TORONTO DECLARATION:
STRATEGIES TO CONTROL AND ELIMINATE VIRAL HEPATITIS GLOBALLY

AVOIDABLE DEATHS DUE TO VIRAL HEPATITIS

Over 400 million people are chronically infected with hepatitis B virus (HBV) and hepatitis C virus (HCV) and thousands of new infections occur every day. Chronic viral hepatitis puts individuals at risk of developing progressive liver disease leading to cirrhosis, liver cancer and ultimately death from liver failure. Collectively these two infections cause an estimated 1.3 million deaths worldwide every year. The enormous global public health burden caused by this ongoing epidemic is largely preventable.

REMARKABLE PROGRESS

The last two decades have witnessed unprecedented scientific and therapeutic advances in the field of viral hepatitis. We now possess the tools to control the epidemic. A highly effective vaccine has made HBV a preventable disease. Well-tolerated, potent medications effectively and safely suppress HBV replication improving clinical outcomes in those already chronically infected. However, although HBV can be controlled with long-term maintenance treatment, true cure remains elusive. HCV is the first persistent viral infection to be cured with medical therapy. Viral eradication leads to improvements in all clinical outcomes, including liver-related and all-cause mortality. A protective HCV vaccine is not yet available; however short treatments with recently developed potent antiviral agents lead to cure in the vast majority of treated individuals. These powerful tools create a scenario in which control and even global eradication of both infections is now a feasible goal.

CALL FOR COORDINATED ACTION

Despite this remarkable progress, major challenges remain. Preventable transmission continues, the majority of infected individuals remain undiagnosed, and only a tiny minority currently receives treatment. In low income countries diagnostic testing for HBV DNA and ad HCV RNA is not generally available, hampering effective monitoring and treatment. Without coordinated action, the recent therapeutic advances will have little effect on the global burden of disease. Individual countries have developed effective national action plans and the World Health Organization recently developed a Framework for Global Action based on 4 specific axes of intervention ranging from raising awareness to increasing access to care and treatment. Building on this solid foundation, The First International Hepatitis Cure and Eradication Meeting presents the ideal forum for proposing an integrated plan to address hepatitis B and C globally with concrete objectives, tangible goals and measurable outcomes. Therefore, in full support of the WHO Global Hepatitis Programme and the World Health Assembly Resolutions on Viral Hepatitis, we, as a group of international experts across multiple disciplines, now call for coordinated action by governments, industry, affected individuals, and healthcare providers to address the many challenges that continue to impede global control and ultimate eradication of viral hepatitis. The present declaration outlines specific public health policies and interventions with tangible but achievable goals that we hope will help guide WHO and national governments as they continue to develop strategies to address viral hepatitis locally, nationally and on a global scale. The Global Viral Hepatitis Summit (International Symposium on Viral Hepatitis and Liver Disease (ISVHLD)) will be held in Toronto in 2018 and as such, we have set this as a target for implementation of the Toronto Declaration.

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Jordan Feld, MD, MPH	*University of Toronto, Canada*
Stephen Locarnini, MBBS, PhD	*Victorian Infectious Diseases Reference Labs, Melbourne, Australia*
Harry Janssen, MD, PhD	*University of Toronto, Canada*
Charles Boucher, MD, PhD	*Erasmus Medical Center, Rotterdam, The Netherlands*
Henry Chan, MD	*The Chinese University of Hong Kong, China*
Pietro Lampertico, MD, PhD	*University of Milan, Italy*
Stanley Lemon, MD	*University of North Carolina, Chapel Hill, USA*
Jürgen Rockstroh, MD	*University of Bonn, Germany*
Lai Wei, MD	*University of Peking, China*
David Thomas, MD, MPH	*Johns Hopkins University, USA*
Mark Sulkowski, MD	*Johns Hopkins University, USA*
John Ward, MD	*Division of Viral Hepatitis, Centre for Disease Control and Prevention, USA*
Mark Thursz, MD	*Imperial College London, United Kingdom*
Gregory Dore, MD	*Kirby Institute, University of New South Wales, Australia*
Jason Grebely, PhD	*Kirby Institute, University of New South Wales, Australia*
Heiner Wedemeyer, MD, PhD	*Hannover Medical School, Germany*
Geoffrey Dusheiko, MD	*Royal Free Hospital, United Kingdom*

HEPATITIS B

National Action Plan

1. All countries should develop a national and/or regional action plan for HBV infection with clearly stated objectives, benchmarks and timelines for implementation.
2. The action plan should follow the principles of the WHO Framework for Global Action and the World Health Assembly Resolution on viral hepatitis and include specific plans for monitoring and evaluation after implementation.

The following targets should be implemented by 2018:

Epidemiology

1. Maintain a national HBV surveillance system that provides data on the burden of infection (acute and chronic) and on HBV-related deaths from liver failure and liver cancer to allow for country-level policy developement
2. Determine accurate population-level estimates of national prevalence of HBV infection including data among sub-populations with high prevalence (e.g. immigrants from HBV-endemic countries, men who have sex with men, people who inject drugs, sex trade workers etc.)
3. Maintain a vaccine coverage registry or alternative system to track HBV vaccination rates locally, regionally and nationally

Disease prevention

1. Eliminate mother to child transmission of HBV through implementation of a combination of the following strategies as appropriate to local epidemiology:
   - Universal neonatal vaccination with >95% coverage of birth-dose within 24 hours of delivery
   - Prenatal screening of all pregnant women with 100% birth-dose vaccination for infants born to HBsAg-positive women
   - Access to antiviral therapy in the third trimester for women with an HBV DNA concentrations above 10^6 (1,000,000) IU/mL
   - Access to a safe supply of Hepatitis B Immune Globulin (HBIG) within 12 hours of birth for infants born to HBsAg-positive mothers, particularly those who are HBeAg-positive or have an HBV DNA level above 200,000 IU/mL
2. Ensure greater than 90% coverage of all 3 doses of HBV vaccine delivered to all children regardless of HBV-status of parents
3. Implement a vaccination catch-up program for children <12 years old for countries with recently introduced or low uptake neonatal HBV vaccination
4. Universal screening of blood and blood products for at least HBsAg and anti-HBc and ideally HBV DNA prior to use
5. Universal implementation of WHO-approved safe injection devices in healthcare facilities
6. Increase education about universal precautions among healthcare providers and the general population to eliminate iatrogenic HBV transmission

Diagnosis

1. Ensure that 75% of infected individuals are diagnosed through
   - Increased awareness among the general population and healthcare providers
   - Implementation of active screening in high-risk populations in low prevalence countries (e.g. household contacts of infected persons, immigrants from endemic countries, men who have sex with men, sex-trade workers etc.)

- Implementation of population and/or targeted screening in countries with intermediate and high prevalence (>2%)

2. Encourage testing for coinfection with HIV or delta infection in HBsAg positive individuals at risk
3. Universal screening for HBsAg and anti-HBc in low prevalence countries (<2%) and HBsAg alone in high prevalence countries for all patients scheduled to receive potent and/or long-term immunosuppressive therapy
4. Universal implementation of WHO-standardized diagnostic tests for surveillance, blood donor screening, diagnosis and disease management
5. Access to post-test counseling in all HBV-testing facilities

Disease Management

1. Ensure new HBV diagnosis prompts linkage to care with access to HBV-trained medical professional in a timely manner (within 6 months)
2. Universal access to quantitative HBV DNA testing for all HBsAg-positive individuals including in low income countries
3. Access to non-invasive assessments of fibrosis (transient elastography, serum panels such as APRI, FIB-4, Fibrotest) or liver biopsy for all individuals with chronic HBV infection
4. Inclusion of antiviral agents with a high barrier to resistance (tenofovir, entecavir, peginterferon) on the 'essential medicines' list with access available for all patients who require antiviral therapy according to international treatment guidelines with the goal of increasing national treatment initiation by at least 25% per year
5. Access to liver cancer surveillance with serial ultrasonography and/or alpha-fetoprotein for those in need according to guidelines provided therapy for early stage liver cancer is available
6. Access to specialty care for those with cirrhosis including liver cancer surveillance, variceal screening and cirrhosis management

HEPATITIS C

National Action Plan

1. All countries should develop a national and/or regional action plan for HCV infection with clearly stated objectives, benchmarks and timelines for implementation.
2. The action plan should follow the principles of the WHO Framework for Global Action and the World Health Assembly Resolution on viral hepatitis and include specific plans for monitoring and evaluation after implementation.

The following targets should be implemented by 2018:

Epidemiology

1. Maintain a national HCV surveillance system that provides data on the burden of infection (acute and chronic) and on HCV-related deaths from liver failure and liver cancer to allow for country-level policy development
2. Determine accurate population-level estimates of national prevalence of HCV infection, including data among sub-populations with high prevalence (e.g. blood-product recipients, people who inject drugs, prisoners, immigrants from endemic countries, HIV-co-infected)
3. Determine local modes of transmission with estimates of disease incidence in both high-risk populations and nationally
4. Determine local estimates of current and future liver-disease burden and related costs

Disease prevention

1. Develop a national policy for people who inject drugs (PWID) including access to harm-reduction initiatives including needle-syringe programs (NSPs) and opioid substitution therapy (OST) leading to a reduction in transmission among people who inject drugs by 25%
2. Universal screening of blood and blood products for anti-HCV antibodies and ideally nucleic acid-based testing for HCV prior to use
3. Universal implementation of WHO-approved safe injection devices in healthcare facilities
4. Increase education about universal precautions among healthcare providers and the general population to eliminate iatrogenic HCV transmission

Diagnosis

1. Ensure that 75% of infected individuals are diagnosed through
   - Increased awareness among the general population and healthcare providers
   - Implementation of active screening in high-risk populations (PWID, immigrants from endemic countries, blood product recipients) and populations with increased prevalence (birth cohort screening in North America, general population in high prevalence countries)
2. Access to HCV diagnostic testing for all
   - Incarcerated individuals
   - HIV-infected individuals
3. Universal implementation of WHO-standardized diagnostic tests for surveillance, diagnosis and disease management with emphasis on point-of-care testing particularly for PWID
4. Confirmatory HCV RNA testing or alternative confirmation of viremia (e.g. HCV core antigen testing) for all anti-HCV-positive samples
5. Access to post-test counseling in all HCV-testing facilities

Disease Management

1. Ensure new HCV diagnosis prompts linkage to care with access to HCV-trained medical professional in a timely manner (within 6 months)
2. Universal access to non-invasive assessments of fibrosis (transient elastography, serum panels such as APRI, FIB-4, Fibrotest) or liver biopsy for all individuals with chronic HCV infection
3. Implementation of models of HCV care appropriate to the local healthcare infrastructure, per capita income, geography and epidemiology including
    - Primary care physician and nurse-led care
    - Comprehensive disease management incorporating liver disease staging, alcohol/drug counseling and HCV treatment initiation and monitoring
4. Ensure that at least 5% of infected population is started on therapy every year
5. Increase treatment among PWID and prisoners to improve health and reduce transmission with goal of treating at least 4% annually
6. Ensure equitable and prompt access (<6 months) to direct-acting antiviral-based HCV therapy for all patients with advanced fibrosis (F3 or F4) and those with severe extra-hepatic disease (symptomatic cryoglobulinemia, porphyria cutanea tarda, lymphoma) or other urgent reasons for therapy
7. Access to specialty care for those with cirrhosis including liver cancer surveillance, variceal screening and cirrhosis management
8. Develop global pricing strategies in collaboration with industry, International Health and Non-governmental Organizations to ensure effective, well-tolerated therapies are affordable and widely available in high, middle and low-income countries
9. Set targets for national disease elimination with a comprehensive monitoring and evaluation plan to assess progress