pmed.1000198]

13 **Gray RR**, Tanaka Y, Takebe Y, Magiorkinis G, Buskell Z, Seeff L, Alter HJ, Pybus OG. Evolutionary analysis of hepatitis C virus gene sequences from 1953. *Philos Trans R Soc Lond B Biol Sci* 2013; **368**: 20130168 [PMID: 23938759 DOI: 10.1098/rstb.2013.0168]

14 **Centers for Disease Control and Prevention**. US Department of Health and Human Services. Factsheet: Hepatitis C. Why should baby boomers be tested? Available from: URL: http: //www.cdc.gov/knowmorehepatitis/Media/PDFs/FactSheet-Boomers.pdf

15 **Volkow P**, Del Rio C. Paid donation and plasma trade: unrecognized forces that drive the AIDS epidemic in developing countries. *Int J STD AIDS* 2005; **16**: 5-8 [PMID: 15705264 DOI: 10.1258/0956462052932638]

16 **Volkow P**, Perez-Padilla R, del-Rio C, Mohar A. The role of commercial plasmapheresis banks on the AIDS epidemic in Mexico. *Rev Invest Clin* 1998; **50**: 221-226 [PMID: 9763887]

17 **Muñoz-Espinosa LE**, Trujillo-Trujillo ME, Martínez-Macías RF, Panduro A, Rivas-Estilla AM, Fierro NA, Silvera-Linares AL, Torres-Valadez R, Cordero-Pérez P, González-Aldaco K, Chen-López CY, José-Abrego A, Zuñiga-Noriega JR, Gutiérrez-Ruiz MC, Roman S. Increase of drug use and genotype 3 in HCV-infected patients from Central West and Northeast Mexico. *Ann Hepatol* 2015; **14**: 642-651 [PMID: 26256892]

18 **Norma Oficial Mexicana NOM. 003/SSA2/1993**. Normas y Técnicas para la Disposición de Sangre Humana y sus Componentes con Fines Terapeúticos. Diario Oficial de la Federación del 18 de Julio del 1994. Available from: URL: http://www.salud.gob.mx/unidades/cdi/nom/003ssa23.html

19 **Roman S**, Panduro A, Aguilar-Gutierrez Y, Maldonado M, Vazquez-Vandyck M, Martinez-Lopez E, Ruiz-Madrigal B, Hernandez-Nazara Z. A low steady HBsAg seroprevalence is associated with a low incidence of HBV-related liver cirrhosis and hepatocellular carcinoma in Mexico: a systematic review. *Hepatol Int* 2009; **3**: 343-355 [PMID: 19669360 DOI: 10.1007/s12072-008-9115-9]

20 **Vivas-Arceo C**, Benavides SA, De Jesús Trujillo J, Panduro A, Rivas-Estilla AM. Hepatitis C virus: prevalence and routes of infection among blood donors of West Mexico. *Hepatol Res* 2003; **25**: 115-123 [PMID: 12644047 DOI: 10.1016/S1386-6346(02)00243-7]

21 **Chiquete E**, Sánchez LV, Panduro A. Routes of infection and clinical outcome of Mexican women reactive to anti-hepatitis C virus antibodies. *Hepatol Res* 2006; **36**: 100-106 [PMID: 16884946 DOI: 10.1016/j.hepres.2006.06.012]

22 **Heredia-Pi I**, Servan-Mori EE, Wirtz VJ, Avila-Burgos L, Lozano R. Obstetric care and method of delivery in Mexico: results from the 2012 National Health and Nutrition Survey. *PLoS One* 2014; **9**: e104166 [PMID: 25101781 DOI: 10.1371/journal.pone.0104166]

23 **Guzman E**, Ludmir J, DeFrancesco M. High cesarean section rates in Latin America, a reflection of a different approach to labor? *Open J Obs Gynecol* 2015; **5**: 433-435 [DOI: 10.4236/ojog.2015.58062]

24 **Chiquete E**, Panduro A. Low prevalence of anti-hepatitis C virus antibodies in Mexico: A systematic review. *Intervirology* 2007; **50**: 1-8 [PMID: 17164551 DOI: 10.1159/000096306]

25 **Santos-López G**, Sosa-Jurado F, Vallejo-Ruiz V, Meléndez-Mena

D, Reyes-Leyva J. Prevalence of hepatitis C virus in the Mexican population: a systematic review. *J Infect* 2008; **56**: 281-290 [PMID: 18343505 DOI: 10.1016/j.jinf.2008.02.001]
26 **Kershenobich D**, Razavi HA, Sánchez-Avila JF, Bessone F, Coelho HS, Dagher L, Gonçales FL, Quiroz JF, Rodriguez-Perez F, Rosado B, Wallace C, Negro F, Silva M. Trends and projections of hepatitis C virus epidemiology in Latin America. *Liver Int* 2011; **31** Suppl 2: 18-29 [PMID: 21651701 DOI: 10.1111/j.1478-3231.2011.02538.x]
27 **Alvarado-Mora MV**, Pinho JR. Epidemiological update of hepatitis B, C and delta in Latin America. *Antivir Ther* 2013; **18**: 429-433 [PMID: 23792375 DOI: 10.3851/IMP2595]
28 **Alonso M**, Gutzman A, Mazin R, Pinzon CE, Reveiz L, Ghidinelli M. Hepatitis C in key populations in Latin America and the Caribbean: systematic review and meta-analysis. *Int J Public Health* 2015; **60**: 789-798 [PMID: 26298439 DOI: 10.1007/s00038-015-0708-5]
29 **Londeix P**, Forette C. New treatments for hepatitis C virus. Strategies for achieving universal access. Medecins Du Monde. Available from: URL: http: //www.hepcoalition.org/advocate/advocacy-tools/article/new-treatments-for-hepatitis-c?lang=en
30 **Graham CS**, Swan T. A path to eradication of hepatitis C in low- and middle-income countries. *Antiviral Res* 2015; **119**: 89-96 [PMID: 25615583 DOI: 10.1016/j.antiviral.2015.01.004]
31 **Phelan M**, Cook C. A treatment revolution for those who can afford it? Hepatitis C treatment: new medications, profits and patients. *BMC Infect Dis* 2014; **14** Suppl 6: S5 [PMID: 25253373 DOI: 10.1186/1471-2334-14-S6-S5]
32 **Stanciu C**, Trifan A. Hepatitis C Virus Treatment Revolution: Eastern European Story. *Hepat Mon* 2015; **15**: e28969 [PMID: 26300932 DOI: 10.5812/hepatmon.28969v2]
33 **Ford N**, Swan T, Beyer P, Hirnschall G, Easterbrook P, Wiktor S. Simplification of antiviral hepatitis C virus therapy to support expanded access in resource-limited settings. *J Hepatol* 2014; **61**: S132-S138 [PMID: 25443341 DOI: 10.1016/j.jhep.2014.09.019]
34 **Strauss E**. Barriers to care of chronic hepatitis patients in Latin America. *Arch Med Res* 2007; **38**: 711-715 [PMID: 17613362 DOI: 10.1016/j.arcmed.2007.02.002]
35 **Botero RC**, Tagle M. New therapies for hepatitis C: Latin American perspectives. *Clin Liv Dis* 2015; **5**: 8-10 [DOI: 10.1002/cld.438]
36 **Lozano-Sepulveda S**, Bryan-Marrugo O, Merino-Mascorro J, Rivas-Estilla AM. Approachability to the new anti-HCV direct acting antiviral agents in the Latin American context. *Future Virol* 2016; **11**: 39-46 [DOI: 10.2217/fvl.15.97]
37 **Silva-Vidal KV**, Méndez-Sánchez N. The good, the bad and the ugly of the new treatments for hepatitis C virus. *Ann Hepatol* 2014; **13**: 574-575 [PMID: 25152995]
38 **Hagan LM**, Schinazi RF. Best strategies for global HCV eradication. *Liver Int* 2013; **33** Suppl 1: 68-79 [PMID: 23286849 DOI: 10.1111/liv.12063]
39 **Suthar AB**, Harries AD. A public health approach to hepatitis C control in low- and middle-income countries. *PLoS Med* 2015; **12**: e1001795 [PMID: 25757228 DOI: 10.1371/journal.pmed.1001795]
40 **Simmonds P**. The origin of hepatitis C virus. *Curr Top Microbiol Immunol* 2013; **369**: 1-15 [PMID: 23463195 DOI: 10.1007/978-3-642-27340-7_1]
41 **Rivas-Estilla AM**, Sánchez LV, Matsui O, Campollo O, Armendariz-Borunda J, Segura-Ortega JE, Panduro A. Identification of hepatitis C virus (HCV) genotypes in infected patients from the west of Mexico. *Hepatol Res* 1998; **12**: 121-130 [DOI: 10.1016/S1386-6346(98)00044-8]
42 **Rivas-Estilla AM**, Cordero-Pérez P, Trujillo-Murillo Kdel C, Ramos-Jiménez J, Chen-López C, Garza-Rodríguez Mde L, Ramírez-Gutiérrez A, Muñoz-Espinosa L. Genotyping of hepatitis C virus (HCV) in infected patients from Northeast Mexico. *Ann Hepatol* 2008; **7**: 144-147 [PMID: 18626432]
43 **Roman S**, Jose-Abrego A, Fierro NA, Escobedo-Melendez G, Ojeda-Granados C, Martinez-Lopez E, Panduro A. Hepatitis B virus infection in Latin America: a genomic medicine approach. *World J Gastroenterol* 2014; **20**: 7181-7196 [PMID: 24966588 DOI: 10.3748/wjg.v20.i23.7181]
44 **Gonzalez-Aldaco K**, Rebello Pinho JR, Roman S, Gleyzer K, Fierro NA, Oyakawa L, Ramos-Lopez O, Ferraz Santana RA, Sitnik R, Panduro A. Association with Spontaneous Hepatitis C Viral Clearance and Genetic Differentiation of IL28B/IFNL4 Haplotypes in Populations from Mexico. *PLoS One* 2016; **11**: e0146258 [PMID: 26741362 DOI: 10.1371/journal.pone.0146258]
45 **Fierro NA**, Gonzalez-Aldaco K, Torres-Valadez R, Martinez-Lopez E, Roman S, Panduro A. Immunologic, metabolic and genetic factors in hepatitis C virus infection. *World J Gastroenterol* 2014; **20**: 3443-3456 [PMID: 24707127 DOI: 10.3748/wjg.v20.i13.3443]
46 **Howes N**, Lattimore S, Irving WL, Thomson BJ. Clinical Care Pathways for Patients With Hepatitis C: Reducing Critical Barriers to Effective Treatment. *Open Forum Infect Dis* 2016; **3**: ofv218 [PMID: 26900576 DOI: 10.1093/ofid/ofv218]
47 **McGowan CE**, Monis A, Bacon BR, Mallolas J, Goncales FL, Goulis I, Poordad F, Afdhal N, Zeuzem S, Piratvisuth T, Marcellin P, Fried MW. A global view of hepatitis C: physician knowledge, opinions, and perceived barriers to care. *Hepatology* 2013; **57**: 1325-1332 [PMID: 23315914 DOI: 10.1002/hep.26246]
48 **Grebely J**, Oser M, Taylor LE, Dore GJ. Breaking down the barriers to hepatitis C virus (HCV) treatment among individuals with HCV/HIV coinfection: action required at the system, provider, and patient levels. *J Infect Dis* 2013; **207** Suppl 1: S19-S25 [PMID: 23390301 DOI: 10.1093/infdis/jis928]
49 **McGowan CE**, Fried MW. Barriers to hepatitis C treatment. *Liver Int* 2012; **32** Suppl 1: 151-156 [PMID: 22212587 DOI: 10.1111/j.1478-3231.2011.02706.x]
50 **Campollo O**, Roman S, Panduro A, Hernandez G, Diaz-Barriga L, Balanzario MC, Cunningham JK. Non-injection drug use and hepatitis C among drug treatment clients in west central Mexico. *Drug Alcohol Depend* 2012; **123**: 269-272 [PMID: 22138538 DOI: 10.1016/j.drugalcdep.2011.11.009]
51 **Chiquete E**, Ochoa-Guzmán A, García-Lamas L, Anaya-Gómez F, Gutiérrez-Manjarrez JI, Sánchez-Orozco LV, Godínez-Gutiérrez SA, Maldonado M, Román S, Panduro A. Hepatitis C virus infection and type 2 diabetes mellitus in Mexican patients. *Rev Med Inst Mex Seguro Soc* 2012; **50**: 481-486 [PMID: 23282259]
52 **Panduro A**, Ojeda-Granados C, Rivera H, Roman S. [h Index and scientific output of researchers in medicine from the University of Guadalajara, Mexico]. *Rev Med Inst Mex Seguro Soc* 2015; **53**: 716-721 [PMID: 26506489]
53 **Panduro A**, Roman S. New challenges for Latin American scientific medical journals: academia or business. *Rev Mex Endocrinol Metab Nutr* 2015; **2**: 163-166
54 **Roman S**, Panduro A. Genomic medicine in gastroenterology: A new approach or a new specialty? *World J Gastroenterol* 2015; **21**: 8227-8237 [PMID: 26217074 DOI: 10.3748/wjg.v21.i27.8227]
55 **Méndez-Sánchez N**, Paraná R, Cheinquer H, Alves de Mattos A, Gadano A, Silva M, Pessôa MG, Gomes-Ferraz ML, Soza A, Mendes-Correa MC, Chávez-Tapia NC, Dagher L, Padilla M, Hernandez N, Sánchez-Avila JF, Contreras F, Moraes-Coelho HS, Parise ER, Bessone F, Uribe M. Latin American Association for the Study of the Liver recommendations on treatment of hepatitis C. *Ann Hepatol* 2014; **13** Suppl 2: s4-66 [PMID: 25185535]
56 **Edwards DJ**, Coppens DG, Prasad TL, Rook LA, Iyer JK. Access to hepatitis C medicines. *Bull World Health Organ* 2015; **93**: 799-805 [PMID: 26549908 DOI: 10.2471/BLT.15.157784]

P- Reviewer: Thompson JR, Trifan A **S- Editor**: Ma YJ
L- Editor: A **E- Editor**: Zhang DN

Published by **Baishideng Publishing Group Inc**
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
http://www.wjgnet.com

ISSN 1007-9327
9 771007 932045 22>