Beyond 20 years of universal vaccination in Italy: achievements and the way forward

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Hepatitis B vaccination in Italy (policy)

Selective vaccination of high risk groups

- Universal vaccination of infants and adolescents (restricted to the first 12 years of vaccination)
- Screening of pregnant women
- Vaccination of high risk groups

1983 February
1991 May, 27
HBV vaccination in Italy
Current status

- Over 95% coverage rate
- Over 21 million individuals (< 34 years) vaccinated
Hepatitis B vaccination: safety & immunogenicity

- Good safety profile and highly immunogenic.

- Seroprotection rates to anti-HBs close to 95-100 % in healthy vaccinees.

- Antibody declines over time, but immunological memory for HBsAg can outlast the antibody detection providing long-term protection.

- Vaccinees who lost Ab usually show a rapid and strong anamnestic response when boosted or exposed to HBV.
The issue of hexavalent vaccines

- 2000: two Hexavalent vaccines (Hexavac® and Infanrix Hexa®) licensed in EU
- 2005: Hexavac suspended
- 10 million doses of Hexavac distributed globally
- ~1.2 million children vaccinated in Italy with Hexavac
Concentration of anti-HBs in 1540 children primed with Hexavac or Infanrix Hexa, 5 years earlier

Hexavac  
- n = 831  
- GMC 4.5 mIU/ml

Infanrix  
- n = 709  
- GMC 61.3 mIU/ml

- 512/831 61.6% (≤10 mIU/ml)
- 319/831 38.4% (>10 mIU/ml)
- 119/709 16.8% (≤10 mIU/ml)
- 590/709 83.2% (>10 mIU/ml)

* p<0.0001
Post-booster anti-HBs concentrations

- Hexavac:
  - n = 444
  - MGT 448.7 mIU/ml
  - 41/549 (7.5%)
  - 508/549 (92.5%)

- Infanrix:
  - n = 105
  - MGT 484.9 mIU/ml
  - 35/444 (7.9%)
  - 409/444 (92.1%)

* p=0.4
Conclusions

- No need for booster injections of vaccine to sustain immunity in children vaccinated in infancy with hexavalent vaccines.
- This observation was specific to the 5-year checkpoint.
- A follow up study - at 10 years distance from priming - is currently in progress.

*Lancet Infect Dis 2010, Vaccine 2012*
Morbidity rate (× 10^5 inhabitants) of hepatitis B in Italy, according to age (1990-2013)

Incidence × 10^5 in 2013:
- 0-14: 0.1
- 15-24: 0.3
- >24: 1.1
- Total: 0.9

Age group:
- 0-14
- 15-24
- 25+
- Total
Impact of hepatitis B vaccination in a highly endemic area of southern Italy (Afragola) (Vaccine, 2007)

Age-specific prevalence of HBsAg

6-14 yrs | 15-20 yrs | >25-58 yrs | Total
---|---|---|---
13.4% | 0.9% | | |

Age-specific prevalence of anti-HBc

6-14 yrs | 15-20 yrs | >25-58 yrs | Total
---|---|---|---
| | | | 66.9%
| | | | 7.6%
Impact of HBV vaccination in Italy

- A generation of children and young people is emerging with at present practically no markers of HBV infection.


Prevalence of anti-HBc in recruits

16.8% 5.8% <1%

Pasquini, D’Amelio et al.
Incidence rates of acute hepatitis B and hepatitis Delta
SEIEVA 1987-2010

Hepatitis B: cases x 100,000
Hepatitis Delta: cases x 1,000,000
Acute hepatitis B in vaccinated people in Italy (SEIEVA, 2001-2012)

5,671 cases

5,156 (91%) vaccination status known

5,000 (97%) subjects not vaccinated

156 (3%) subjects vaccinated
  mean age 35.9 yrs
  67.7% males

325 (6.5%) escaped mandatory vaccination

86% Italians
14% Immigrants

86% Italians
14% Immigrants
Hepatitis B in vaccinated people in Italy (SEIEVA, 2001-2012)

- 37 cases vaccinated properly
- Molecular characterization:
  - 14/21 wild type
  - 7/21 escape mutants
- In Italy, estimated 3-4 vaccination failures annually
- Correctly vaccinated: 156 cases of hepatitis B in vaccinated people (24%)

In Italy, estimated 3-4 vaccination failures annually
Changing patterns of hepatitis B in Italy

Conclusions

Hepatitis B has progressively declined during the last 20 years as a result of:

- Social, behavioural, and demographic changes.
- General improvements in the standards of living and hygiene.
- Introduction of public health measures such as refinement in blood screening, use of universal precautions in medical settings and implementation of vaccination programmes.
HBV infections in vaccinees

✔️ Cases of hepatitis B in vaccinated people are very rare and generally confined to those who did not complete schedule of vaccination properly.

✔️ Infections of vaccinated people with S-gene mutants (G145R) are rare and do not pose a public health threat.
Italy versus other countries

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

- 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 vaccination in Italy: what the future holds

• Maintaining vaccination of infants.
• HBsAg testing of pregnant women.
• Increasing HB vaccination coverage in high-risk groups, including households of HBsAg carriers, immigrants and travellers to and from highly endemic countries.