

Lessons from previous VHPB technical meetings and plans for the future

Daniel Shouval
Liver Unit

Hadassah-Hebrew University Hospital
Jerusalem, Israel



TECHNICAL MEETINGS

Technical meetings: broad range of topics covered (1)

- **Surveillance best practice**
- **Universal Immunisation programs (transition from risk groups)**
- **Injection safety and safe blood supply**
- **HBV mutants and variants**
- **Prevention and control of viral hepatitis in migrants and refugees**
- **Behavioural issues in hepatitis B vaccination**
- **How to reach risk groups**
- **Combined vaccines**
- **Economic evaluations**

Technical meetings: broad range of topics covered (2)

- Hepatitis B vaccination safety issues
- Hepatitis A and B vaccine and long term efficacy
- Hepatitis infections and immunization strategies in HCW
- Prevention of perinatal transmission
- Adolescent vaccination programs
- Patient and advocacy groups
- Hepatitis A and E
- Identification and management of persons with HCV
- Treatment of hepatitis B and C

Perinatal HBV transmission:



Prevention and control of perinatal hepatitis B
virus (HBV) transmission in the WHO
European Region
Istanbul, Turkey, March 15-17, 2006

Meeting conclusions

Journal of Viral Hepatitis, 2004, **11**, 198–205

REVIEW

Prevention of hepatitis C virus infection*

M. Kew,¹ G. François,² D. Lavanchy,³ H. Margolis,⁴ P. Van Damme,² P. Grob,⁵ J. Hallauer,⁶
D. Shouval,⁷ G. Leroux-Roels⁸ and A. Meheus² ¹*South African Medical Research Council/Cancer Association of South*

Reports



VIRAL HEPATITIS

Published by the Viral Hepatitis Prevention Board (VHPB)

October 2009
Volume 18 - Number 1

CONTENTS

EDITORIAL..... 1

Editorial

This issue of *Viral Hepatitis* reviews topics covered at the Viral Hepatitis Prevention Board (VHPB)'s spring meeting on *Hepatitis A and E: Update on Prevention and Epidemiology*, held on March 12-13, 2009 in Antwerp, Belgium.

Vaccine 28 (2010) 583–588

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine



Conference report

ARTICLE INFO

Keywords:
Hepatitis A
Hepatitis E
Prevention
Epidemiology
Vaccines

ABSTRACT

In March 2009 the Viral Hepatitis Prevention Board (VHPB) organized a meeting in Antwerp, in order to review the status of epidemiology and prevention of both hepatitis A and E. International hepatitis experts from the public health and academic sector provided the state of the art on HAV and emphasized the growing public health importance of the disease, in particular in intermediate endemicity regions, and the need for control at global level. The information shared on HEV showed clearly that it is emerging, but still a lot of efforts are needed to clarify among others the transmission routes, the clinical presentations and the burden of disease. First data on hepatitis E vaccines were discussed, showing a promising safety and efficacy profile. The meeting was concluded with lessons learnt, challenges, needs and proposed step forwards for both diseases.



VIRAL HEPATITIS

PUBLISHED BY THE VIRAL HEPATITIS PREVENTION BOARD (VHPB)

November 2005
Volume 14 - Number 1

CONTENTS

EDITORIAL 1

Editorial

This issue of *Viral Hepatitis* examines the important topic of blood-borne infections in healthcare workers (HCWs), as discussed at the meeting of the Viral Hepatitis Prevention Board (VHPB) held in Rome, Italy, from 17-18 March 2005. The meeting was hosted by the team of experts based at the *Istituto Nazionale per le Malattie Infettive IRCCS 'Lazzaro Spallanzani'*.

Incentives and barriers regarding immunization against influenza and hepatitis of health care workers. [FitzSimons D¹](#), [Hendrickx G²](#), [Lernout T³](#), [Badur S⁴](#), [Vorsters A³](#), [Van Damme P³](#) [Vaccine](#). 2014 Aug 27;32:4849-54

Hepatitis B virus, hepatitis C virus and other blood-borne infections in healthcare workers: guidelines for prevention and management in industrialised countries

D FitzSimons,¹ G François,² G De Carli,³ D Shouval,⁴ A Prüss-Üstün,⁵ V Puro,³ I Williams,⁶ D Lavanchy,⁷ A De Schryver,⁸ A Kopka,⁹ F Ncube,¹⁰ G Ippolito,³ P Van Damme²

Occup Environ Med 2008;**65**:446–451. doi:10.1136/oem.2006.032334

Vaccine 32 (2014) 4849–4854



ELSEVIER

Contents lists available at [ScienceDirect](#)

Vaccine

journal homepage: www.elsevier.com/locate/vaccine



Conference report

Incentives and barriers regarding immunization against influenza and hepatitis of health care workers

WHAT DID WE LEARN FROM PREVIOUS TECHNICAL MEETINGS AND WHAT NEEDS FURTHER FOLLOW UP OF VHPB

- Perinatal HBV transmission: Istanbul, Turkey, March 15-17, 2006
- Control of hepatitis A and E: *Update on prevention and epidemiology*, Antwerp, Belgium March 2009
- How to reach Healthcare workers
Barcelona, Spain, 15-16 November 2012
- Control of hepatitis C (public health issues)
Split, Croatia Nov 14-15, 2013

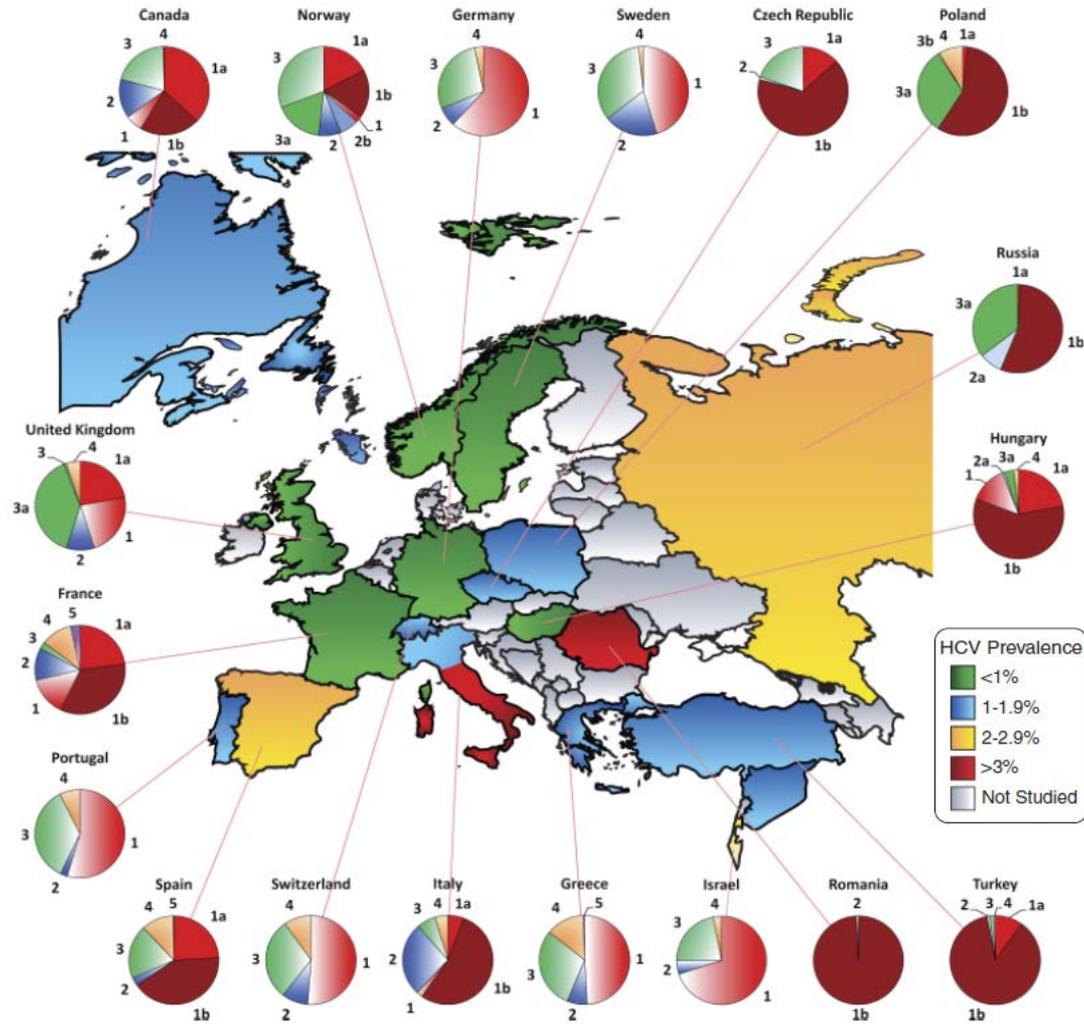
Control of hepatitis C: Public health issues

Split, Croatia Nov 14-15,2013

Epidemiology of HCV infection in Europe

Systematic review of HCV epidemiology in Europe

Cornberg et al.



Objectives

- An overview of the developments in hepatitis C therapy and their potential for controlling the disease
- To review country examples of screening and treatment strategies and their impact on the public health
- To identify barriers to the identification and treatment of patients with hepatitis C, and to discuss equal access to treatment and the perspectives of different stakeholders (hepatologists, patients, public health experts)
- To examine the impact of the increasing number of patients seeking care on existing public health resources (financial and human)
- To provide an overview of the status of the development of hepatitis C vaccines

Background

- Large number of chronic HCV infections (170 million globally, 6.1 million in EU, up to 4.4 million in USA; 10 million infected IDUs, globally; 4-5 million co-infected with HIV) and considerable under-reporting.
- Prevalence varies – relatively low (0.4-4.0%) in developed world but high in some other countries (e.g. Egypt)
- Incidence: steady overall in Europe but falling in North/ West, rising in South/East; rising in some countries (e.g. Australia, Uzbekistan); rural spread a problem (Canada and USA)
- Routes of transmission: IDU, but globally many infections due to suboptimal infection control
- “Epidemic” of HCV-related chronic liver disease including HCC expected to peak around 2020s-2030s

Strategies for control and “burning” questions

- Concern: Diagnosis of HCV without offering treatment in countries with limited resources
- Strategies for treatment – treat to prevent transmission and disease, treat all or selected patients? (F3/F4)
- Treatment regimens (are) were complex, with different protocols for naïve subjects, relapsers, and partial and non-responders, for different viral genotype
- Toxicity still an issue with current regimens but expected to be significantly lower with second generation DAAs
- PegIFN/Ribavirin may remain the standard of care in countries with limited resources

Severity of Disease Increases Need for HCV Therapy but Also Impairs Response

- May not need immediate treatment
- BUT
 - Easier to treat
 - High likelihood of response

- Greater need for treatment
- BUT
 - Response to current IFN-based therapy may be impaired



Mild disease

**Advanced disease/
cirrhosis**

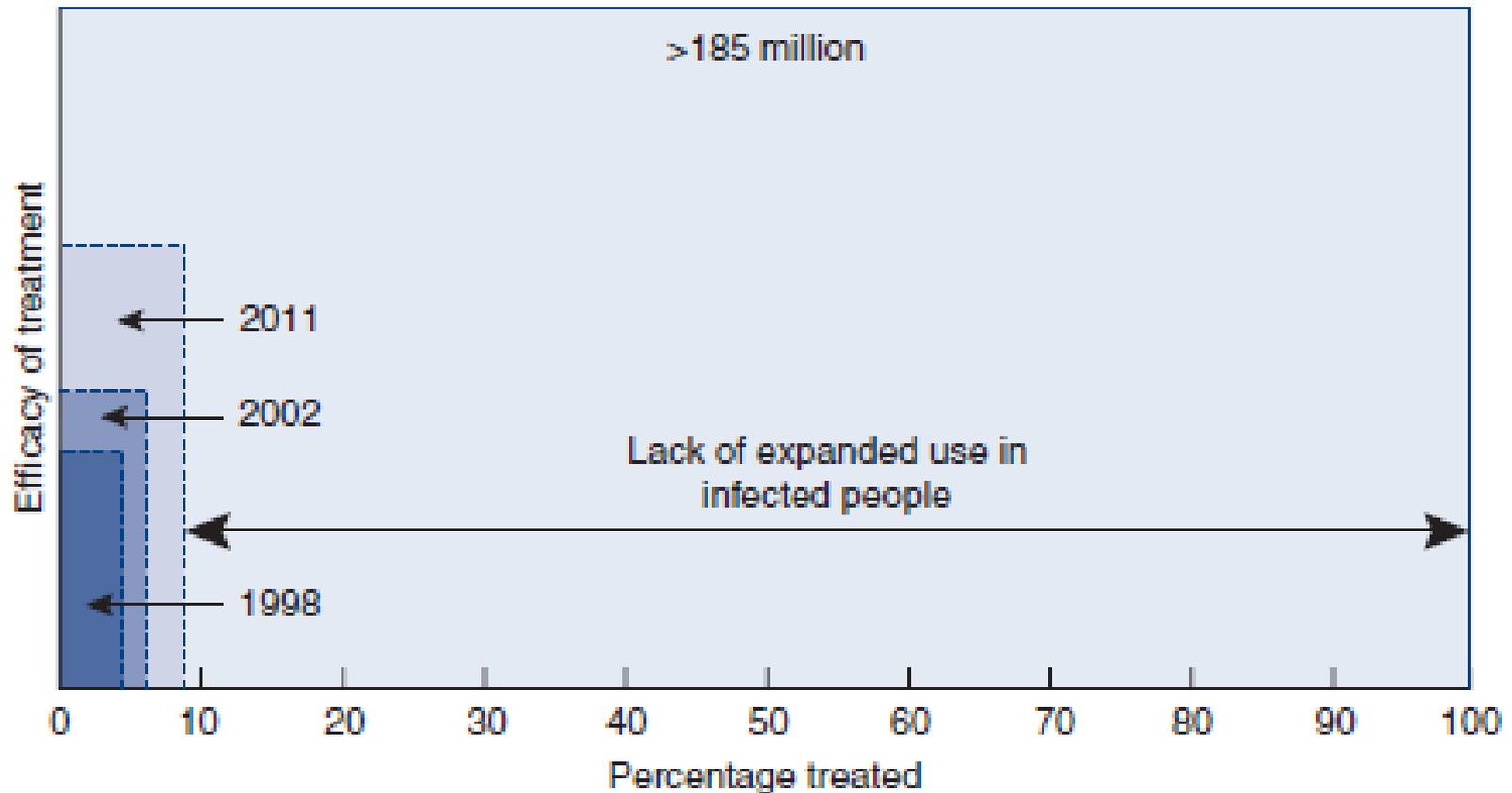
Changing therapeutic landscape

- Steady improvements in SVR with combination therapy - modelling indicates impact of treatment in terms of predicted deaths averted (in USA screening of the 1945-65 birth cohort expected to increase the HCV patients pool)
- Success rates with available therapies (until 2014) vary with genotype (up to 90% for GT2 but progressively lower for GT3, 1b and 1a)
- Introduction of direct acting agents improving benefits of treatment; new treatments recently licensed-(87-98% SVR in all genotypes excl GT3)
- More antiviral agents in pipeline (different classes with different mechanisms of action) – rapid progress, revolutionizing treatment and breaking down barriers to treatment
- All-oral, IFN-free treatment regimens can lead to dramatically increase in number of candidate patients treated (including IDUs) but cost is prohibitive

Different Strategies



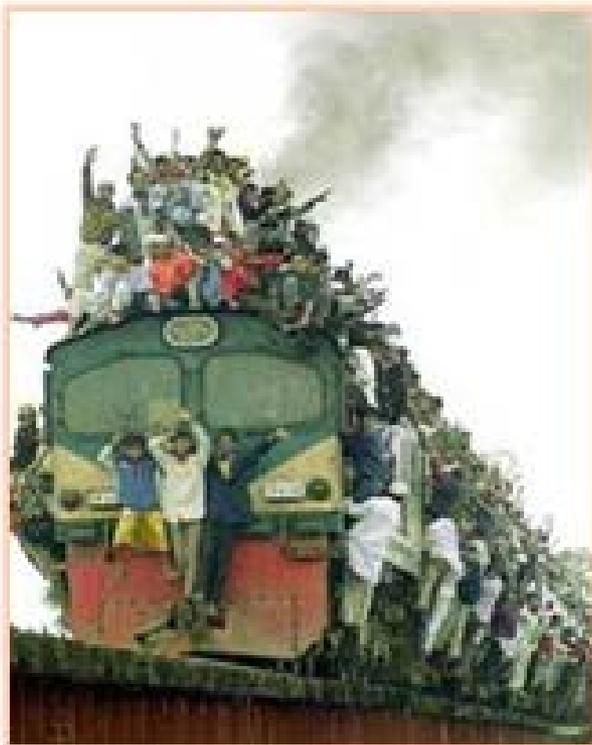
Global control of hepatitis C: where challenge meets opportunity



Progress in development of anti-viral agents for HCV

Candidate anti-viral agents for HCV

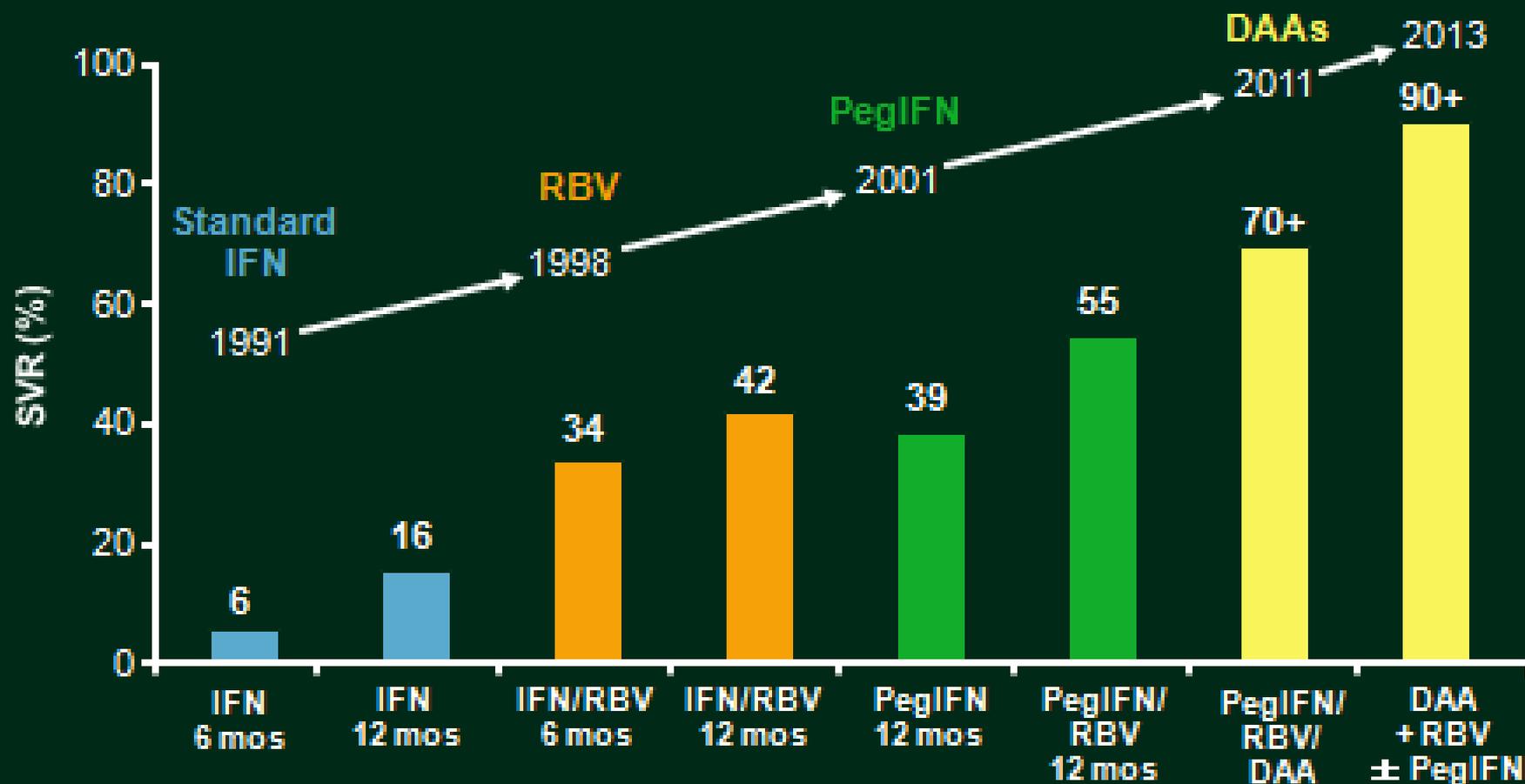
2012



2014



The Good News



Adapted from the US Food and Drug Administration, Antiviral Drugs Advisory Committee Meeting, April 27-28, 2011, Silver Spring, MD.

Cost of treatment

- Price of treatment – likely to be high (around US\$ 80,000-120,000) for the next few years
- Reimbursement covered by the state or private health insurance in some countries; lack in other countries means that new treatments will be unavailable
- Support must be provided to countries to scale up HCV testing and treatment
- Comparison of prices a useful approach for countries before negotiations on purchases - other approaches include national procurement, tiered-pricing or rebates
- Urgent need to explore innovative funding methods

Barriers to treatment

- Barriers seen at all steps of care and at all levels: health system, providers, patients and pharmaceutical industry
- Underserved populations – little or no access to testing
- Surveillance of treatment
- Solutions – from decriminalization of drug use to public awareness and education (including physicians), and provision of need-adapted care systems

Matters for consideration I

- How to raise awareness about hepatitis C as a global health problem and create and maintain greater political will and commitment?
- How to generate more and better data, including burden of disease and health economic studies (cost-effectiveness of treatment and screening)?
- Other experiences from HIV/AIDS – treatment as prevention, expanding access
- Examples: action plans (France and Scotland)

Matters for consideration II

- Injecting drug users: Learn from successful national action plans. Consider decriminalizing injecting drug use
- How to develop screening recommendations that destigmatize hepatitis C
- How to overcome major barriers at all levels: lack of awareness, poor knowledge and inadequate education? Need for accurate information and for consensus within the medical community

Matters for consideration III

- What policy should be adopted for those diagnosed with HCV infection but without access to treatment?
- How can we apply the new treatments to lower the barriers to treatment?
- Need for education and training, sharing of best practices, monitoring and evaluation, networks and partnerships between public health experts and policy-makers, clinicians, funders, doctors and patients
- Some high-level of support and interest (e.g. ECDC, DG Sanco, EU's Seventh Framework Programme)

Matters for consideration IV

- Periodic update of guidelines – at present they are rapidly becoming obsolete
- Need for more work on nosocomial infections and improvements in infection control
- Stigmatization is a real problem and its drivers need to be better understood; health care workers, especially in primary health care, need training to counter it
- Recognition of HCV as a carcinogenic virus

Impediments for developing an HCV vaccine

- Complex nature of immune response to HCV
- Existence of multiple HCV genotypes (differences in ~30% in nucleotide position)
- HCV exists as a population of related viral quasi-species which enables emergence of HCV variants eluding the immune response
- Risk of HCV re-infection
- Limited availability of animal models
 - Chimpanzees
 - Immuno-deficient mice
 - Cell culture systems

Pros and Cons for development of HCV vaccine(s)

Pros

- Control of global HCV infection
- Reduction in rates of cirrhosis and hepatocellular carcinoma
- Control of HCV infection in specific risk groups

Cons

- Priorities and cost
- Limited knowledge on protective immune response post acute HCV
- Anticipated duration of clinical trials
- Lack of predictive modeling how combined vaccination with DAA will reduce global pool and interrupt transmission in rural and urban populations
- Scarcity of candidates for controlled clinical trials on protective vaccines as well as ethical considerations

Debate

In view of the immense progress in development of anti-viral agents against HCV:

What is the rational for developing a vaccine against HCV?

– Preventive vaccine (i.e. for specific risk groups Vs universal mass vaccination)

– Therapeutic vaccine

- *Inability of anti-virals to restore protective immunity may justify induction of HCV T cell mediated responses to maintain an SVR*
- *Combination with anti-viral agents with vaccine to prevent relapse after cessation of anti-virals (variable timing in administration of anti-virals)*
- *Induction of viral suppression and control of HCV infection without complete viral clearance*

Summary -

- Key messages: an abundance of HCV and HCC cases expected, HCV is about to become a global public health emergency, need for testing campaigns linked to action (e.g. treatment, prevention and adherence to infection control procedures), issues of access must be resolved, and urgent need for public health measure
- The goal of control of hepatitis C (through increased treatment and prevention) appears to be feasible in the long-term – but only with political will, infrastructure and health system capacity-building

“Some” of the future challenges for the VHPB

- Surveillance of the epidemiology including burden and control of hepatitis A, B, C and E in the European regions and in specific risk groups
- Surveillance of vaccination efforts against HAV and HBV including monitoring of timely administration of a birth dose HBV vaccine
- Continuous monitoring of immune memory to specific vaccines and need for boosting
- Maintenance of protection and prevention measures against hepatitis B in healthcare workers
- Special attention regarding the disparities and impact of access to testing and introduction of the new DAAs against HCV in the various European regions
- Maintain the position of a public health “watch dog” and be prepared to respond in a timely manner to emerging new issues

The Hadassah Medical Center in Jerusalem

Thank You

