Prevention of Hepatitis B

SIAVASH MANSOURI, MD.
N.I.O.C. HOSPITAL
HBV: A Global Problem

- Hepatitis B infection is of major global importance
  - large pool of patients
  - serious nature of disease sequelae
  - significant economic burden

- Urgent actions are needed to address the problem
  - immunisation programmes
  - therapeutic intervention for chronically-infected patients
  - education initiatives to prevent transmission/ infection
Schematic Representation of HBV

DNA polymerase

Inner protein core (HBcAg)

HBV DNA

Outer lipid envelope containing HB surface antigen

HBsAg

HBeAg
“The primary objective of hepatitis B immunisation is to prevent chronic HBV infections, which result in chronic liver disease later in life. By preventing chronic HBV infections, the major reservoir for transmission of new infections is also reduced.”
Vaccination (2)

- Stimulates the body to produce immunogenic levels of anti-HBs
- Confers immunity to HBV in 95% of recipients
- Prevents development of chronic hepatitis B and associated liver disease
- Reduces HBV transmission rates
Vaccination (3)

- Vaccination
  - WHO recommends that HBV vaccination be included in national immunisation programmes
  - Universal immunisation programmes have not been adopted in many countries
- For those chronically infected with HBV, treatment is the sole option to prevent the devastating sequelae of HBV infection
Prevention of Hepatitis B

• 1-Primary Prevention
• 2-Secondary Prevention
Vaccine Indications

- HBIG and HB vaccine to infants of HBsAg+ mothers
- Routine vaccination of infants and adolescents
- Catch-up vaccination of children
- Vaccination of adults at risk of infection
- Positive HBC ab in non endemic area
Indications in Adults

- Sexual and household contacts of carriers
- Sexually active individuals with multiple sex partners and men who have sex with men
- Injection drug users
- Hemodialysis patients and patients under immune suppressive drugs
- Recipients of clotting factor concentrates
- Families of adoptees from endemic areas
- Diabetic patient (19-59)-chronic elevated LFT
<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Age Group</th>
<th>Dose (ug)</th>
<th>Volume (ml)</th>
<th># Doses</th>
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<tbody>
<tr>
<td><strong>Engerix-B</strong></td>
<td>0-19 yr</td>
<td>10</td>
<td>0.5</td>
<td>3 (mo 0,1,6)</td>
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<tr>
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<td>40</td>
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<tr>
<td></td>
<td>(Optional 2-dose)</td>
<td>11-15 yr</td>
<td>10</td>
<td>2 (mo 0,4-6)</td>
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*Special Formulation
Safety

- Most common adverse event -- soreness and erythema at the injection site
- Systemic symptoms -- transient low-grade fever, headache, malaise and myalgia in ~10%
HBV - Vaccine

Serious adverse events of HBV vaccines

Proven relationship
- Anaphylaxis ~ 1 in 600,000 doses

No proven relationship
- Arthritis
- Demyelinating CNS diseases
- Sudden Infant Death Syndrome
- Autism
# Dose schedule of HBV vaccine

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Factors that Reduce Vaccine Efficacy

Host Factors

- **Age:**
  - ~95% response in children
  - ~85% response in adults > 40 years
  - ~70% response in adults > 60 years
- Immunosuppression, chronic medical illness
- Smoking, obesity
- HLA haplotype

Other factors

- Inadvertent freezing of vaccines
- Inadvertent SC injections (gluteal)
- Incomplete vaccination series
### Immunogenicity and efficacy of HBV vaccines

#### Vaccine Efficacy

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<th>Definition of protective response</th>
<th>Anti-HBs &gt;10 IU/L</th>
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<td>Prevention of infection</td>
<td></td>
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<tr>
<td>- Pre-exposure</td>
<td>Immunocompetent adults and children &gt;95%</td>
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<tr>
<td>- Post-exposure</td>
<td>Infants born to HBsAg + mothers</td>
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- Vaccine alone: 65%-95%
- Vaccine + HBIG: 85%-95%
Management of non-responders

Primary series

No response

Repeat 3-dose series

5-10%

Respons e

50% - 75%

Immunocompetent adults

No response

Test for HBsAg
Pre-vaccination Testing

Not recommended for

- Routine infant, childhood or adolescent vaccination
- Worker at occupational risk

May be cost-effective in adult populations with

- HBsAg carrier rate > 2%, or
- Overall infection (anti-HBc+) rate > 30%
HBV - Vaccine

Neonates of HBsAg+ Mothers

Vaccine

HBIG

Birth

0 1 6

Months
HBV S escape mutants
New Developments

**Improving delivery**
- Combining vaccines - e.g. hepatitis A and B vaccine
- Incorporating HB vaccine into Expanded Program of Immunization
- Developing oral vaccines

**Enhancing response**
- Use of more potent adjuvants
- Development of DNA vaccines
- Incorporation of pre-S antigens
Long-term efficacy of hepatitis B vaccination in healthcare workers of Oil Company Hospital, Tehran, Iran (1989–2005)

• Seyed-Moayed Alaviana, Siavash Mansouri, Mehdi Abouzaria, Shervin Assarib, Mirmohsen Sharifi Bonabb and Seyed-Mohammad Miria
Long-term efficacy of hepatitis B vaccination in healthcare workers of Oil Company Hospital, Tehran, Iran (1989–2005)

• This study was conducted to evaluate the 16-year efficacy of hepatitis B virus (HBV) vaccine in healthcare workers of Oil Company Hospital, Tehran, Iran.
Long-term efficacy of hepatitis B vaccination in healthcare workers of Oil Company Hospital, Tehran, Iran (1989–2005)

• Method:
• After explaining the objectives of the study and obtaining informed written consent, 200 consecutive healthcare workers of Oil Company Hospital who had not received HBV vaccine previously were enrolled in the study in 1989.
Long-term efficacy of hepatitis B vaccination in healthcare workers of Oil Company Hospital, Tehran, Iran (1989–2005)

1-questionnaire
2-blood sample was taken before vaccination and
3- HBV markers HBsAg, HBsAb, HBcAb, HBeAb and HBe AG were tested
4-positive HBV marker and positive HCV Ab or HIV were excluded from study
all participants were inoculated with three doses of 20 mg hepatitis B recombinant vaccine (Recombinant HB, Ho¨chst,Belgium) at intervals of 0, 1, and 6 months.
Routine blood counts and liver function tests (aminotransferase activities) were also performed for all participants to establish the fact that the healthcare workers were otherwise healthy.
Sixteen years later, in 2005: all individuals were reevaluated. All HBV markers were tested with the same method.
The levels of anti-HBsAb above 10 IU/l were defined as protective. The data were analyzed using w2 and Student’s t-test statistical methods. The analysis was performed using the SPSS 15.0 software package (SPSS Inc, Chicago, Illinois, USA), and P value of less than 0.05 was considered significant.
Long-term efficacy of hepatitis B vaccination in healthcare workers of Oil Company Hospital, Tehran, Iran (1989–2005)

• RESULT:

• Of the 200 participants who enrolled in this study in 1989, 87 (43.5%) participants were lost to follow-up and 30 (15%) participants were excluded owing to anti-HBcAb above 10 IU/l (free of clinical hepatitis and negative for HBsAg).
Of the remaining 83 participants, 38 (45%) were male and 45 (55%) were female. None of the participants were HBsAg positive in either 1989 or 2005.
Protective levels of anti-HBsAb were absent in all participants in 1989, but present in 67 (80.7%) participants in 2005 (P<0.001).
HBsAb titer after vaccination was significantly higher in female than in male (P=0.01). and the lowest protective titer was 12 IU/l.

The mean HBsAb titer after vaccination was not significantly different regarding participants’ jobs or occupational wards.
Long-term efficacy of hepatitis B vaccination in healthcare workers of Oil Company Hospital, Tehran, Iran (1989–2005)

The results obtained in this study are in agreement with the results of other studies done in Iran and also in other countries.
80.7% of vaccinees had protective levels of antibody in their sera even after 15 years. The mean antibody titer after 16 years was in the range which means maintenance of immunological memory for at least 10–15 years.
Although all anti-HBc positive participants were free of clinical hepatitis and were negative for HBsAg, hepatitis vaccination was proved to be highly effective in preventing clinically significant infection and chronic carrier status up to 16 years after the primary vaccination.
No one will manufacture a lock without a key.

Similarly God won't give problems without solutions.
Every successful person has a painful story. Every painful story has a successful ending.

Accept the pain and get ready for success.