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Report from the HA React Conference, Vilnius, Lithuania, April 2017

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Introduction by Prof. Massimo Colombo M.D.

In Europe, chronic infection with the hepatitis C virus (HCV), which together with alcohol bears the responsibility for most cases of cirrhosis and liver cancer, causes approximately 60,000 deaths annually - more than the combined mortality from hepatitis B (31,000) and HIV (8,000). Worryingly, the health threats of HCV infection are not confined to the liver, as the virus has clearly been implicated in cases of lymphoma, renal failure and cardiovascular accidents, thus making the clinical consequences of hepatitis C not fully appreciated by statistics.

From the public health perspective, even more worrisome is the changing pattern of epidemiology of the infection that is taking place in most Mediterranean and eastern regions of Europe, where the HCV epidemic was originally established as a consequence of unsafe medical procedures and appeared to be under control with sanitation interventions. In these regions, the pool of individuals infected through unsafe sexual and life style behaviours is on the rise to progressively erode the prevalent cohort infected in the early 1960s and '70s through unsafe medical procedures, an event that leads these regions to progressively have the epidemiological pattern of HCV typical of central and northern Europe regions, where infection has mainly been spread through parenteral risk behaviours. The clear consequence of this is the expansion of an infected cohort of young and middle age individuals where persons who inject drugs (PWID) and HIV infected men who have sex with men (MSM) are classified as high transmitters, i.e. having an high propensity to spread HCV. Along this line, it should also be noted that these individuals are more prone than others to be reinfected with HCV following a cure with direct acting antivirals.

It is no surprise therefore that in the WHO guidelines for the elimination of hepatitis C by 2030, the importance of treatment of hepatitis C among high transmitters is underlined. This has clearly been shown to be the case in a number of studies in Scotland, Australia and Canada, where modelling studies pinpointed at the difficulty of eliminating HCV among the PWID community at high prevalence of hepatitis C and the importance of articulated interventions to be delivered in parallel with an effective harm reduction programme. While most experts concur on the social and medical benefits provided by the delivery of combined programmes of harm reduction and highly effective antiviral therapy among those mostly likely to transmit HCV, funding such a campaign of public health intervention has met with reluctance if not real cultural barriers by the general population and less inspired stakeholders owing to social stigmas attached to the beneficiaries.

In April, the Hepatitis B and C Public Policy Association was in Vilnius, Lithuania, to participate in a meeting entitled: "The Financing and Sustainability of Harm Reduction Services in the EU." This meeting was a part of the *European Joint Action on HIV and Co-infection Prevention and Harm Reduction (HA-REACT), which is co-funded by the European Commission. The overall aim of the Joint Action is to help eliminate HIV and reduce viral hepatitis and TB*

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among people who inject drugs (PWID) in the European Union by 2020. HA-REACT focuses on member states with gaps in effective, evidence-informed interventions. The Joint Action also encourages the implementation of comprehensive harm-reduction programmes throughout the EU as an essential strategy for improving the prevention and treatment of HIV, viral hepatitis and TB.

Below, Prof Jeffrey Lazarus sums up some of the highlights from the Vilnius meeting "The Financing and Sustainability of Harm Reduction Services in the EU.

The meeting focused on the part of the Joint Action devoted to the sustainability and long-term funding of harm reduction programmes, and the 27 participants came from 15 EU countries and included both NGO and government representatives.

The bulk of the meeting was devoted to two subjects: how to make the case for funding harm reduction programmes, and the use of alternative funding mechanisms, particularly bonds.

Charles Gore, founder of the World Hepatitis Alliance, began by sketching out some of the main funding issues. He said that in the absence of major external funders, the biggest challenge now is to get countries to increase their commitment to harm reduction. Advocacy is critical, and the key argument to make is that harm reduction saves money. He also suggested framing it more positively, saying, “Perhaps we should start talking about it as health promotion rather than harm reduction.”

Gore identified several ways to make existing resources stretch farther, including pooled procurement, integrating harm reduction efforts with existing disease efforts and generally working more efficiently. For instance, it should be simple to provide direct-acting antivirals at the same time as methadone or buprenorphine – not only cutting costs, but also expanding the number of people on each treatment. He concluded that the costs of harm reduction are small in comparison with the significant investment going into HCV drugs, while economising on harm reduction will increase the number of new cases requiring expensive treatment.

Since it is difficult for governments to finance a scale-up of harm reduction through conventional methods of funding health expenditure, they should take advantage of the many alternative funding mechanisms used by public-private partnerships in other sectors.

Rob Walton, presenting on behalf of the Hepatitis B & C Public Policy Association, argued that since it’s difficult for governments to finance a scale-up of harm reduction through conventional methods of funding health expenditure, they should take advantage of the many alternative funding mechanisms used by public-private partnerships in other sectors. These mechanisms fall into four categories: secured lending, unsecured lending, bond financing, and equity or quasi-equity investment. As an example, he described how floating a 30-year bond issue to scale up harm reduction would require little or no public outlay, while investors made money, the government saved on long-term health costs – and public health improved.

I remember how the investment case developed by experts was key in changing the HIV landscape; now we need to develop the investment case for scaling up harm reduction. While it will not end drug addiction, and would in fact save more money on treating HIV than HCV, people with HCV can actually be cured – and that is the strongest argument for scaling up.

If we are to eliminate hepatitis C, we have to find ways to fund harm reduction now.
Use hepatitis C elimination to fund harm reduction – and vice versa

The evidence shows that harm reduction has numerous health and social benefits, and one way forward is to frame it in terms of hepatitis C elimination. And conversely, harm reduction needs to be the cornerstone of any hepatitis elimination strategy. Across the WHO European Region, half of PWID are living with hepatitis C. Yet even in the EU, only half of people who use opioids are on OST, and access to NSPs is similarly limited. If we are to eliminate hepatitis C, we have to find ways to fund harm reduction now.

Parts of this article appeared on the BioMed Central “On Health” blog: https://blogs.biomedcentral.com/on-health/2017/05/03/use-hepatitis-c-elimination-to-fund-harm-reduction-and-vice-versa/

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Occupational exposure and liver disease

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Q. What liver disorder has been linked unequivocally to professional exposure?

A variety of liver diseases associated with work place exposures includes acute hepatitis, Toxic Associated SteatoHepatitis (TASH) and malignancy. Most of them are linked to various solvents (such as chlorinated hydrocarbons and mixtures of organic solvents), metals (such as berillium and cobalt), viruses (hepatitis viruses) and pesticides (paraquat) occurring after acute/subacute or chronic exposures [1,2]. However, given the improved hygienic conditions and an increased awareness of risks most of these cases should be traced back in time. Nevertheless, they may still occur occasionally because of accidental exposures. Among malignancies, strong evidence of causal relationship is available

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for angiosarcoma of the liver and the exposure to vinyl chloride monomer occurring in the manufacture of polyvinyl chloride [3,4] and, of course, for HCC as a long-term consequence of hepatitis infection in hospital staff and other medical professions.

Q. The literature is abundant with alarms about cases of hepatotoxicity and carcinogenicity in occupational environments. Was there any evidence-based link proven in all cases?

Not really! Cross-sectional studies on workers exposed to potentially hepatic toxins are numerous, showing higher percentages of alterations of liver function biomarkers. However, results are inconsistent and often the assessment of exposure is missing or inadequate. Thus, it is difficult to assess the clinical significance of these alterations and the role of occupational exposures. Somehow, similar problems are encountered in epidemiological studies where, in addition, the strength of positive associations, when detected, is small. An example is given when looking at the literature of a possible association between exposures to the common solvent trichloroethylene (TCE) and HCC. A meta-analysis based on nine studies gave an overall RR of 1.3 (95% CI, 1.1–1.4), but an inconsistent dose-risk relationship. The authors concluded that the evidence was inconclusive [5]. However, TCE was classified as carcinogen to humans (Group 1) by the International Agency for Research on Cancer [6]. Another study gave a RR of 1.91 (95% CI, 1.2–3.0), and concluded that TCE is possibly associated with excess of HCC [7]. However, another record–linkage study from four Nordic countries did not report excess HCC among workers occupationally exposed to TCE [8]. An earlier meta-analysis based on 14 occupational cohort studies gave a RR of 1.1 (95% CI, 1.0–1.3) for workers exposed to TCE [9]. In conclusion, strong evidence of causality should be based upon toxicological evidence of exposure and coherence with expected clinical findings, in workers' health surveys upon accurate assessment of exposures and in epidemiology when studies are coherent and the strength of association is robust.

Q. Why is this area of medicine difficult to explore with an evidence-based approach?

A key factor is the absence of pathognomonic signs across toxic diseases of the liver. In addition, currently available biomarkers of liver toxicity are in certain instances not sensitive enough. An example is given by TASH associated with solvent exposures that may occur without alterations of liver enzymes [2]. Another important factor that makes these studies difficult is the presence of much more common risk factors such as alcohol, smoking, viruses and pre-existing diseases. In these circumstances, the interactions with the effects of occupational exposures are difficult to disentangle, although their occurrence has been documented. For instance, high alcohol intake and the subsequent cytochrome P-450 enzymes induction had a severe potentiating effect on occupational exposures to carbon tetrachloride [10] and to other chemicals that are activated by the same enzymes [11]. Similarly, pre-existing liver diseases, drug treatments [12] and metabolic polymorphisms [13] may account for the higher susceptibility of certain individuals to hepatotoxicity. Also the alterations of gut microbiota induced by several chemicals may modulate bile acid profiles and thus influence the development of liver diseases from other causes [14]. The functional reserve of the liver may also represent another factor that hampers the detection of minor toxic liver injuries.

Q. What can be done to make the future of this field of health care brighter?

First of all, in the clinical setting by increasing physicians' awareness that work places may have an etiological role in the disease they observe. In fact, an accurate occupational history is of paramount importance and in most cases represents the only criterion for attribution, based upon the identification of chemical(s), and the length and intensity of exposures. Thus, the understanding that exposures to hepatotoxic agents may occur in a variety of workplaces is essential. These include agricultural environments, hospitals, dry cleaning shops and in several industries where they are used as solvents and degreasing agents, such as polymer synthesis, resins, leather, printing industries and others. The help of occupational medicine physicians who are familiar with work environments may be useful. Another important step is the development of new liver function biomarkers to be used for the prevention and diagnosis of occupational-related injuries. In this respect, a recent study on exposure to TCE may pave the way, showing among exposed workers an association with selected metabolomic markers of hepatotoxicity [15]. Finally, record linkage ("big data") studies should help in the identification of exposures deserving epidemiological studies.

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References

1. Warnes TW, Smith A. Hepatotoxic effects of workplace exposure. Hunter's diseases of occupations, Tenth ed. London: Hodder Harnold; 2010. p. 1171-1195.
2. Wahlang B, Beier JI, Clair HB, Bellis-Jones HJ, Falkner KC, McClain CJ, et al. Toxicant-associated steatohepatitis. Toxicol Pathol 2013;41:343-360.
3. Mundt KA, Dell LD, Austin RP, Luippold RS, Noess R, Bigelow C. Historical cohort study of 10 109 men in the North American vinyl chloride industry, 1942-72: update of cancer mortality to 31 December 1995. Occup Environ Med 2000;57:774-781.
4. Ward E, Boffetta P, Andersen A, Colin D, Comba P, Deddens JA, et al. Update of the follow-up of mortality and cancer incidence among European workers employed in the vinyl chloride industry. Epidemiology 2001;12:710-718.
5. Scott CS, Jinot J. Trichloroethylene and cancer: systematic and quantitative review of epidemiologic evidence for identifying hazards. Int J Environ Res Public Health 2011;8:4238-4272.
6. IARC Monographs on the evalutaion of carcinogenic risks to humans. Vol 106. Trichloroethylene, Tetrachloroethylene, and Some Other Chlorinated Agents. IARC, Lyon 2014.

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7. Hansen J, Sallmen M, Selden AI, Anttila A, Pukkala E, Andersson K, et al. Risk of cancer among workers exposed to trichloroethylene: analysis of three Nordic cohort studies. J Natl Cancer Inst 2013;105:869-877.
8. Vlaanderen J, Straif K, Pukkala E, Kauppinen T, Kyyronen P, Martinsen JI, et al. Occupational exposure to trichloroethylene and perchloroethylene and the risk of lymphoma, liver, and kidney cancer in four Nordic countries. Occup Environ Med 2013;70:393-401.
9. Alexander DD, Kelsh MA, Mink PJ, Mandel JH, Basu R, Weingart M. A meta-analysis of occupational trichloroethylene exposure and liver cancer. Int Arch Occup Environ Health 2007;81:127-143.
10. Manno M, Rezzadore M, Grossi M, Sbrana C. Potentiation of occupational carbon tetrachloride toxicity by ethanol abuse. Hum Exp Toxicol 1996;15:294-300.
11. Hills BW, Venable HL. The interaction of ethyl alcohol and industrial chemicals. Am J Ind Med 1982;3:321-333.
12. Mahieu P, Geubel A, Rahier J, Scailteur V, Dieryck JP, Lauwerys R. Potentiation of carbon-tetrachloride hepato-nephrotoxicity by phenobarbital in man, a case report. Int J Clin Pharmacol Res 1983;3:427-430.
13. Bolt HM, Roos PH, Thier R. The cytochrome P-450 isoenzyme CYP2E1 in the biological processing of industrial chemicals: consequences for occupational and environmental medicine. Int Arch Occup Environ Health 2003;76:174-185.
14. Jin Y, Wu S, Zeng Z, Fu Z. Effects of environmental pollutants on gut microbiota. Environ Pollut 2017;222:1-9.
15. Walker DI, Uppal K, Zhang L, Vermeulen R, Smith M, Hu W, et al. High-resolution metabolomics of occupational exposure to trichloroethylene. Int J Epidemiol 2016;45:1517-1527.

The control of HCV in Egypt

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Ten years ago, Egypt was renowned for having the highest prevalence for hepatitis C virus (HCV) infection worldwide, as 15% of Egyptians were seropositive for HCV. Genotype 4 represented more than 90% of this figure [1]. The parenteral antischistosomal mass treatment programs that lasted for more than 30 years using non-disposable syringes were accused of being the cause of such an epidemic [2]. Despite the considerable reduction in this prevalence rate falling to 6.3% in 2015 [3], reports about ongoing transmission of the disease in the community have been published [4,5].

There was an estimation of a sharp increase in the incidence of hepatocellular carcinoma (HCC) among other liver-related complications, with an expected doubling of HCV-related mortalities between 2000 and 2020 [6].

Back in 2006, Egypt announced the launch of the National Committee for Control of Viral Hepatitis (NCCVH) to take responsibility for managing HCV in the country and to secure a framework for control of HCV infection, aiming at reducing the prevalence and burden of the disease, and aimed to eliminate HCV in Egypt by 2030. The main goals of NCCVH were to improve access to diagnosis and management, with efforts to stop transmission of the disease [7]. At the time, and in a country with limited resources like Egypt, there were many barriers that needed to be addressed before implementing a nationwide project to combat HCV: the high cost of the antiviral therapies, the lack of accurate data about HCV prevalence in the country and the absence of specialized centers and personnel that could work as a basis for implementing an HCV elimination program. To overcome these, NCCVH issued the "National Control Strategy for Viral Hepatitis" that represented the road map for its mission [8]. The preparation of this strategic plan was one of the NCCVH missions, besides issuing the standardized treatment protocols, establishing a nationwide network of viral hepatitis specialized treatment units covering the whole country, training of the staff working in these centers and negotiating for the prices of the supplied antiviral therapies [7]. The first of these centers was opened in 2007 within the facilities of Egyptian Ministry of Health and Population. A plan was implemented to cover Egypt's territory with these centers that now exceed 54 in number in 2017 [7]. During the first years of the program, the standard of care for HCV patients was the combination of Pegylated Interferon (PEG IFN) with Ribavirin (RBV). NCCVH succeeded in securing access to this therapy for free –or with a much reduced price for more than 350,000 patients over the period from 2007 to 2013 [7,9]. With the rapid changes in HCV treatment guidelines and the appearance of new directly acting antivirals (DAAs), NCCVH maintained the same strategy with securing access to the new DAAs at very reduced prices that has enabled the treatment of more than a million patients since 2014. Treatment protocols that were utilized in NCCVH affiliated centers were constantly changing according to the repeated changes in treatment guidelines and the availability of antiviral drugs in the program. Accordingly, Sofosbuvir/RBV, Sofosbuvir/PEG IFN/RBV regimens were initially used followed by the introduction of other IFN free regimens like Sofosbuvir/Semiprevir, Sofosbuvir/Daclatasvir and Paritaprevir/Ombitasvir [7]. The availability of cheap locally produced generics of many DAAs helped a lot in reducing the cost of the program and hence, the ability to increase the number of the treated patients over time. In a trial to connect the treatment centers with the headquarters

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in NCCVH, a specialized intranet network was used to register data of all treated patients in different treatment centers since 2010. Also, the introduction of online registration through the NCCVH electronic site helped the organization to select patients for attendance to the nearest treatment center to their localities. The cost of this program was about 2.8 billion L.E. (350 million US dollars), and nearly 90% of the treated patients were sponsored through governmental supported funds [7]. Screening programs to detect undiagnosed infected patients, awareness programs to know the modes of HCV transmission and its prevention, and the enhancement of infection control programs are currently the main pillars of the future strategy in the Egyptian battle against HCV. The Egyptian program for control of HCV provided a successful model for managing HCV in a resource limited country with a high prevalence of the disease.

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References

1. El-Zenati F, Way A. Knowledge and Prevalence of Hepatitis C. Egypt demographic and health survey 2008. [ONLINE]. Available from: https://dhsprogram.com/pubs/pdf/FR220/FR220.pdf. Accessed 10 April 2017.
2. Frank C, Mohamed MK, Strickland GT, et al. The role of parenteral antischistosomal therapy in the spread of hepatitis C virus in Egypt. Lancet. 2000; 355:887–889.
3. Ministry of Health, Egypt, El-Zanaty and Associates, Egypt, ICF International. Egypt Health Issues Survey. Cairo, Egypt and Rockville, MD, USA: Ministry of Health and ICF International; 2015.
4. Kandeel A, Genedy M, El-Refai S, Funk AL, Fontanet A, Talaat M. The prevalence of HCV infection in Egypt 2015: implications for future policy on prevention and treatment. Liver Int. 2016; 37:45–53.
5. Miller FD, Abu-Raddad LJ. Evidence of intense ongoing endemic transmission of hepatitis C virus in Egypt. Proc Natl Acad Sci USA. 2010;107:14757–14762.
6. Waked I, Doss W, El-Sayed MH, Estes C, Razavi H. The current and future disease burden of chronic hepatitis C virus infection in Egypt. Arab J Gastroenterol. 2014;15: 45–52.
7. El-Akel W, El-Sayed MH, El Kassas M, El-Serafy M, Khairy M, Elsaeed K, Kabil K, Hassany M, Shawky A, Yosry A, Shaker MK, ElShazly Y, Waked I, Esmat G, Doss W. National treatment programme of hepatitis C in Egypt: Hepatitis C virus model of care. J Viral Hepat. 2017 Apr;24(4):262-267.
8. Egyptian National Control Strategy for Viral Hepatitis 2008-2012. Available at: http://www.pasteur.fr/ip/resource/filecenter/document/01s-00002i-03t/nsp-10-april-2008.
9. Centers for Disease Control and Prevention (CDC). Progress toward prevention and control of hepatitis C virus infection—Egypt, 2001– 2012. MMWR Morb Mortal Wkly Rep. 2012;61:545–549.

Hepatitis E

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Q. What is hepatitis E?

The term 'hepatitis E' refers to an illness caused by infection with hepatitis E virus (HEV). Till some years ago, this infection was believed to cause acute hepatitis only in developing countries (in Asia, Africa, and Mexico). However, the infection is now known to occur also in developed countries of Europe and North America, and to become persistent (chronic hepatitis E) in some people.

Q. What do we know about hepatitis E virus?

Hepatitis E virus (HEV) is a small virus with RNA genome, which primarily affects liver cells. HEV strains that cause human disease have been classified into four genotypes, namely 1-4. Genotype 1 and 2 HEV isolates are prevalent in developing countries of Asia and Africa and infect only humans. By contrast, genotype 3 and 4 HEV isolates are primarily animal viruses, with occasional zoonotic transmission to humans; of these, genotype 3 isolates have been particularly found in industrialized countries and genotype 4 in South-East Asia, with occasional cases from the rest of the world.

The viral isolates from different genotypes appear to share epitopes, such that antibodies to these are cross-reactive.

Q. How does hepatitis E virus infection usually occur and in whom?

The virus enters the body primarily through the enteral route, and is excreted in the faeces of infected individuals. The modes of transmission of HEV however vary in different geographic regions, with two major epidemiologic patterns: high-endemic and low-endemic.

In most parts of Asia and Africa, HEV infection (with genotype 1 or 2 virus) is highly endemic, with the major route of spread being contamination of drinking water supplies with human faeces,

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leading to water-borne outbreaks of acute hepatitis. In these areas, hepatitis E is also often the most common cause of acute sporadic hepatitis. The highest attack rates are observed in young adults, in particular pregnant women, whereas children are affected quite infrequently. Transmission of infection from HEV-infected pregnant women to newborns is known, but it is only a minor contributor to the overall disease burden.

By contrast, in Western Europe and other developed countries (e.g. Japan, USA, Australia), though indigenous transmission is known, the disease occurs as infrequent sporadic cases. These cases are often related to ingestion of undercooked meat, in particular products that contain liver and liver products, from pigs and deer. The liver injury following such infection, usually with genotype 3 (and sometimes genotype 4) HEV usually causes a milder form of liver injury. In these areas, the disease occurs more often among elderly men, in particular those with other associated diseases.

Q. Can HEV infection also be transmitted through blood transfusion?

In low-endemicity areas, a low-level, genotype 3 HEV viremia can be detected in a small proportion of healthy blood donors, raising a concern about the safety of blood and blood product supply chain. The contribution of blood-borne transmission to the overall burden of HEV infection remains unclear and may be small. However, immunosuppressed persons may be at a particular risk because of their need for transfusions for underlying diseases and propensity for chronic infection.

Q. What are the clinical manifestations and natural history of HEV infection?

In areas with high disease endemicity, hepatitis E manifests almost exclusively as acute hepatitis-like illness. The illness usually resolves spontaneously in 1-5 weeks; however, a few cases develop acute liver failure, which may be fatal. Pregnant women with hepatitis E are at particular risk of acute liver failure; the mortality rates among these women reach 15% to 25%. Persons with pre-existing chronic liver disease may present with acute-on-chronic liver failure and form another group with risk of poor outcome.

Cases in low-endemicity areas appear to have a milder liver injury. However, individuals with impaired immune response, e.g. organ transplant recipients on immunosuppressive drugs, may fail to clear the virus, leading to persistent infection. This results in chronic hepatitis E, defined as HEV infection lasting beyond 6 months, which can progress to liver cirrhosis.

Some cases with illnesses of other organ systems, e.g. neurological syndromes, haematological manifestations, etc. have been reported in association with HEV infection. These cases have been labelled as having extrahepatic manifestations of hepatitis E. However, further studies are needed to clarify the exact relation of these illnesses with HEV infection.

Q. Can HEV infection be asymptomatic?

Anti-HEV antibodies can be identified in a proportion of healthy people residing in both high- and low-endemicity areas, who lack past history of liver disease. This indicates that a large proportion of HEV infections are asymptomatic. The seroprevalence rates are somewhat higher in the high-endemicity areas; however, this difference is less marked than that in the clinical disease rates.

Q. Should HEV infection be treated? If so, how?

Acute hepatitis E is usually self-limited, and hence only symptomatic treatment suffices. In such cases, no specific anti-viral treatment is indicated. A few reports of treatment of acute severe hepatitis E with ribavirin in persons with or without underlying chronic liver disease have been published; however, the need and efficacy of such therapy remains unclear.

In persons with chronic HEV infection who are receiving immunosuppressive drugs (such as organ transplant recipients), discontinuation or reduction of immunosuppression, if possible, leads to clearance of HEV viremia in about one-third of patients. In organ transplant recipients in whom this is not possible or fails to clear the virus, treatment with oral ribavirin for 3 months, is often successful in eradicating chronic HEV infection. In other immunosuppressed patients with chronic hepatitis E, interferon-alpha, ribavirin, or a combination of these drugs have shown good results in individual cases or short case-series. However, no comparative trials are available to assess the relative efficacy of these treatments.

Q. Can vaccination prevent HEV infection?

Two vaccines, based on 56-kilodalton (kDa) and 26-kDa recombinant HEV capsid proteins, respectively, each expressed as virus-like particles, have been developed. These vaccines have undergone human trials in Nepal and China, respectively. In these trials, both vaccines showed high rates of protection against clinical hepatitis E, and were safe except for mild pain and swelling at the injection site. In the Chinese trial, the vaccine-induced protection was shown to last for at least 4.5 years.

The 26-kDa vaccine is was approved and marketed in China in 2012; however, it is not yet available in any other country. The immunogenicity of this vaccine among immunosuppressed persons and the protection offered by it against genotype 3 virus and chronic HEV infection, which constitute the main disease burden in Europe, have not been studied. Its role in the European population thus remains unclear.

The other vaccine has not yet been marketed.

Q. How else can one prevent HEV infection?

HEV infection can be prevented by interrupting the fecal-enteral route of transmission. In hyperendemic areas, this can be done by ensuring safe drinking water supplies and proper disposal of human faeces.

In low-endemicity areas of Europe, this can be done by ensuring that animal meats are cooked thoroughly before consumption. This may be particularly important in relation to food products that contain pork liver (e.g. figatelli in France) and for persons who are at a potential risk of developing chronic hepatitis E.

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