

VIRAL HEPATITIS PREVENTION BOARD MEETING



PREVENTION AND CONTROL OF VIRAL HEPATITIS IN ISRAEL: LESSONS LEARNT AND THE WAY FORWARD

Jerusalem, 14 and 15 March 2013

The Viral Hepatitis Prevention Board (VHPB) convened a meeting in Jerusalem (14 and 15 March, 2013) in order to share Israeli experiences in the prevention and control of viral hepatitis and to examine how presented data have been and may be used to shape policy.

Background and health system in the state of Israel

Israel has a heterogeneous, relatively young population of 8.08 million, of whom about 80% are Jewish and 20% non-Jewish, mainly Arab (2012). It has experienced massive waves of immigration including in the late 1940s and 1950s migrants from North Africa, Arab countries, Romania and Poland followed by immigration from former USSR countries in the 1990s and from Ethiopia from the 1980s and onwards. Beside legal immigrants, many people from Africa have entered the country illegally, often as refugees or migrant workers.

The health system rests on the principles of equity, justice and solidarity, with universal health care coverage. The government regulates health care through policy setting and implementation as well as financial support. Data presented herewith derive from annual reports of the Israeli Central Bureau of Statistics 2010-2012 and http://apps.who.int/iris/bitstream/10665/85397/1/9789241564632_eng.pdf. The gross national income per capita is US\$27,110 (2011). The health expenditure as % of GDP is 7.63% as compared to 9.3% in OECD countries (2010). The per capita health expenditure is \$1319 (2010). Overall life expectancy at birth is 82 years (2009), 83.6 years for females and 79.9 years for males. The median age of the population is 30 years (2010) and the total fertility rate per woman is 2.9 (2010). The number of physicians per capita is decreasing and at present stands at 3.3 per 1000. The annual need for replacing retired physicians is estimated at 800-900 per year.

The health service is financed mainly through tax revenues (health tax) which is proportional to individual income. The government regulates national health insurance funds among four competing health maintenance organizations (HMOs, also called sick funds) on a capitation basis. Care is also delivered through public not-for-profit organizations. The private sector is increasingly providing and financing service delivery, and the proportion of private sector funding reached almost 40% of total expenditure on health in 2011.

The National Health Insurance Law, adopted in 1995, makes health insurance compulsory (even for those without an income), and defines the national list of health services and medications (the “basket”) that the health insurance services have to provide. Each year, the health ministry solicits recommendations from all interested parties for new technologies to be included in the public health “basket”. The list currently covers some 2600 pharmaceuticals and 1100 technical applications, including six antiviral agents for hepatitis B, several new treatment regimens for hepatitis C, viral load assays and assessment tools for hepatic fibrosis for chronic hepatitis C.

Vaccine-preventable diseases feature as a specific element of the national “Healthy Israel 2020” initiative. The Ministry of Health’s Advisory Committee on Infectious Diseases and Immunization sets policy for immunization (including vaccination of travellers). It decided in 1991 to introduce routine-universal vaccination of neonates against hepatitis B and, in 1999, universal vaccination of toddlers against hepatitis A.

The Ministry of Health (MOH) also covers agencies such as the non-profit organization Magen David Adom emergency and ambulance service, whose responsibilities include the collection, processing, testing and distribution of blood units and blood products throughout the country. Blood donors are not remunerated. The MOH also funds the infra structure of the National Hemophilia Center while pharmaceutical agents and blood products for patients are covered by the individual health insurance agencies. A serum bank was established in 1997 by the MOH, collecting residual samples from diagnostic laboratories or blood donors from all regions of the country.

Civil society is becoming active: The Israeli Association for the Health of the Liver (<http://www.hetzliver.org/Page.asp?id=1>), a non-governmental organization and advocacy group, provides support for patients, the first to do so in the country. Recently it organized seminars for patients in medical centres to mark World Hepatitis Day, with media coverage.

Surveillance and control of viral hepatitis (including hepatitis A and B vaccination policies) *

There is a written national strategy that focuses primarily on the prevention and control of viral hepatitis, and also integrates other diseases.

It includes components for surveillance, vaccination, prevention of transmission via injecting drug use and in health-care settings, treatment and care, and co-infection with HIV.

**Modified from: Global policy report on the prevention and control of viral hepatitis in WHO Member States, page 121, WHO 2013.*

http://apps.who.int/iris/bitstream/10665/85397/1/9789241564632_eng.pdf

There is routine MOH surveillance for acute hepatitis A, B and C using standard case definitions, but not for any type of chronic hepatitis. Reporting rates of acute hepatitis cases are relatively low, estimated for hepatitis A at 1:5 and most probably lower for hepatitis B and C. Deaths, including from hepatitis, are reported to a central registry. Liver cancer cases are registered nationally, but cases with HIV/hepatitis co-infection are not. There is no designated governmental unit/department responsible solely for coordinating and/or carrying out viral hepatitis-related activities, including introduction of vaccines and vaccine coverage, screening policies and surveillance systems.

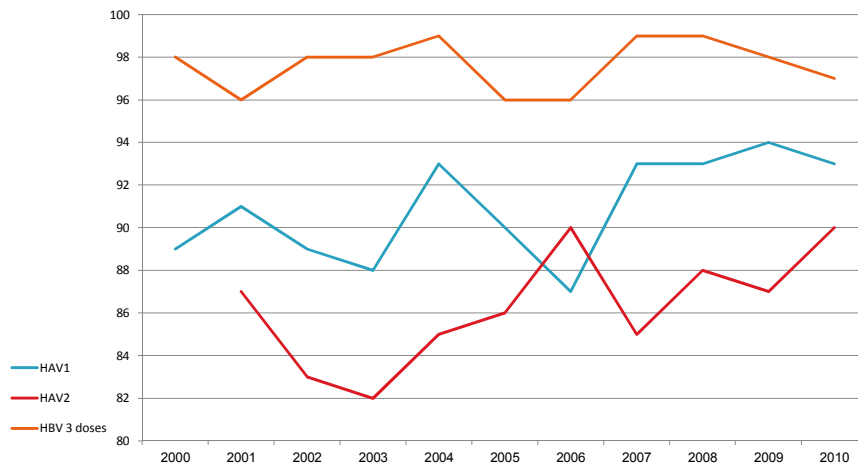
The government has a viral hepatitis prevention and control program that includes activities targeting the following specific populations: health-care workers (including health-care waste handlers), people who inject drugs, patients with HIV and travelers. Hepatitis outbreaks are required to be reported to the government and are further investigated. There is adequate laboratory capacity nationally to support outbreak investigations and other surveillance activities for hepatitis A, hepatitis B, C and D. Serologic and molecular diagnosis for hepatitis E is provided at present by a single laboratory in the country.

There is a national policy on hepatitis A and B vaccination[1]. The government has not established a goal of eliminating hepatitis B. Nationally, 98% of newborn infants in a given recent year received the first dose of hepatitis B vaccine within 24 hours of birth and 98% of one-year-olds (ages 12–23 months) in a given recent year received three doses of hepatitis B vaccine (Figure 1).

A third-generation, mammalian cell derived recombinant hepatitis B vaccine that contains glycosylated S, Pre-S and Pre-S2 components of the hepatitis B surface antigen has been developed in Israel [2-5]. In early comparative studies in adults and in children, it appears to be highly immunogenic (3 doses of 10 µg given at 0,1 and 6 months for adults and 3 doses of 2.5 µg in children), inducing higher and faster protective levels of antibody to those produced by second-generation yeast-derived vaccines at comparable smaller doses and only one booster dose [6-8]. The vaccine was instrumental in bypass of non-response to immunization with yeast derived vaccines [9]and in patients with end-stage renal failure[5, 10] who were in part non-responders to vaccination with second generation, yeast-derived vaccines. In a pilot study, in previously vaccinated end-stage renal failure patients, 3 doses of 20 µg Sci-B-Vac were comparable to 4 doses of 40 microgram Engerix B, achieving 88% seroprotection [5].In vaccine-naïve patients 3 doses of 10 µg Sci-B-Vac were comparable to 4 doses of 40 µg of Engerix B, leading to 70% seroprotection.

At present, the vaccine is licensed in Israel where it is used mainly for universal immunization of newborns against HBV as well as for immunization of patients with end-stage renal failure. Studies are ongoing in HIV patients. It is also licensed in several countries in East Asia.

Figure 1: HAV & HBV National Vaccine Coverage, 2000-2010



Division of Epidemiology, Ministry of Health, Israel

The country boasts an extensive network of mother and child health clinics (free of charge) throughout the country[1]. Every child resident in Israel is entitled to receive health services in the public well-baby clinics, regardless of the legal civil status of the family. They provide low-cost, universal preventive services, including comprehensive immunization programmes, among other vaccinations against hepatitis A and B. School health services have been operating for more than 40 years; their activities include delivery of vaccines and provision of catch-up doses for the estimated 7% of children not immunized at birth. Clinics and schools report vaccination data to the health ministry.

In recent years, non-compliance with recommendations of immunization by the MOH is rising. For example, resistance to vaccination was documented among some Jewish ultra-orthodox communities where several outbreaks of measles and mumps were linked to refusal of parents to immunize their children. Anti-vaccination activists in Israel have recently resorted to threatening critics with defamation suits over comments in online social-media discussions. Furthermore, recently, the Izun Hozer "Association for Dissemination of Health Education" has petitioned the Israeli High Court of Justice in an effort to halt the ongoing vaccination campaign against Polio. The petition was rejected. Regardless of these activities, vaccine coverage rates remain very high in Israel.

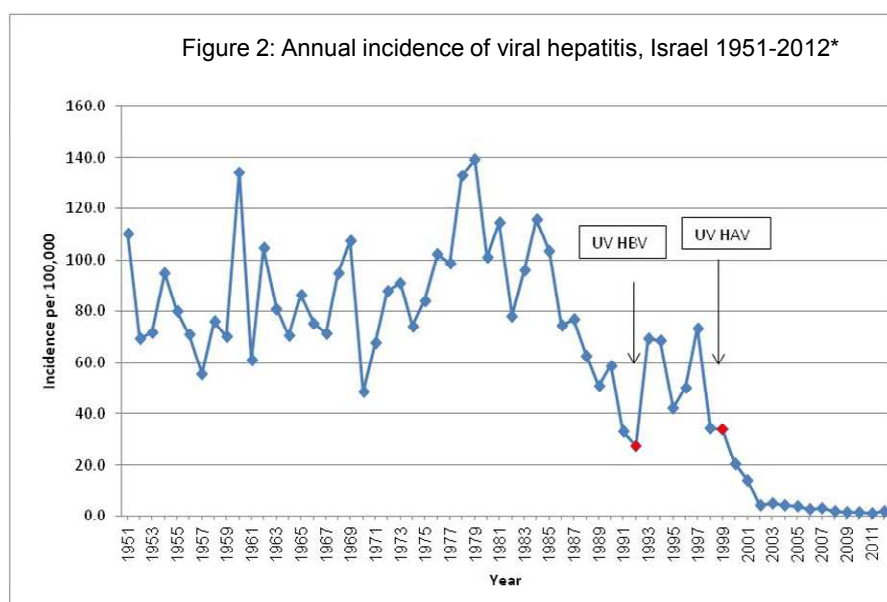
Through a series of regulations and guidelines, health care facilities carry the responsibility of providing a safe environment for patients and protecting their personnel. Circulars issued by the MOH in 2011 and 2013 cover vaccination of students in the health professions and health care workers themselves. As of March 2013, vaccination recommendations for health professionals include hepatitis B (for all those at risk of exposure to blood and bodily fluids), hepatitis A (for laboratory workers) and seasonal influenza. Current policy for both health professionals and students demands that they must present evidence of complete vaccination against hepatitis B before starting work or studies and by the end of 2013 hepatitis B vaccination of health care workers will be mandatory. Health care workers who refuse vaccination must sign a declaration of exemption. Those who practice exposure-prone procedures must provide evidence of protective anti-HBs antibody levels prior to

engagement in such activities. HBsAg carriers involved in exposure prone procedures must present evidence for suppression of viral load (HBV-DNA <2,000 IU/ml). The MOH Committee on Employment of Healthcare workers infected with hepatitis B or C issued in 2006 extensive guidelines for protecting healthcare workers against hepatitis B and handling health care personnel infected with hepatitis B or C viruses. These recommendations are in the process of implementation nationwide. (Shouval D. et al.

<http://www.old.health.gov.il/pages/default.asp?maincat=1&catid=6&pageid=4366>)

Viral hepatitis epidemiology and disease burden

Notifications and surveillance data, such as incidence of viral hepatitis (figure 2) and vaccine coverage data (figure 1), are reported through district health offices to the health ministry for analysis and dissemination of information as weekly and annual reports. Inevitably, under-diagnosis of asymptomatic infections and under-reporting of viral hepatitis are common, the latter being estimated at around 1:5 or less for hepatitis C.



*Source: Israel MOH. Since 1993, the list of notifiable diseases has included serologically confirmed acute hepatitis A, B, C and "other viral hepatitis"; chronic disease is not reportable. Each notification includes information about prior vaccination history, if known. *UV HBV-universal vaccination; HBV- hepatitis B virus; HAV- hepatitis A virus

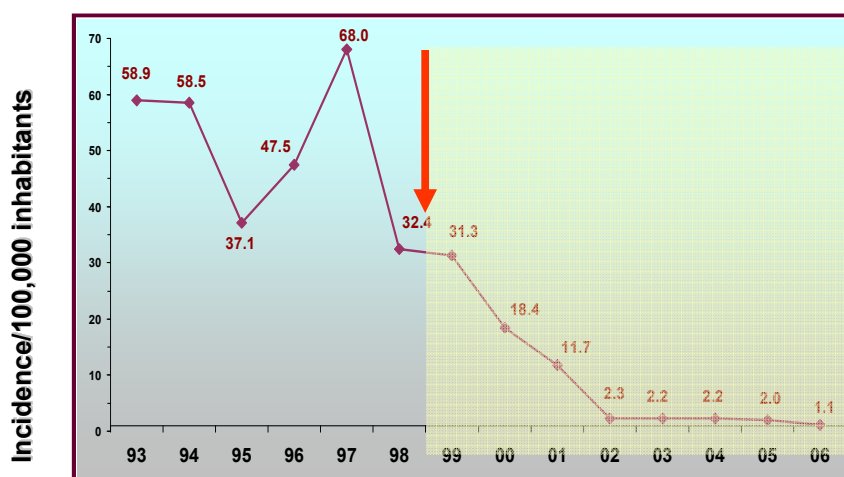
Electronic reporting of data will soon be the norm. In 2008, work began on an electronic national registry of childhood vaccinations. Information, including data on the vaccines used, is provided by well-baby clinics through a web-based interface. The registry is linked to the national population demographic database. The National Immunization Registry, due to be finalized soon, will connect all health services in the country that provide immunization. A central cancer registry exists, which includes data on hepatocellular carcinoma, but aetiological data (i.e. on HBV, HCV, alcoholic liver disease or non-alcoholic fatty liver disease) are not always available. In order to improve that situation, a two-centre collaborative project (Hadassah and Ichilov Sorasky medical centers) has recently begun, and initial findings show that about 50% of the 80 cases of hepatocellular carcinoma are related to HCV (Shibolet O and Levi I., personal communication). Another Ministry of Health database is the

National Case Registry of all patients treated in methadone maintenance centres, and this is expected to be online by the end of 2013.

Hepatitis A

Until the late 1990s, hepatitis A had been the most common viral hepatitis in Israel, with often large outbreaks in military and civilian populations, and even up to the year 2000 it caused a third of all cases of fulminant hepatitis in Jerusalem. Between 1993-1998, the overall incidence of HAV infection fluctuated between 37 and 68 cases/100,000, reaching 120 cases/100,000 in 5–9 year-old children (Figure 3). In 1999, universal paediatric vaccination was introduced, offering vaccine free of charge to 18 month-old toddlers with a booster dose at 24 months of age. Vaccination coverage of 90% and 85% was achieved for the first and second dose, respectively. Within 2–3 years of programme initiation, annual immunization of toddlers, which comprise about 3% of the population, led to a marked decrease in infection rates of HAV in all age groups (reflecting herd immunity) and a shift from intermediate to very low endemicity of 2.5 cases/100,000 (figure 3)[11].

Figure 3: Reduction in reported hepatitis A disease following introduction of universal vaccination to toddlers in Israel



Thus at present, hepatitis A has been virtually eliminated nationwide – a development that would have been unimaginable 20 years ago[11-14]. This dramatic achievement came as a result of the introduction of universal childhood hepatitis A vaccination in 1999; Israel was the first (and until 2004 the only) country to include hepatitis A vaccine in its national routine vaccination programme.

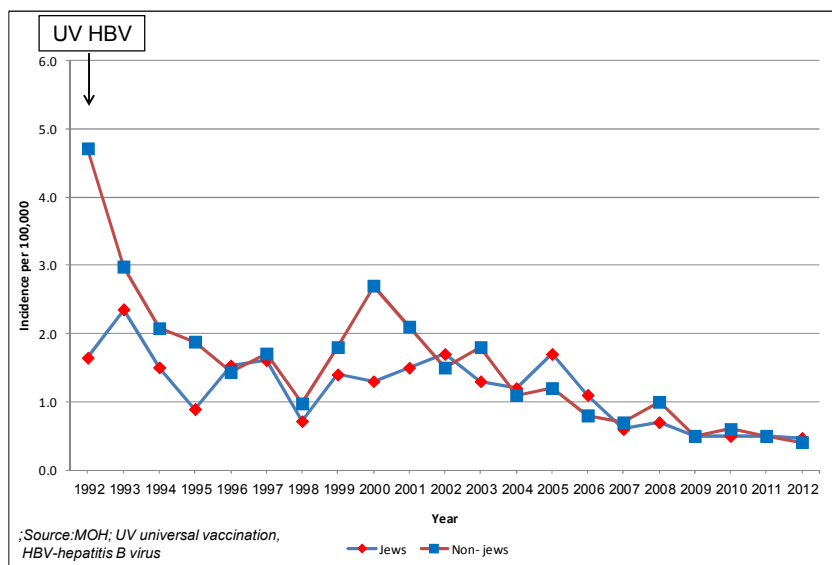
One of the triggers for action was a large outbreak that occurred in a socioeconomically deprived Arab village in 1996[15]. After two rounds of administration of immune globulin failed to halt the epidemic, the decision was taken to introduce mass immunization. More than 1100 children aged 12-72 months were vaccinated, and, within two weeks, transmission was interrupted and the epidemic extinguished four weeks later. A cost-benefit analysis was also instrumental in obtaining governmental support for introduction of universal vaccination in toddlers[16]. A subsequent evaluation of the universal vaccination programme found much higher than expected field effectiveness, with significant herd immunity [13].

Most of the older adult population born in Israel, including the Jewish and Arab communities as well as immigrants from endemic countries, will have been infected with hepatitis A virus and thus have developed immunity. In contrast, the continuously improving socio-economic and sanitary conditions in Israel over the past 5 decades lead to emergence of susceptible populations among adolescents, young adults and infants between the age at which they clear maternal antibodies (around 6 months) and the age at which the first dose of vaccine is given (18 months). Despite high vaccination coverage rates and herd immunity, small outbreaks of hepatitis A continue to occur every year. The characteristics of the outbreaks have changed since the 1990s. They now occur in older age groups (10-19 year olds compared with 1-6 year olds), affecting more specifically the cohort born in 1993-1997, in urban rather than rural communities and can only be controlled through catch-up vaccination programmes [17].

Hepatitis B

Since the introduction of universal newborn hepatitis B vaccination in 1992 the number of reported cases of acute hepatitis B has declined from about 140 a year to less than 40 in both 2009 and 2010, with cases shifting to older age groups. Incidence rates have similarly dropped to around 0.5/100,000 population. (figure 4).

Figure 4: Incidence of acute hepatitis B in Israel, 1992 – 2012, rate/100.000, by population groups



Most early data on prevalence of HBV and HCV markers derive from screening of volunteer blood donors[18]. Up to date population based data on the epidemiology of both hepatitis B and C are limited. In a recent and the largest retrospective epidemiological study to date, HBsAg seropositivity was investigated using data held in the computerized records of the largest sick fund in the country which provides healthcare insurance to a population of 3.8 million (Zuckerman E. personal communication). Results for the 340,000 males and 530,000 females for whom test results were available since 2000, show an estimated overall HBsAg prevalence rate of 1.8%. Lower rates were seen in women (1.2% compared with 2.7% in men), people under 19 years of age (1.5%) and in Jewish communities (0.5-1.7%) compared with non-Jewish populations (mean 2.98% but with rates of up to 9% in some Arab

villages) ; 4.5% for immigrants from North Africa and 6.3% for immigrants from Ethiopia). Tests of 12,475 HBsAg positive individuals identified a small rate of HBe antigen positivity at 9%. The prevalence rate of HBsAg among blood donors has been falling steadily for a decade, reaching less than 0.1% in 2012. From 2008 until 2012, occult HBV infection as determined by nucleic acid testing was found in 52/1,463,899 tested blood donors, resulting in at least one infection in a recipient of donated blood.

The proportion of pregnant women in Israel who are carriers of HBsAg ranges between 0.4% and 4.4%¹, with variations between ethnic groups. A recent survey in the city of Jerusalem revealed a 3.9% carrier rate in pregnant Arab women as compared to 1.6% in the Jewish women [19]. In contrast only 0.4% of pregnant Jewish women in the city of Beer Sheba tested positive for HBsAg [20]. The majority are HBeAg negative and it has been estimated that most familial infections of HBV occurs through horizontal transmission.[21, 22]. Currently, screening of pregnant women is limited to testing of risk groups only, while the definition of risk is vague. In 1991, the Ministry of Health's Advisory Committee on Infectious Diseases and Immunization voted against universal screening of pregnant women for HBsAg on the grounds that perinatal transmission contributed little to the overall transmission of hepatitis B virus in Israel, that hepatitis B immunoglobulin had little benefit provided newborns are vaccinated on the day of birth, according to the schedule, and that the cost of the programme would double if screening would be done. It is quite likely that the epidemiologic basis for this decision has changed. A recent extrapolation, based on prevalence data extracted from the sick fund laboratory testing mentioned above suggests that there are approximately 16,000 HBsAg positive women in child bearing ages in Israel (Zuckerman E. personal communication). Consequently, the 1991 decision of the committee to abstain from HBsAg screening during pregnancy needs re-evaluation.

From the available data it is estimated that there are between 60,000 and 100,000 carriers of HBsAg in the country, most of whom are unaware of their infection status. Efforts to reach those at risk with vaccination have not been successful and it was argued that universal screening was the solution. At present, two decades have passed since the introduction of universal vaccination of HBV in newborns. The evaluation of the impact of this intervention requires improved monitoring. Better epidemiological data should provide useful additional information for review of policies on screening and for planning treatment.

Hepatitis C

Most of the data on epidemiology of HCV infection in Israel is derived from ongoing monitoring of HCV prevalence over the past two decades in volunteer blood donors [18] as well as from monitoring HCV cases at the laboratory of the largest health insurance agency [23]. Prevalence of anti-HCV in blood donors (some of whom are repeat donors) dropped from 0.16% in 1996 (N=193,806) to 0.03% (N=235,211) in 2011(Yahalom V et al. personal communication).

Few investigations have been made into the population based epidemiology of hepatitis C in Israel; only 12 studies have been published in the past two decades. In the recent, largest epidemiological study referred to above (Zuckerman E, personal

communication), 2.3% of nearly 800,000 people tested for infection with hepatitis C virus were anti-HCV positive. In contrast to the results for hepatitis B, much higher rates of HCV infection were found in Jewish than the Arab population. About 70% of HCV carriers in the Jewish population are immigrants born in endemic countries, including those of the former USSR. Data for blood donors confirm this higher rate[18]. Few and sporadic cases of acute HCV infection (which is frequently subclinical and difficult to detect) do occur, mainly in healthcare setting[24].

Quoted estimates of the number of HCV carriers fell in the range 60,000-120,000, and as with hepatitis B, most carriers are unaware of their infection. The number of newly diagnosed cases of chronic hepatitis C in Israel in fact fell substantially between 2002 and 2010 (from 3510 to 1329) but rose thereafter (70% genotype G1), possibly owing to the availability of new treatments, leading to increased testing. Although patients diagnosed with chronic hepatitis C (F2-F4) are eligible for antiviral treatment, less than 20% are treated. In the absence of a look-back program for risk groups (i.e. recipient of blood transfusions prior to 1992) referral for treatment is influenced by unawareness of HCV carriers regarding their infection, as well as delays in initiation of treatment due to shortage of specialist physicians.

Cirrhosis due to hepatitis C is the main reason for referral for liver transplantation in the country[25]. The annual need for liver transplantation, regardless of etiology of liver failure, is estimated to range between 10-18 donors/million of the general population[26], while recent donation rates are around 6-8 donors/million. Most patients eligible for a transplant are increasingly elderly men, including a rising number of patients with hepatocellular carcinoma[27]. HCV graft re-infection after liver transplantation, contributes to a reduced post transplant survival as compared to patients with non-HCV cirrhosis[25]. Patients with hepatitis B who receive a liver transplant may expect excellent outcomes due to prevention of post-transplant HBV re-infection through hepatitis B immune globulin and nucleos(t)ide-analogue treatment.

Specific groups

Hepatitis B (1.8%) and C (0.9%) seroprevalence rates in Israeli health care workers are comparable to the rates reported in the general population[28-30]. Over a five-year period in one medical centre in 2006-2010, 0.6% of health care workers who reported an injury with exposure to a potential source of infected bodily fluids were found to be infected with HBV; the figure for HCV was 1.6%. Investigation of nearly 1300 reported incidents showed that 4.5% of the reported sources were positive for HBV and 10.2% for HCV (*Rubinowitch B., Personal communication*).

Some 4500 injecting drug users are being treated with substitution therapy in 14 treatment centres. At their entry in the centre, about 13% tested positive for markers of HBV infection and 40% for HCV infection. Viral hepatitis is the third leading cause of death in the methadone-maintenance patients (Roska P., personal communication)[31]. A new project has been launched with the help of the Hetz Liver advocacy organization and ministerial support to increase awareness, knowledge and referral. It was suggested that the care model, with daily visits and a high level of health services, could be applied in other countries.

Most haemophilia patients born before 1986 are infected with HCV (and 15% co-infected with HIV), except immigrants from the countries of the former USSR, where

they had been given treatments other than factor VIII concentrates[31, 32]. The prognosis for HCV/HIV co-infected patients is worse than for HCV mono-infected subjects, with poorer success rates of antiviral therapy[33].

Combined and other hepatitis virus infections

Co-infections (HBV, HCV, HDV and/or HIV) are occasionally identified. In the population-based study referred to above, at least 7% showed signs of dual infection with HBV and HDV and 1% with HBV, HCV and HDV[33, 34].

Hepatitis D, previously affecting up to 25% of chronic hepatitis B patients [35] is by now relatively rare.

Sporadic cases of hepatitis E have occasionally been diagnosed in Israel[36, 37] and in travellers to East-Asia. HEV RNA sequencing suggests that a few patients may have been infected in Israel by a genotype 1a HEV (Shouval D., personal communication).

Hepatocellular carcinoma

Limited data on hepatocellular carcinoma (HCC) exist in Israel [25, 27, 37]. Recent data suggest that the disease burden is increasing, irrespective of better informed doctors and improved diagnosis HBV and HCV (which are the most common risk factors for HCC) . However, the prevalence of non-alcoholic fatty liver disease among HCC patients is rising. Alcohol intake is also recorded as a co-factor regarding the risk of HCC in patients persistently infected with HCV. A two-centre collaborative project has recently been launched. The case for primary and secondary prevention is clear and facilitated through guidelines of the Israel Association for the Study of the Liver. These include non-invasive HCC screening methods for chronic liver disease , vaccination against hepatitis B and suppression of viral load in HBV as well as treatment of chronic hepatitis C with anti-viral agents.

Discussion and potential future activities

Achievements:

Israel could be regarded as the "Italy of the Middle East" in preventing and controlling viral hepatitis - that was the comparison prompted by the enormous progress documented at the meeting and the remarkable collaboration and teamwork demonstrated. The dramatic control of hepatitis A through a programme of universal vaccination of toddlers provides a good example of how data can be used for sound policy-making. The great fall in incidence rates of hepatitis B provide further testimony to the value of universal childhood vaccination against hepatitis B. Other achievements include the high vaccination coverage rates, the creation of registries and databases, and improvements in electronic reporting. The development of a third-generation hepatitis B vaccine holds promise.

Concerns:

Despite the successes, several concerns were identified or raised by VHPB members:

- No national policy exists on screening for hepatitis B and hepatitis C in defined risk groups (i.e. recipients of blood products prior to 1992 and former immigrants from endemic countries).
- In particular, in contrast to a large number of countries with intermediate endemicity for HBV, there is no overall national policy for screening of

pregnant women for HBsAg. The current recommendation to screen pregnant women at risk for HBV infection requires re-evaluation, especially in view of the heterogeneous and multi-ethnic population, which includes Israeli born Jews and Arabs as well as immigrants from countries endemic for HBV where universal immunization against hepatitis B was not available.

- Other policy issues concern the lack of monitoring of post vaccination immunity against hepatitis B of the generation vaccinated at birth since 1992.
- National surveillance data on prevalence of chronic hepatitis B and C were not presented during the meeting
- Of notice is the report that the country has a serious shortage of organ donors.
- The number of hepatologists and supporting services is not enough to cope with the existing and expected rising burden of hepatitis C patients who require up to date anti-viral therapy, let alone the expected increase of hepatocellular carcinoma. Expanding and training of physicians and nurses needs to start now.
- Other concerns, not unique to Israel, relate to forecasting disease burden for hepatitis B and hepatitis C, the quality of surveillance, under-reporting and in some cases lack of data, not to mention perennial worries about funding.

General comments and guidelines:

- ❖ It is highly recommended to establish a national registry for chronic hepatitis B and C
- ❖ High priority should be given to creating a national plan for improved and sustained prevention and control of viral hepatitis with special emphasis on hepatitis C and hepatitis B.
- ❖ Such a plan should include among others the systematic screening of pregnant women for hepatitis B on the basis of robust, rigorous and defensible evidence and proposals that cover all stages from screening to treatment.
- ❖ In the case of HCV, the target population for screening needs to be defined before a plan can be contemplated. Economic modelling of options for screening for HCV and outcomes could provide valuable information for policy development. Steps are needed to improve the early detection of chronic HCV infection. To support the policy-making process, more and better data are needed; this could be done especially through systematic sero-surveys at population level and in risk groups for both HBV and HCV infection and improved data analysis. Policy development also needs to cover the design of programmes to monitor the impact of universal vaccination against hepatitis B 20 years after its introduction, including quality control of the assessment of immunization.
- ❖ High vaccination rates need to be sustained and the need of catch-up vaccinations for hepatitis A assessed.
- ❖ Sustain momentum and enforcement of universal precautions and prevention of viral hepatitis in health care workers, including students who should routinely receive regular education and training on safe injection practices, starting as early as possible in their careers. The strict observation of universal precautions in health care facilities needs to be enforced, possibly through the introduction of legislation comparable to the Needlestick Safety and Prevention Act in the USA. The design of such facilities should facilitate the optimum use of safety equipment. Policies for health care workers exposed to

or infected with blood-borne pathogens need to be regularly evaluated, updated and applied. Health care facilities have to respect their responsibility to ensure the safety of processes, technologies and equipment (including its provision). Specific areas identified for further research include: the epidemiology of hepatocellular carcinoma in Israel; occult hepatitis B infection and the associated risk of infection of recipients of donated blood, and the question of what is the clinical and public health significance of occult hepatitis B virus infection; further evaluation of the use of the third-generation hepatitis B vaccine manufactured in Israel, in particular for patients with end-stage renal failure, diabetes and HIV-infected subjects; evaluation of introduction of more effective, interferon-free treatments for hepatitis C and non-invasive monitoring of liver disease.

- ❖ Associations that work with and between patients, their families, family physicians and treating doctors, and whose functions include raising public awareness, need further support (in terms of both human and financial resources).

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