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Evolving epidemiology of hepatitis C virus

D. Lavanchy
Interlifescience, Massagno Ticino, Switzerland

Abstract

More than 20 years after the discovery of the hepatitis C virus (HCV), it is now well established that HCV is of global importance affecting all countries, leading to a major global health problem that requires widespread active interventions for its prevention and control. Chronic hepatitis C was linked to the development of cirrhosis and hepatocellular carcinoma in many areas of the world. Current epidemiological assessments have identified complex patterns with highly variable local prevalence rates between countries and within countries. HCV infection patterns have not significantly changed in most parts of the world since 1997, when first analyzed, partly due to the lack of new and more accurate data. The assessment of the national HCV prevalence and transmission modes should be completed to enable national authorities to prioritize preventive measures and to make the most appropriate use of available resources. The 'patchy' epidemiological situation in some areas will continue to complicate the task of the establishment of global, regional and national base line data. The present assessment finds a global prevalence of 2.35%, affecting 160 million chronically infected individuals. There is an urgent need for more accurate Information on the costs and burden of HCV to society. Twenty-one year after the discovery of HCV, the assessment is far from being complete and little progress has been made in the past 10 years in many countries. In some countries significant increases have been reported and this may also apply to countries were insufficient data exist. A safe and efficient vaccine against HCV is urgently needed.

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Corresponding author: D. Lavanchy, ruelle des Chataigniers 1, CH-1026 Denges VD, Switzerland
E-mail: lavanchyd@gmail.com

Introduction

After the discovery of the hepatitis C virus (HCV) in 1989 and its linkage to non-A, non-B hepatitis, HCV was first thought to be an infection of minor importance, affecting selected drug user and blood product recipient populations in developed countries. More than 20 years later, it is now well established that HCV is of global importance, affecting all countries, leading to a major global health problem that requires widespread active interventions for its prevention and control. This is no surprise as the spread of HCV (based on the rate of development of molecular diversity) can be estimated to date back about 500–2000 years [1].

Chronic hepatitis C has been linked to the development of hepatocellular carcinoma (HCC) in many areas of the world. Of the more than 500 000 new cases of liver cancer that occur each year, 22% (>100 000) are attributable to HCV infection [2]. Prospective studies have shown that 80% of cases of acute hepatitis C progress to chronic infection; 10–20% of these will develop complications of chronic liver disease, such as liver cirrhosis, within two to three decades of onset, and 1–5% will develop liver cancer [3–7], making HCV a health problem of global importance [8]. Heavy alcohol consumption, particularly in females, age and HCV/human immunodeficiency virus (HIV) co-infection may be associated with more rapid progression of HCV liver disease, especially fibrosis [9]. Additional prospective longitudinal studies are needed to determine whether other factors, such as schistosomiasis and clonorchiasis, and exposure to toxic solvents, a common occurrence in developing countries, are associated with disease progression. There is an urgent need for more accurate information on the long-term outcome, with its consequences for, and costs and burden , to, society.

Transmission

There are still large gaps in our knowledge of the global epidemiology of HCV. The relative contributions of the various

sources of infection have rarely been investigated in population-based epidemiological studies in most geographical areas. The assessment of national HCV prevalence and transmission modes should be completed to enable national authorities to prioritize preventive measures and to make the most appropriate use of available resources. In addition, many unanswered questions exist concerning the roles of risk factors and lifestyle conditions that may be associated with HCV spread in different regions of the world. Epidemiological studies on the roles of potential risk factors, such as medical procedures, injections for medications and immunizations, injections applied outside of medical settings, tattooing, and scarification techniques, have shown wide geographical variations with major implications for local populations and potential prevention and control programmes.

As HCV can be sexually transmitted (albeit rarely between healthy individuals), the role of co-infection with other sexually transmitted diseases, such as HIV/AIDS, need to be further studied, especially for those that can result in open genital sores, such as chlamydial infection, chancroid and syphilis.

Hepatitis C Global Prevalence

HCV has been shown to have a worldwide distribution, occurring among persons of all ages, genders, races and regions of the world. The socio-economic burden of HCV has not yet been defined in most countries. Where the epidemiology of hepatitis C has been studied, the consequences of chronic hepatitis C, HCC and end-stage liver cirrhosis have been shown to increasingly impact on national health systems [10]. New infections still occur, because of the continued use of unscreened or inappropriately screened blood transfusions and blood products, the failure to sterilize medical equipment adequately, and the increase in intravenous drug use in previously unaffected areas. Global, regional and national monitoring will be necessary to evaluate results and address shortcomings. The quality and coverage of population-based HCV prevalence should be improved, by using: (i) a representative population sample; and (ii) accurate diagnostic tests. To better evaluate the incidence trends and burden of chronic disease, the prevalence of HCV infection should be stratified according to age, ethnicity and gender. Since the first publication in 1997 [8], published evidence for the prevalence of HCV still remains disappointedly limited, as information is still inadequate in many countries, most published prevalence studies being of limited scope, representing only a segment of the population [11–13] (e.g. pregnant women, blood donors or hospital admissions), with only a few studies using sampling techniques that represent the entire population.

Prevalence of hepatitis C worldwide

As most acute HCV infections (60–70%) are asymptomatic [14–16], data on the incidence of new cases of HCV infection are difficult to obtain and therefore scarce. Some risk groups, such as haemophiliacs, haemodialysis patients, patients transfused with unscreened blood and unscreened blood products, inmates of long-term correctional facilities, and persons with occupational exposure, clearly have a high incidence and prevalence of HCV infection [17–24].

As measurement of incidence fails to produce reliable numbers, because of the mostly asymptomatic form of acute infection, most approximations are based on reviews of published prevalence data, which estimated that 130–170 million persons, or 2–3% of the world's population, are infected with HCV [25–27]. The current estimates are given in Fig. 1 and Tables 1 and 2. Prevalence estimates are 400 000 chron-

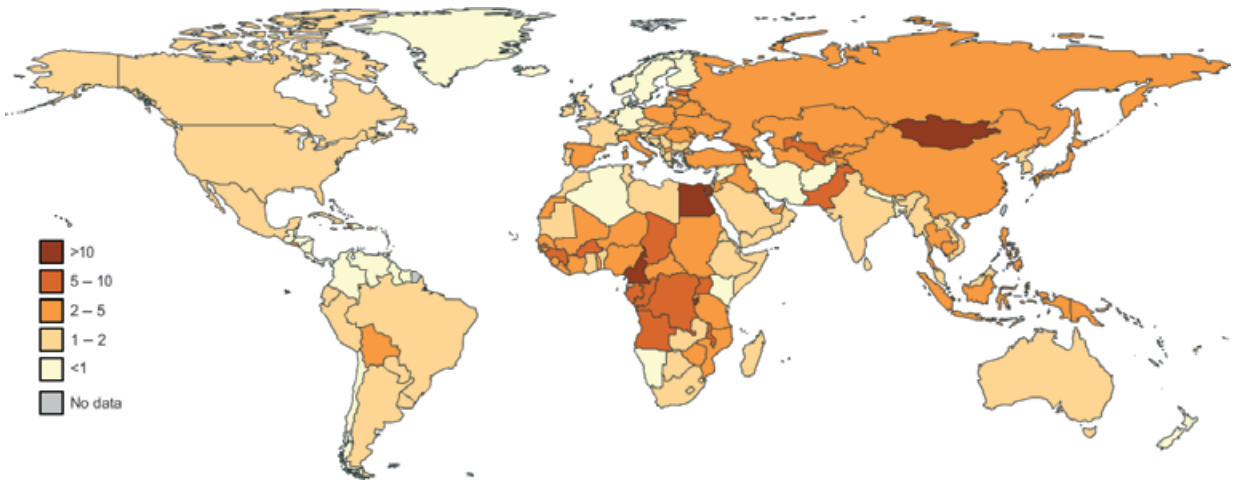

FIG. 1. Hepatitis C global prevalence 2010 (%).

TABLE 1. Hepatitis C global prevalence country data 2010[a]

Country	Anti-HCV (%)	No. infected
Afghanistan	0.5	147 735
Albania	1.5	53 172
Algeria	0.2	70 846
Angola	5	950 000
Antigua and Barbuda	0.75	525
Argentina	1.9	743 750
Armenia	4	133 012
Australia	1.1	227 831
Austria	1	81 748
Azerbaijan	4	314 735
Bahamas	0.75	2250
Bahrain	1.8	12 240
Bangladesh	0.6	986 550
Barbados	0.75	2100
Belarus	2.2	226 600
Belgium	0.9	93 134
Belize	0.75	2100
Benin	1.6	147 392
Bhutan	1.3	28 412
Bolivia	4.7	471 457
Bosnia and Herzegovina	1.5	58 605
Botswana	1.6	31 648
Brazil	1.4	2 609 670
Brunei	2.9	10 846
Bulgaria	1.8	139 068
Burkina Faso	5.2	846 924
Burundi	11.3	888 067
Cambodia	4.1	617 173
Cameroon	13.8	2 754 204
Canada	1	322 680
Cape Verde	3	15 390
Central African Republic	2.4	108 144
Chad	5	575 300
Chile	0.85	134 530
China	2.2	29 791 212
Colombia	0.97	425 191
Comoros	1	7980
Congo	5.5	206 745
Cook Islands	1.5	270
Costa Rica	0.75	32 453
Croatia	1.5	68 265
Cuba	1.8	202 842
Cyprus	0.5	4175
Czech Republic	1.5	153 300
Denmark	0.5	27 155
Djibouti	0.3	2637
Dominica	0.75	593
Dominican Republic	0.75	66 713
Democratic Republic of Congo	6.4	4 010 240
Ecuador	1.4	195 605
Egypt	14	11 826 360
El Salvador	2.5	164 689
Equatorial Guinea	1.7	11 781
Eritrea	1.9	85 500
Estonia	5	70 097
Ethiopia	1.9	1 500 734
Federal States of Micronesia	2	2200
Fiji	2	16 960
Finland	0.5	26 245
France	1.3	814 281
Gabon	9.2	138 092
Georgia	6.7	328 945
Germany	0.75	620 168
Ghana	1.7	413 661
Greece	1.5	166 800
Greenland	0.5	280
Grenada	5	5150
Guatemala	0.8	115 016
Guinea	5.5	567 820
Guinea-Bissau	4.7	77 409
Guyana	0.75	5633
Haiti	4.4	448 272
Honduras	0.5	36 025
Hungary	2.2	219 582
Iceland	0.5	1500
India	1.5	18 216 960
Indonesia	3.9	9 436 986
Iran	0.9	630 450
Iraq	3.21	834 600
Ireland	1.1	44 682

TABLE 1. (Continued)

Country	Anti-HCV (%)	No. infected
Israel	1	70 000
Italy	3.2	1 923 136
Ivory Coast	3.3	717 783
Jamaica	0.75	20 250
Japan	2.4	3 058 008
Jordan	2.1	114 660
Kazakhstan	3.2	474 592
Kenya	0.9	367 767
Kiribati	2	2020
Kuwait	3.1	68 634
Kyrgyzstan	4	205 880
Laos	1.1	70 796
Latvia	2.2	50 732
Lebanon	0.7	31 850
Lesotho	1	22 660
Liberia	3	123 060
Libya	1.6	104 736
Lithuania	2.2	75 086
Luxembourg	1	4630
Macedonia	2	40 800
Madagascar	1.7	342 482
Malawi	6.8	1 067 056
Malaysia	1.5	397 515
Maldives	1	2850
Mali	3.3	439 659
Malta	1	4000
Marshall Islands	1.5	900
Mauritania	1.1	37 026
Mauritius	2.1	27 237
Mexico	1	1 106 450
Moldova	2.3	99 498
Mongolia	10.7	303 048
Morocco	1.93	624 953
Mozambique	3.2	748 992
Myanmar	1	505 190
Namibia	0.9	19 908
Nauru	2	256
Nepal	0.64	181 037
New Zealand	0.3	11 820
Nicaragua	0.35	19 803
Niger	3.2	50 851
Nigeria	2.1	3 323 439
Niue	2	30
North Korea	1	231 130
Norway	0.55	25 328
Oman	1.2	34 836
Pacific Islands (Palau)	2	606
Pakistan	5.9	9 422 403
Panama	0.75	22 500
Papua New Guinea	2	117 740
Paraguay	1.23	76 162
Peru	1	284 100
Philippines	2.2	1 932 854
Poland	2	770 360
Portugal	1	105 240
Qatar	1.8	15 120
Reunion	0.14	1172
Romania	4.5	1 003 680
Russia	4.1	5 796 498
Rwanda	4.9	452 466
Samoa	0.75	1875
Sao Tome and Principe	10	17 580
Saudi Arabia	1.8	437 292
Senegal	3	385 830
Serbia	1.5	156 345
Seychelles	0.34	289
Sierra Leone	2	117 680
Singapore	1	46 090
Slovakia	1	54 240
Slovenia	1	19 980
Solomon Islands	2	9560
Somalia	1	83 040
South Africa	1.7	858 364
South Korea	1.68	823 956
Spain	2	906 340
Sri Lanka	1	207 180
St Kitts and Nevis	2.2	880
St Lucia	0.75	1232
St Vincent and the Grenadines	1	1180
Sudan	2.8	1 209 376

TABLE 1. (Continued)

Country	Anti-HCV (%)	No. infected
Suriname	0.75	3278
Swaziland	1.5	18 030
Sweden	0.5	46 465
Switzerland	1	74 190
Syria	0.5	94 405
Tajikistan	4	292 840
Thailand	2.2	1 499 058
The Gambia	2.4	42 024
The Netherlands	1	163 360
Togo	3.3	223 740
Tonga	2	2200
Trinidad and Tobago	3.9	50 583
Tunisia	1.2	124 488
Turkey	2.2	1 549 108
Turkmenistan	4	268 960
Tuvalu	2	220
Uganda	6.6	2 230 536
UK	1.1	659 032
Ukraine	4	1 864 840
United Arab Emirates	2.3	81 052
United Republic of Tanzania	3.2	1 441 280
Uruguay	1	34 000
USA	1.8	5 367 834
Uzbekistan	6.5	1 774 955
Vanuatu	2	4060
Venezuela	0.94	272 976
Vietnam	1	835 360
Western Sahara	3	15 900
Western Samoa	2	3540
Yemen	1.7	412 352
Montenegro	1.5	10 980
Zambia	1.5	198 855
Zimbabwe	2	262 400
Total infected		158 910 617
% population	2.35	

[a]Based on published data.

TABLE 2. Hepatitis C regional prevalence 2010

Region	Anti-HCV (%)	No. HCV-infected
Africa	3.2	28 100 000
Americas	1.5	14 000 000
Asia	2.1	83 000 000
Australia and Oceania	1.2	400 000
Europe	2.3	17 500 000
Middle East	4.7	16 000 000
Total	2.35	159 000 000

ically infected subjects in Australia and Oceania, 14 million in the Americas, 16 million in the Middle East, 17.5 million in Europe, 28 million in Africa, and 83 million in Asia [12].

The published data suggest that most populations in the Americas, western Europe and Southeast Asia have prevalence rates of antibody to HCV (anti-HCV) under 2.5%. Anti-HCV prevalence rates for eastern Europe average from 1.5% to 5%, those for the Western Pacific region from 2.5% to 4.9%, and those for the Middle East and Central Asia from 1% to more than 12% [27]. In terms of absolute numbers, the majority of infected people live in Central/Southeast Asia and the Western Pacific regions (Table 2), a finding similar to that for chronic hepatitis B infection.

Only a few studies on cost estimates are available. In the USA, the current estimate of the annual costs of acute and chronic hepatitis C exceeds US$600 million [29], and over the period 2010–2019, the total costs are expected to be US$184 billion [30], giving an indication of how important the burden of chronic HCV infection can be for national health systems, even in a low-endemicity country (1.8%). The European Monitoring Centre for Drugs and Drug Addiction estimated the HCV-related costs in ten European Union countries to be €50 million, excluding HCV drug therapy and monitoring, thereby demonstrating that, even with no public health action, HCV causes significant costs to society. The estimates for Spain were approximately €3 billion for the period 2010–2030 [31], and in Canada the costs are estimated at CD$150 million annually until 2040 [32].

Epidemiological trends

As representative prevalence data are still not available from many countries, and progress since 1997 has been scarce, the local, national and regional baseline estimates of the rate of infection, the number of individuals chronically infected and the burden of disease are not established, making it impossible to assess correctly the impact of control and prevention measures. In addition, highly significant differences in subnational population groups have been documented.

For instance, in China, Bao *et al.* [33] found that the prevalence in non-injection drug users varied from 0% (Anhui) to 40.00% (Fujian). Intravenous drug use is increasing in China, posing a new challenge to public health authorities for the implementation of harm reduction programmes [34]. Only a few studies have addressed the prevalence of HCV in China. In a cross-sectional study conducted in six different regions of the country, the overall prevalence of HCV was 0.58%, which was much lower than the 2.7% estimated by the WHO [35]. On the other hand, the prevalence in the general population was found to be 2.1% in Fujian province [36], 9.6% in Henan province [37] and 25% in a rural community of elderly people [38]. Therefore, in China, the geographical distribution of HCV infection is heterogeneous, and patterns differ between rural and urban settings, but, with the significant increase in intravenous drug use, it is expected that the prevalence will generally increase in China.

Hepatitis C is an emerging infection in India as well, and is already responsible for a significant proportion of liver disease in various states. However, the prevalence appears to be highly variable ('patchy'), according to the geographical site or the population group analysed (0.09–7.89%) [39]. Most of the studies of prevalence have been conducted in blood banks, and have shown prevalence rates of <2%, but in professional donors prevalence rates between 55.3% and 87.3% have been found. The consequences of chronic HCV infection will probably be significant increases in morbidity and mortality in India in the years to come.

Changing trends in HCV over the past 50 years have also been observed in Japan, where 70% of cases of HCC are attributable to HCV, and HCC is the fourth leading cause of death in males and the fifth in females. HCV started to spread in the 1930s among intravenous drug users (amphetamines) before, during and after World War II, or through medical procedures such as blood transfusion and the use of contaminated syringes. The prevalence of HCV infection is much lower in the younger generation than in the older generation aged >55 years (0.1–0.2% vs. >2%) [40]. Therefore, the total number of patients with HCV infection is considered to have decreased. The incidence of HCC has steadily increased over the last 50 years, but it is now decreasing in Japan, mainly because of the decreased prevalence of HCV-related HCC. A similar trend has been observed in Italy [41,42].

Pakistan is a developing country of 170 million people, and recent investigations have shown that about 10 million (5.9%) people are presumed to be infected with HCV [43]. Public health authorities are raising awareness about viral hepatitis among healthcare workers and the general population, but tremendous efforts are still required to combat various risk factors involved in HCV transmission, particularly because of the non-implementation of international standards regarding blood transfusion and safe injection practices.

Egypt has a very high prevalence of HCV, reaching as much as 32% in the population of young males requesting visas for foreign travel [44–47], and the country suffers high morbidity and mortality from chronic liver disease, cirrhosis and HCC. Approximately 20% of Egyptian blood donors are anti-HCV-positive [44]. Geographically, the desert areas of Egypt have the lowest rates of anti-HCV positivity; rural areas tend to have higher rates than cities; and rates in the Nile Delta (Lower Egypt) are higher than in the Nile Valley (Middle Egypt and Upper Egypt) [44,46,47]. The strong homogeneity of HCV subtypes found in Egypt (mostly 4a) [48–50] suggests an epidemic spread of HCV [49]. The risk factor(s) originally responsible for the establishment of HCV in the general population may not necessarily be the same as those responsible for transmitting the virus today. Therefore, both traditional risk factors and risk factors that may be unique to Egypt need to be considered in explaining the transmission of HCV in this country. The prime candidate to explain the high prevalence of HCV in Egypt is the past practice of parenteral therapy for schistosomiasis with tartar emetic (potassium antimony tartrate), and the data suggest that Egypt's mass campaigns do indeed represent the world's largest example of iatrogenic transmission of a blood-borne pathogen [51]; the large reservoir of chronic HCV infection established in the course of these campaigns remains the most likely reason for today's high prevalence of HCV, which may be largely responsible for the continuing endemic transmission of HCV today [52]. Egypt has a unique HCV prevalence pattern that is not comparable with those of its eastern Mediterranean neighbours. However, in the recent past, intravenous drug use has been shown to have increased in the Middle East, as documented for Iran [53]. It is therefore expected that the prevalence of HCV will increase in the next 10 years.

For Africa, HCV prevalence data are incomplete, but show considerable variation from one population studied to another, with prevalence rates from 0% to 51% [54–57]. More than 28 million people are chronically infected with HCV on this continent. It is currently difficult to determine trends concerning current and future infection rates.

In Europe, too, the HCV prevalence data are often incomplete, outdated or inconclusive. The current estimates are that 7.3–8.8 million people (1.1–1.3%) are chronically infected in the European Union, a figure that is almost double the first estimates performed in 1997 [27], indicating that HCV is also a major health problem in Europe [58], and an increase is forecasted for the next decade [59–61]. For the whole of the European continent, it is estimated that 17.5 million individuals are infected. Recently, a 3-month pilot study carried out by the Hepatitis C Trust in pharmacies in England found that the prevalence of HCV infection was almost four times as high as previously estimated. The pilot study found a prevalence of 15%, which is significantly more than the 4% determined by tests carried out in general practitioner surgeries in 2008 [62], emphasizing that the study design has major consequences for outcomes in population-based studies, and calling for caution when evaluating published HCV prevalence figures, even in well-studied countries.

In addition to anti-HCV-based prevalence studies, longitudinal genotype observation adds a further tool for monitoring epidemiological trends. Measurement of the spatial introduction of new genotypes in a population, and the rate of sequence evolution or natural recombinations in viruses introduced at a given time in a cohort, provides the possibility of evaluating the history of the past geographical spread of HCV through different populations, shedding light on the demographic, social and biological factors that are at the basis of ancient and current unrecognized routes of transmission. Genotypes 1–3 have a worldwide distribution [48,63–65]. Genotypes 4 and 5 are found principally in Africa, and genotype 6 is distributed in Asia [66]. Endemic areas for specific genotypes are found in West Africa (types 1 and 2), West Central Africa (type 4), the Indian subcontinent (type 3), Central Africa (type 4) and Southeast Asia (type 6). An endemic area for genotype 5 has not been found [49,67–73], except for a local county in central France, where

HCV 5a contamination of the local population was associated with living in a rural area called Vic-le-Comte. Abergel *et al.* suggest that HCV 5a spread by an iatrogenic route before 1972, and then via transfusion to the whole county [74]. When a limited diversity of HCV subtypes is found in a certain geographical area, it may be attributed to the recent introduction of HCV into the population, as was documented for Canada [75] or Australia [76]. The molecular epidemiology of HCV genotype 2 points to West and Central Africa, mostly along the African Atlantic coast, as its endemic place of origin. Markov *et al.* have found an eastwards spread from the West African coast to Cameroon that took place over several centuries [77]. Molecular clock analysis dates the common ancestor of HCV to Guinea-Bissau, around 1470 (1414–1582). Isolates from Madagascar and Martinique suggest that the historical slave trade and the possible parenteral HCV exposure during public health campaigns undertaken during the colonial era may have played a role in the dissemination of HCV genotypes 2a and 2c. In summary, the geographical distribution of HCV genotypes and the rate of genetic variation are consistent with the global distribution of HCV, and are compatible with a long history of infection in most populations of the world, preceding, in many geographical locations, the era of modern medicine by many centuries.

HCV-related cirrhosis and deaths from HCC are likely to increase dramatically within the next decade, e.g. in Australia [78,79], Canada [80], France [81], the UK [59–61] and the USA [82]. Owing to the increase in intravenous drug use in China, India and the Middle East, increases are likely to occur within this decade in these regions too, and because China and India are the countries with the largest populations, a 1% increase in both would result in an additional 25 million HCV-infected subjects. If patients are left undiagnosed and untreated, the future burden of the disease for healthcare resources and society will be substantial. A declining burden in the years to come is expected only in Italy [42,83], Japan [84], South Korea [84] (accompanied by a decrease in the incidence of HCC in these two countries) [85] and the USA [86].

Strategies for Prevention in Light of the Undetermined Epidemiology

HCV-prevention programmes are needed at the local, national, regional and global levels if the spread of HCV and the burden of hepatitis C are to be reduced. To achieve these objectives, the implementation of measures that reduce the risk of contracting HCV infection is required, a task that was unfulfilled in many areas in 2010. Such programmes need to ensure that blood supplies and related products are free of infection, and that safe injection methods are practised within and outside medical settings. The use of disposable syringes for immunization and injections is particularly crucial in developing countries. Risk-education counselling for professionals and the public is of paramount importance. Where this is affordable, persons with chronic hepatitis C should be identified and targeted for special counselling and medical management, in order to reduce the risk of them developing HCV-related disease complications. Healthcare professionals and the public, who are crucial for the effective prevention of HCV transmission, should be educated about the risk of transmission of blood-borne pathogens (HCV, hepatitis B virus and HIV) by contaminated injection and other medical equipment, as well as by traditional and folk medical procedures or practices [87–89], and should receive appropriate education and training concerning the importance of controlling such infections in all medical, surgical and dental facilities, including the use of standard precautions, safe injection practices, proper sterilization techniques, and high-level disinfection where appropriate, avoiding the re-use and sharing of contaminated equipment and supplies, and avoiding contamination of multi-use supplies, such as medication vials. The use of devices or products that prevent re-use or contamination of medical and dental equipment should be encouraged (e.g. autodestruct syringes), noting that cost-effective devices are available [90–92].

Conclusions

From the above, it can be seen that the assessment of the national, regional and global prevalence of chronic HCV represents an enormous task that may never be fully achieved. The 'patchy' epidemiological situation in some areas will continue to complicate the task of the establishment of global, regional and national baseline data, and this will also apply to the use of modelling that is currently undertaken by the CDC and by others. Therefore, new and inventive methodologies may have to be applied in order to estimate the actual baseline of the HCV epidemic and to evaluate future prevention and control activities. There is a need for better public awareness, coordinated national and regional action plans, and better data that take into account representative population samples. Improved assessment of risk factors in high-risk groups, the different genders and 'forgotten' ethnic groups is needed. Education should be culturally appropriate and address the concerns of all populations with HCV. Twenty-one years after the discovery of HCV, the assess-

ment is far from being complete, and little progress has been made in the past 10 years in many countries. The global figures have not changed significantly, with a global estimate of 160 million infected people and a global prevalence of 2.35% (Tables 1 and 2). However, in some countries, significant increases have been reported, and this may also apply to countries where insufficient data exist.

Physicians, healthcare workers and public health officials should be aware—and many are not—that many subjects are unaware of their infections, provide timely testing and antiviral treatment when needed, and avoid further iatrogenic transmission. It is a public health responsibility to ensure that prevention and control measures, in particular drug treatment, should be accompanied by the appropriate assessment and monitoring, using inventive and locally adapted methodologies for the evaluation of the baseline and the follow-up activities. Targeted populations should have equitable access to care and guaranteed, sustained supplies of medications, as well as clinical monitoring. Needless to say, in today's context a safe and efficient vaccine against HCV is urgently needed, and even a vaccine with suboptimal efficiency will probably help to better control HCV.

Transparency Declaration

The author declares no conflict of interest.

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