

# Viral Hepatitis Prevention Board



## **Prevention and control of viral hepatitis in Belgium and Luxembourg: lessons learnt and the way forward**

**BRUSSELS, BELGIUM**

**7-8 November 2017**

# Context

- In the 2030 Agenda for Sustainable Development, adopted in 2015, Goal 3 (ensure healthy lives and promote well-being for all at all times) has a target “to combat viral hepatitis”
- In 2016, the World Health Assembly adopted the global health sector strategy on viral hepatitis. Later in 2016, the WHO Regional Committee for Europe adopted an action plan for the health sector response to viral hepatitis in the WHO European Region
- The Regional Action Plan sets the goal of elimination of viral hepatitis as a public health threat by 2030 by reducing the transmission of hepatitis viruses; reducing morbidity due to viral hepatitis and its complications; and ensuring equitable access to comprehensive prevention, and recommended testing, care and treatment services for all. It also sets viral hepatitis control targets to be achieved by 2020, including:
  - 95% coverage with the three-dose hepatitis B vaccine for children;
  - 90% coverage with timely hepatitis B birth-dose vaccination within 24 hours of birth for countries that implement universal newborn vaccination
  - 90% of mothers screened for HBsAg prenatally and 95% of infants of infected mothers treated with HBIG plus birth dose of hepatitis B vaccine in countries that implement selective vaccination
  - $\leq 0.5\%$  of hepatitis B surface antigen (HBsAg) prevalence in vaccinated cohorts
  - 50% of all persons with chronic HBV, HCV and HDV diagnosed and 90% of them linked to care and adequately monitored; 75% of the diagnosed eligible patients with chronic HCV infection receive effective treatment and at least 90% of them are cured



# Health care systems

- In **Belgium** the population (11.2 million) perceives the country's health care system as satisfactory, probably because of its high and easy overall accessibility and affordability; the State spends about 8% of its GDP on health
- The system is shaped by the consequences of the country's complex federal, regional and subnational structure and the historical vertical division into sectors ("pillarization")
- Health care is financed through both compulsory social security contributions and taxation; health insurance is compulsory and covers 99% of the population
- Health care is delivered through private non-profit organizations, with independent medical practitioners, within a framework set by the State; services are payable by the patient and reimbursed later by health insurance institutions – that can pose problems for vulnerable or hard-to-reach populations
- The system performs well in general, but attention needs to be given to access for the most vulnerable, to adequacy and variations in quality, the centrality of hospitals in the system, and government policies to address these issues
- Belgium has a national plan for hepatitis C (2014-2019) but not for hepatitis B and D or viral hepatitis generally; the plan has 6 strategic axes (from prevention and screening to follow-up) and 22 actions – but a low implementation rate: few actions have been undertaken or completed and the prospect of achieving WHO's objectives by 2030 were not seen as encouraging. An inter-cabinet working group aims to allocate tasks to stakeholders by end of 2017



# Health care systems

- **Luxembourg** (population about 560,000) operates a free market affiliated to its national health insurance system, which enjoys an accumulation of financial resources, although as the population ages it expects problems; currently the system covers some 800,000 people, including non-residents
- Its social welfare model is based on solidarity, operates through several institutions in particular the national statutory health insurance body, aims to provide equitable and unlimited access to high quality health care with a free choice of provider, has strong health promotion and disease prevention programmes
- Most health expenditures (83%) are covered by the public sector; for 2018 the health ministry's budget is €166 million (which pays for most disease-prevention activities) and the ministry of social security about €3310 million (which includes health insurance) - together 23% of the total national budget)
- A law due to be enacted before the end of 2017 will mandate reporting of notifiable diseases by laboratories; that reporting will complement the existing mandatory reporting by clinicians
- Both Belgium and Luxembourg have relatively large but different immigrant populations and are multilingual
- **National plans** for viral hepatitis: Belgium has a written plan for hepatitis C and Luxembourg is aiming to finalize its national plan on viral hepatitis by end-2017 following analysis of other countries' plans; it has five strategic axes. Both emphasize prevention, screening (epidemiology), access and linkage to care. In both countries the plans focus primarily on hepatitis C and there is no real plan for hepatitis B.



# Vaccination

- The major issue is the prevention of perinatal transmission and the importance of maternal screening and administering the birth dose in a timely manner. Outstanding questions are: what proportion of mothers are screened, what proportion of babies born to HBsAg-positive mothers are treated, and what follow-up is instituted?
- **Belgium:** Universal vaccination began in 1999 for infants and adolescents, and is mandatory for health care workers and reimbursed for several groups at risk. Flanders and Wallonia have independent but closely related policies for hepatitis B vaccination; the Flemish Government successfully made its political commitment to the goal of lifetime immunity through vaccination. Strengths include use of Well Baby clinics, School Health Services and mobile vaccination teams (for outbreaks and catch-up vaccination), high vaccination coverage, and rapid and coordinated multidisciplinary response to rumours. Hepatitis A vaccination only applied for outbreak management.
- Wallonia and Brussels also work through Well Baby clinics (with mobile well baby clinics) and School Health Services, as well as antenatal consultations. Service coverage is better in Wallonia than in Brussels. Low rates of refusal of hepatitis B vaccination were seen (1.3%) but vaccine hesitancy has increased
- Hexavalent vaccine was introduced in Belgium in 2004, raising coverage rates to high levels nationwide
- Vaccination coverage is assessed every three years
- WHO Regional Office for Europe calls for verification of HBV carrier prevalence in immunized cohorts of children



# Vaccination (continued)

- **Luxembourg:** vaccination is not mandatory in the country but vaccines are fully funded by the State and the costs of consultations for administration of vaccine are reimbursed. Vaccination is mostly given in private medical practices, not in public health settings, and financial incentives are provided for attendance at well baby clinics. Hepatitis A vaccine is not reimbursed.
- Hepatitis B vaccine is part of the universal infant immunization programme. There is a catch-up programme for 12 year olds and vaccine is available free for 12-15-year olds. Vaccination is recommended for many risk groups but reimbursed only for haemodialysis patients, PWIDs and health care professionals in training. The refusal rate was low (1%).
- Vaccination coverage is not routinely assessed by seroprevalence data but is surveyed every five years



# Epidemiology

## HAV

- Different sources of data in Belgium provide good quality surveillance and a nationwide seroprevalence study is planned for 2018
- In Belgium, incidence has declined to levels comparable with its neighbours, but the corollary is that there is a growing pool of susceptibles - most cases are now travel-related or in children. Outbreaks increasingly occur in MSM, and a pan-European increase in cases has been seen in 2017 (probably associated with travel to an increasing number of events such as Gay Pride activities), with three strains of HAV circulating simultaneously
- Sexual practices of MSM carry risks of infection and some doctors are neither comfortable nor sufficiently knowledgeable to discuss and advise about changing sexual behaviour; MSM need information and advice about HAV vaccination (especially during outbreaks)
- Food-related outbreaks: a Belgian federal agency has issued advice for management of food-handlers; genotyping and phylogenetic analysis need to be done at the time of outbreaks in order to identify and trace sources. Health professionals need to be informed and made aware
- Only a few cases in Luxembourg in 2017, with no evidence of outbreaks.



# Epidemiology

## HBV, HCV and HDV

- Both hepatitis B and C viruses cause morbidity and mortality (including hepatocellular carcinoma) – the fact needs re-emphasizing, as some bodies refuse to recognize it and the contribution of HBV and HCV to HCC is not defined. Alcohol exacerbates the risk of HCC. The implication is that stopping disease progression (through antiviral treatment) and paying attention to avoidable risk factors such as alcohol can reduce mortality
- There are multiple surveillance systems in Belgium, including a sentinel laboratory network, with each providing information at different levels. Nevertheless it is not a comprehensive system – there is no evaluation of screening of pregnant women for HBV, meaning that opportunities for treatment and prevention may be missed as in some situations no birth dose might be given
- HCV seroprevalence studies are under way in Belgium; for future studies the use of protocols based on those of ECDC will be recommended



# Epidemiology (continued)

## HBV, HCV and HDV

- *HCV in risk groups*: in **Belgium**, there have been several studies, but the most solid data on HCV in PWIDs dates from 2005, showing a seroprevalence rate of 50% in ever and current PWIDs; another study showed HCV infection in 10-15% of prisoners, and a prevalence of 1.6% in HIV-infected patients; many HCV patients are migrants, and in Luxembourg a higher proportion of hepatitis B case are in migrants
- Genotype 1 accounts for at least 50% of HCV infections with a significant contribution from genotype 3
- No screening policy or strategic plan in Belgium for HBV (infected subjects as well as pregnant women)
- In **Luxembourg**, three databases were merged in 2015, allowing better estimates of incidence; a new law being enacted will mandate laboratory-based notification of all infectious diseases
- PWIDs account for 43% of HCV-infected population in Luxembourg and more than 75% of PWIDs are infected (anti-HCV-positive); the epidemic is being modelled but real-world estimates are better
- Laboratory-based estimates substantially higher than clinical notifications; data suggest 70% prevalence in PWIDs (with 38% of infections due to genotype 3)

**HDV**: On average nine confirmed cases are confirmed by the National Reference Laboratory a year in Belgium, but probably many more cases are not reported; a study in 2008-2009 showed 5.5% of HDV superinfections in HBsAg-positive cases, mostly in males



# Epidemiology

## HEV

- In Belgium in 2010 the National Reference Laboratory was established and became the main source of data, Sentinel surveillance was introduced in 2014, providing complementary data. There is no mandatory reporting. A cross-sectional seroprevalence study is planned for 2018
- The incidence rate is increasing (possibly owing to increased awareness) but is still low; genotyping shows that 90% of typed strains are genotype 3, mostly 3f and 3c (now dominant) with similar subtypes seen in pigs and wild boars. Chronic hepatitis E infection in immunocompromised subjects is often unrecognized and can be confused with transplant rejection
- HEV RNA has been found in faeces of most fattener pigs and liver sausages and pate prepared at low temperature, and is resistant to heating at 71 °C for 20 minutes or more. What are the heating time and temperature that inactivate the virus is not known. Advice to immunosuppressed subjects is not to eat such foods
- Regional differences are seen across Belgium but the notification and seroprevalence rates are lower than those reported in some other EU countries
- Blood is currently not screened for HEV in Belgium



# Prevention and control, besides vaccination

*PWIDs*: good achievements have been made by the Free Clinic, one of the few drug treatment centres with a well-established HCV care programme in Belgium

- The main message to emerge is to focus on currently injecting PWIDs, when the aim is to reduce incidence
- Modelling exercise concluded that more than 10% of infected PWIDs would have to be treated in order to meet WHO's target of reducing prevalence by 90% by 2030. However, although treatment uptake through the Free Clinic's activities exceed 10% that covers all PWIDs, not just current injectors. PWIDs presenting at the clinic are less stable and more precarious.
- Luxembourg has introduced a drug consumption room and opening of another is planned for 2018, but for Belgium to follow suit would need a change in the law and an increase in resources

## *Prisons*

- An innovative programme in a large prison in Luxembourg, with many subjects detained for drug-related offences, in Luxembourg has produced good results. The medical service provides testing (for HAV, HBV, HCV and other pathogens), treats and prevents (including vaccination, harm reduction measures, needle-exchange programmes and a unique safe tattoo project). A nurse practitioner coordinates a clinic for infectious diseases, including a considerable burden of viral hepatitis. Loss to follow-up is a major problem.

- Working with NGOs inside the prison proved to be a valuable approach.
- VHPB country meeting: Prevention and control of Viral Hepatitis in Belgium and Luxembourg: lessons learnt and the way forward. Brussels, Nov 2017



# Prevention and control, besides vaccination (continued)

## *Commercial sex workers*

- Men, women and transgender people, they are not a homogenous group, working in different locations and sites. They are a very mobile population.
- Ghapro and PASOP, NGOs in Antwerp and Ghent, offer effective screening and prevention services, including free hepatitis B vaccination for the whole of Flanders. For Ghapro, over 17 months in 2016-2017, six carriers of HBV markers and one case of HCV infection were found in 643 newly identified sex workers who attended the clinic.
- The federal Government recognizes the need to work with other similar bodies across the country.

## *Migrants*

- Comparison of two approaches to screen for HBV and HCV a large representative sample of Chinese migrants in four centres in three cities across Belgium (apparently covering large proportion of the Chinese immigrant population) showed the value of the use of point-of-care tests and immediate delivery of results. This Community Partnership approach was cost-saving compared with the Community Outreach approach that used blood samples. Among 559 subjects 37 tested positive for HBsAg and one for HCV infection



# Treatment

- The Belgian Association for the Study of the Liver (BASL) has issued no specific guidelines on hepatitis B, relying on EASL's 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection; criteria for reimbursement have been established
- BASL issued revised recommendations for chronic hepatitis C in 2017 and new reimbursement criteria now applied (with an e-health platform); several DAAs available
- Luxembourg has no specific guidelines for hepatitis B and C, using those of EASL (as recommended in the national hepatitis action plan), but there are no restrictions on choice of antiviral; about 10% of HCV patients have been treated (nearly 300 in 2016)
- Luxembourg paying high prices for DAAs and overall costs exceed those of OST and needle exchange programmes
- Some 60% of HIV-infected PWIDs are treated in Luxembourg; about 20 cases a year were diagnosed in 2016 but the number seems to be falling as a result of awareness-raising and other preventive activities. DAAs are used in a prison medical clinic to treat HCV
- Prison offers an opportunity to treat and provide information for health promotion, as well as fostering links with care
- Treatment of chronic hepatitis E in immunosuppressed subjects with ribavirin was recommended, but doubts were cast as to its appropriateness as a therapy
- There is currently no recommendation in Belgium to treat pregnant women who are HCV positive



# Issues

- Complexity - multiple layers of legislation and different authorities concerned with public health and health care (with seven health ministries alone in Belgium), different mandates, multiplicity of entities
- Work on strategies and action plans is a call for political action, advocacy for viral hepatitis to be on the agendas of decision- and policy-makers in government
- Shortages of vaccines (HAV and HBV) in many countries in Europe (and elsewhere) – a continuing and serious problem
- Activity of anti-vaccine groups, more pronounced in Wallonia; increasing vaccine hesitancy as well as resistance to hepatitis B vaccination
- Changing drug use practices, for instance cocaine and consequent marked increase in frequency of injection and undermining of needle and syringe exchange programmes (in both countries); also, increased precarity of PWIDs



# Issues (continued)

- “Treatment without prevention and screening makes no sense” – the importance of evaluation of screening for HBsAg in pregnancy was repeatedly emphasized
- The high cost of DAAs means prioritization of resources and interventions; other countries (e.g. Australia) have good experience with lowering costs and generics
- Negotiation with pharmaceutical companies is excluded by law in Luxembourg; coordinated or pan-European negotiations should be considered
- At what stage of liver fibrosis to treat? It has become increasingly clear that to meet WHO’s goals treatment has to be given irrespective of stage of fibrosis
- A suggestion was made to consider introduction of filters into irrigation systems for vegetables to capture HEV in areas such as the pig belt in north-western Europe where the virus was abundant in pigs



# Needs

- Countering negative messages and rumours about vaccines, with consistent and uniform information communicated and disseminated through various media
- Creation of national hepatitis registries and databases, including data on recipients, vaccinations and vaccines issued
- Risk communication (for example, for MSM about HAV, about HBV for migrants and HEV for immunosuppressed subjects)
- Research into why three strains of HAV are co-circulating in Europe and causing large outbreaks
- More DNA sequencing data for investigating food-borne outbreaks
- Vital need for good seroprevalence data on HCV – in general populations and specific groups (e.g. prisoners) – and their use to expand criteria for reimbursement; similarly, there is a need for a screening policy and plan to increase the number of patients treated
- Vital need for good seroprevalence data on HBV in order to measure the impact of the universal vaccination programme



# Needs (continued)

- Creation and introduction of electronic registries of HBV and HCV patients
- Much more and better information about the cascade of care of hepatitis C
- Guidelines for the clinical management of hepatitis E (in immunosuppressed patients)
- Further work on epidemiology and molecular epidemiology of HEV in humans, in the apparent animal reservoir (in particular pigs) and possibly in shellfish
- Extra efforts and investment into reaching “hard-to-reach” populations
- Evaluation of the recommendations of National Immunization Technical Advisory Groups (NITAGs) on immunization



# Recommendations

- In working groups at the meeting, participants identified needs for the two countries to reach WHO's milestones and targets for 2018 and 2020
- Improve knowledge about the molecular epidemiology of HAV in Belgium for monitoring and tracking outbreaks
- Public funding should be made available for vaccinating children aged 1-12 years who travel to countries with high prevalence rates of HAV
- Policy should be to vaccinate MSM and PWIDs against hepatitis A and B, with consideration being given to offering outreach vaccination at specific events (and to the means of raising appropriate funding), and awareness should be raised in such groups about preventive measures
- Monitor, evaluate and strengthen implementation of recommendations for screening of pregnant women (Belgium) for HBsAg positivity, preferably during the second trimester, and consider antiviral therapy when relevant, and ensure administration of a timely birth dose of HBV vaccine and HBIG
- Measure HBV DNA at end of second trimester to ensure detection of pregnant women with high viral load so as to be able to initiate antiviral treatment, benefiting mother and child
- Vaccination against hepatitis B should be extended to specific risk groups as is the case for sex workers
- Maintain current high vaccination coverage rates (in both countries)



# Recommendations (continued)

- Screen pregnant women for HCV; approaches to screening (B and C) should be standardized
- Determine the quality-adjust life years (QALYs) for treating HCV infection in each country; if not nationally then supranationally
- Improve knowledge of HEV epidemiology in swine and possible links with human infection; involve the veterinary sector
- Prepare and disseminate official recommendations on prevention of HEV infection in risk groups such as immunocompromised subjects, patients with chronic liver disease and organ transplant recipients
- Promulgate recommendations for testing populations for HCV and emphasize the value of being tested
- Encourage and support the work of NGOs, including clinics for hard-to-reach populations and prisoners, encourage coordination between centres and expand the use of peer-to-peer advocacy
- Encourage coordination of actions and funding when responsibilities are spread across different ministries
- Consider introduction of drug consumption rooms for PWIDs in Belgium



# Recommendations (continued)

- Better coordination and collaboration between countries to lower prices of DAAs
- Treatment criteria should be broadened to include hepatitis patients at all stages of fibrosis
- Belgium is encouraged to bring reimbursement criteria into line with international standards (EASL) and cover diagnostic tools
- Belgium and Luxembourg should participate in the validation process of the WHO Regional Office for Europe for meeting regional elimination targets. Necessary actions are: serosurveys of cohorts of immunized children and adolescents (target seroprevalence rate of HBsAg-positivity of 0.5%) and monitoring of perinatal transmission of HBV through maternal screening and consider routine birth dose of hepatitis B vaccine
- The need for good data is paramount, and the creation of linked central national registries and databases is a priority
- Continue efforts to raise political will; use strategies and action plans as calls to political action
- Attention should be paid urgently to the issues surrounding vaccine shortages



# VHPB, Brussels meeting

Thank you for your attention

