Hepatitis B: the burden

✓ 2 billion people have been globally infected with HBV
✓ Over 350 million chronically infected
✓ An estimated 500,000-700,000 people die each year
✓ 4.5 million new HB cases/year (of whom a quarter progress to CLD)

Source: WHO

Vaccination against Hepatitis B

- Strategies for vaccination initially targeted to groups at increased risk.
- Failure of such policies led WHO to recommend that all countries should introduce universal infant or adolescent (or both) hepatitis B vaccination into their national immunisation programmes by 1997.

Types of Hepatitis B vaccines

I generation  plasma derived (1981)
II generation  yeast-derived (1986), rec-DNA
III generation  - Combined vaccines (HA + HB; hexavalents)
               - preS1-S2 vaccines
               - novel adjuvanted vaccines

Hepatitis B vaccination: immunogenicity

- Several hundred million vaccinations have been administered worldwide with an outstanding record of safety and efficacy.
- Seroprotection rates to anti-HBs are close to 100% in healthy children and ~95% in healthy adults.
- Immunocompromised individuals, the elderly, the obese and heavy smokers may have suboptimal responses.
- Rapid protection (i.e. HCWs exposed to HBV) can be achieved through the adoption of an accelerated schedule (0, 1, 2 and 12 m).
Hepatitis B vaccination: long-term immunogenicity (1)

- Vaccine-induced antibodies are long-lasting (at least 15-20 years).
- Anti-HBs duration is related to the antibody peak level achieved after primary vaccination.
- Antibody declines over time, but clinically significant breakthrough infections are rare.

Hepatitis B vaccination: long-term immunogenicity (2)

- Vaccinees who have lost antibodies over time, usually show a rapid anamnestic response when boosted.
- Immunological memory for HBsAg can outlast the antibody detection thus providing long-term protection.

Hepatitis B vaccination: to boost or not to boost?

- Routine administration of booster doses are not necessary to sustain long-term protection.
- Such conclusions are based on data collected during the past 15-20 years of vaccination.

HBV vaccination: Safety profile (1)

- Vaccination is well-tolerated.
- Local side effects are generally mild and confined to symptoms at the site of injection (i.e. erythema, swelling, induration).
- Systemic reactions (i.e. fatigue, nausea, headache, fever) are uncommon.
- Contraindications: known hypersensitivity to any component of the vaccine or a history of anaphylaxis to a previous dose.

Hepatitis B vaccination: Safety profile (2)

- In 1998 case reports from France raised concern that HB vaccination may lead to new cases or relapses of MS or other demyelinating diseases such as G-B.
- In 2008, the same findings were put forward (Mykaeloff Y, Neurology 2009).
- However, no clear causality link has been established, and WHO stated that there were no reason to change current vaccination policy.

Impact of Hepatitis B mass vaccination in hyperendemic areas: Taiwan

- Annual average incidence (x 10^5) of HCC among children 6-14 yrs (Chang, 1997 and 2004)
- HBsAg prevalence in individuals <20 yrs (Chang, 2004)
Impact of Hepatitis B mass vaccination in hyperendemic areas: **Taiwan**

July 1984: mass vaccination of newborns

Impact of Hepatitis B mass vaccination in hyperendemic areas: **the Gambia**

1986: universal infant vaccination

Impact of Hepatitis B mass vaccination in hyperendemic areas: **Malaysia**

- 1990: universal infant vaccination

Impact of Hepatitis B mass vaccination in hyperendemic areas: **Hawaii**

- 1991: universal infant vaccination

Impact of Hepatitis B mass vaccination in hyperendemic areas: **Alaska**

- 1981: universal vaccination of children
- Sharp decline incidence of acute hepatitis B (next to zero).
- Trend towards decreasing incidence of HCC in subjects <30 years of age.

Hepatitis B vaccination in Italy (Strategies)

- Selective vaccination
  - 1983
  - 1991
- Universal vaccination
- Screening of pregnant women
- Vaccination of high risk groups

Morbidity rate ($x 10^5$ inhabitants) of hepatitis B in Italy, according to age (1990-2009)

Incidence $x 10^5$ in 2009:
- 0-14 aa 0.01
- 15-24 aa 0.5
- >24 aa 1.3
- Total 1

Impact of hepatitis B vaccination in Afragola, a highly endemic area of Southern Italy (Da Villa et al., 2007)

- Age-specific prevalence of HBsAg
- Age-specific prevalence of anti-HBc

Impact of HBV vaccination in Italy

- A generation of children and young people (30 age cohorts) is emerging with practically no markers of HBV infection.

Prevalence of anti-HBc in individuals aged <30 years

Incidence rates of acute hepatitis B and hepatitis Delta

SEIEVA 1990-2006

- Italy’s programme of vaccination has resulted in substantial progress towards the prevention and control of hepatitis B.

World wide impact of hepatitis B vaccination

- Our findings compare well with data reported elsewhere (e.g. Taiwan, the Gambia, Alaska) where the impact of vaccination in terms of reduction in incidence, in carrier rate, and in HBV-related mortality has been impressive.

HBV infections in vaccinees

- Cases of hepatitis B in vaccinated people are very rare and generally confined to those who did not complete the schedule of vaccination properly.
- Breakthrough infections (anti-HBc +, transient ALT↑) have been occasionally observed in successfully vaccinated people.

HBV escape mutants

- Breakthrough infections caused by S gene mutants (G145R) have been reported in babies born to HBsAg carrier mothers (Zanetti, 1988; Carman, 1990).
- Despite concern that these mutants could evade the vaccine-induced immune response and infect vaccinated individuals, at present they do not pose a real public health threat.
**Conclusions (1)**

- Safe and effective vaccines have been available since the early 80’s, offering the opportunity to exert substantial prevention and control of the disease and its long-term severe consequences on a global scale.

- Globally, a remarkable significant progress in implementation of vaccination against HB has been achieved in recent years, but much remains to be done to meet the WHO goal of controlling HB in the community at large.

**Conclusions (2)**

- At present most of the countries that are not yet covered by vaccination are those economically underprivileged.

- Efforts should be undertaken so as to override social and economic barriers hampering the introduction of HB vaccination in countries with low resources, which are those with the highest endemicity.

- Migration and travels from and to highly endemic countries may increase the risk of exposure to the virus requiring a global strategy to make control and elimination of HBV feasible.