Hepatitis B: long-term protection through vaccination and treatment

Virtual meeting

29 and 30 March 2022

Day 1 – Long-term protection of HBV vaccination

Objectives

- To assess the long-term protection resulting from hepatitis B vaccination, and the scientific evidence from recent and/or ongoing follow-up studies
- to assess the long-term impact of hepatitis B vaccination strategies, illustrated by success stories
- to discuss the impact of growing vaccine hesitancy on long-term vaccination coverage
- further to discuss long-term hepatitis B vaccination in relation to the 2030 elimination goals of the World Health Organization (WHO)

Long-term protection after hepatitis B vaccination

- A 35-year follow-up of people including children 6 months of age vaccinated with a plasma-derived HB vaccine in western Alaska showed gradual declines in anti-HBs concentrations but solid evidence of protection with overall 85% having evidence of immunity (>=10 mIU/ml), including one group that had not received a booster dose in the interim. The data support vaccinating children younger than 6 months.
- At 30 years of follow-up, cell-mediated immunity had been demonstrated.
- Higher anti-HBs antibody titres after the primary series of vaccination were associated with protective antibody titres at 35 years.
- Poor immune response was not found to be associated with age, sex, body mass, diabetes or comorbidities.
- Over 35 years only 27 cases of anti-HBc antibody were detected, none with detectable illness and none was immunocompromised.

Murine model of hepatitis B

- Replication-competent transgenic mice depleted of circulating HBsAg and implanted with HBV-specific CD8+ T cells were used to study host-virus interactions.
- Clearance of serum HBsAg had only minimal effect on the expansion of HBV-specific naïve CD8+ T cells undergoing intrahepatic priming; it had no effect on the antiviral activity of IL-2-based immunotherapeutic strategies.
- The results have implications for the treatment of chronic hepatitis B virus infection.

Responses to vaccination and policy implications

- Variations in the responses to HBV vaccination were found in one study to be due to age at vaccination, sex, time interval before study of antibodies and the level set for antibody titre being “protective”.
- Variable modifying the response include sex steroidal hormones, sex chromosomal genes and immune gene polymorphisms; females appeared to have stronger responses than males when vaccinated at ages above one year.
- The findings lead to a proposal to consider 2 mIU/ml as a lower band for considering anti-HBs antibodies as protective, with implications for optimizing vaccination schedules and surveillance of healthcare workers, professionals and medical students.

Impact of vaccination in Europe

- The 53 countries of the WHO European Region have seen major advances in implementing HBV vaccination over 25 years with striking results, with only three countries in central Asia having high prevalence rates and 25, mainly in western Europe with low rates.
- Few countries have done population-based representative serosurveys but several showed much higher of HBsAg prevalence in foreign-born subjects compared with the indigenous populations.
- Policies vary but every country is implementing vaccination. Many have net coverage targets for 3 doses of hepatitis B vaccine, the birth dose, and for hepatitis B screening of pregnant women. Italy and the Netherlands have achieved control of hepatitis B.
- COVID-19 caused coverage of vaccine with three doses to fall, but otherwise regional rates have held steady since 2016.
- A regional strategy for achieving the 2030 elimination targets is being finalized, and the process of validation of target attainment has begun.

Vaccine hesitancy, COVID-19 and responses

- WHO has a working group on vaccine hesitancy, and there are concerns that loss of confidence in vaccines will derail vaccine campaigns generally and decrease coverage of HB vaccine with consequent undermining of progress towards viral hepatitis elimination.
- Recent findings in 19 countries of increased willingness to accept COVID-19 vaccine are encouraging but the requirements and mandates for HBV vaccination are many and varied, presenting complexities Health professionals need to set examples about vaccination but even they report hesitancy. More advocacy and coherent messaging are needed.
- The arrival of COVID-19 caused viral hepatitis outreach programmes in Spain to rethink approaches, favouring the introduction of aspects of these into COVID-19 vaccination and using novel strategies to overcome health system barriers and bringing marginalized populations into contact with health and community services. Success with HCV has the potential for introducing services for HBV; experience is minimal because of the focus on COVID-19, although Albania has introduced a web-based system for linking surveillance and vaccination data.

Group discussion: 1. Based on the available scientific evidence should booster dose for hepatitis B be recommended in general population and/or healthcare professionals, medical students, other risk groups?

- Hepatitis B vaccine prevents disease (rather than infection) and the response of vaccinees to boosters (natural or administered) indicates the presence of cell-mediated immunity to HBV.
- The data from the 35-year follow-up of vaccinated children in Alaska are convincing and encouraging about the success of vaccinating against hepatitis B. They and many other studies confirm the view that for the general population there is no need for a booster dose.
- Certain groups may benefit from screening and boosting as appropriate.

Group discussion, question 1 (continued)

- There was consensus that groups at risk (e.g. healthcare workers and professionals, medical students, injecting drug users, dialysis patients and people living with HIV), especially in low-resource settings, could benefit from being boosted; different strategies could be evaluated – boost all and then test or test and then boost those with anti-HBs concentrations of <10 mIU/ml or antibody-negative.
- Surrogate markers are needed to identify people who need boosting because of low or no anti-HBs antibody levels but without changing policy.

Group discussion, question 1 (continued)

- Given a lack of solid data, a meta-analysis of studies on antibody responses to HB vaccination, including vaccinees those whose antibody concentrations lie in the range 1-10 mIU/ml, and morbidity in vaccine recipients would be useful, together with cost-effectiveness studies of preventing HBV infections through a booster dose and the necessary programmes.
- Cost-effectiveness analyses of preventing HBV infections through programmes of both boosting and screening before boosting would also be valuable for decision-making.
- Door-to-door screening of household contacts also good model: finger stick HBsAg, with links to care or vaccination

Group discussion: 2. Can we continue as we are or are there threats to the high coverage rates and is it necessary to take special initiatives to counter these threats?

- Maintaining high coverage rates of hepatitis B vaccination is crucial, especially given the long-term prevention of liver cirrhosis and hepatocellular carcinoma; raising rates of birth doses needs to be continued in countries where they are low and HBsAg prevalence is high or intermediate.
- With high coverage of young people in many countries, attention could turn to raising average figures and to older people including those with comorbidities, those among whom coverage rates are low, and other groups such as refugees and immigrants from countries with high prevalences.

Group discussion: question 2 (continued)

- The dangers of politicization of vaccines and public health need to be recognized and countered, especially with other challenges than viral hepatitis to public health.
- Growing hesitancy towards vaccines including those against vaccine-preventable diseases and potentially hepatitis B too, exacerbated by reactions to the COVID-19 vaccines, is a major concern.
- Continuing education, communication and advocacy are vital, with messaging that is specific for hepatitis and its long-term and anti-cancer benefits.
- Novel strategies for outreach and overcoming health system barriers need developing
- The elimination goal set for 2030 needs to be kept high on the agenda.