Objectives of the presentation

- Review progress in the prevention and control of hepatitis B in Italy, 12 years after the implementation of universal vaccination.

- Present a recent study on the duration of immunity and on the need of a booster policy to mantain lifelong protection.

Burden of hepatitis B in Italy in the early 1980s

- 1.5 million chronic carriers
- 9000 deaths per year due to HBV-related diseases
- Annual incidence for acute hepatitis around 12 per 10^5 (nearly 8000 new cases per year)
- Number of infections per year at least 5-10 times the number of reported cases (40.000-80.000)
- Highest attack rate (41 x 10^5) for acute hepatitis B observed in people 15-24 old, reflecting risk behaviours like i.v. drug use and multiple sexual partners
- Wide spread of hepatitis delta, especially among IVDUs

Italian strategy for hepatitis B vaccination

Rationale:

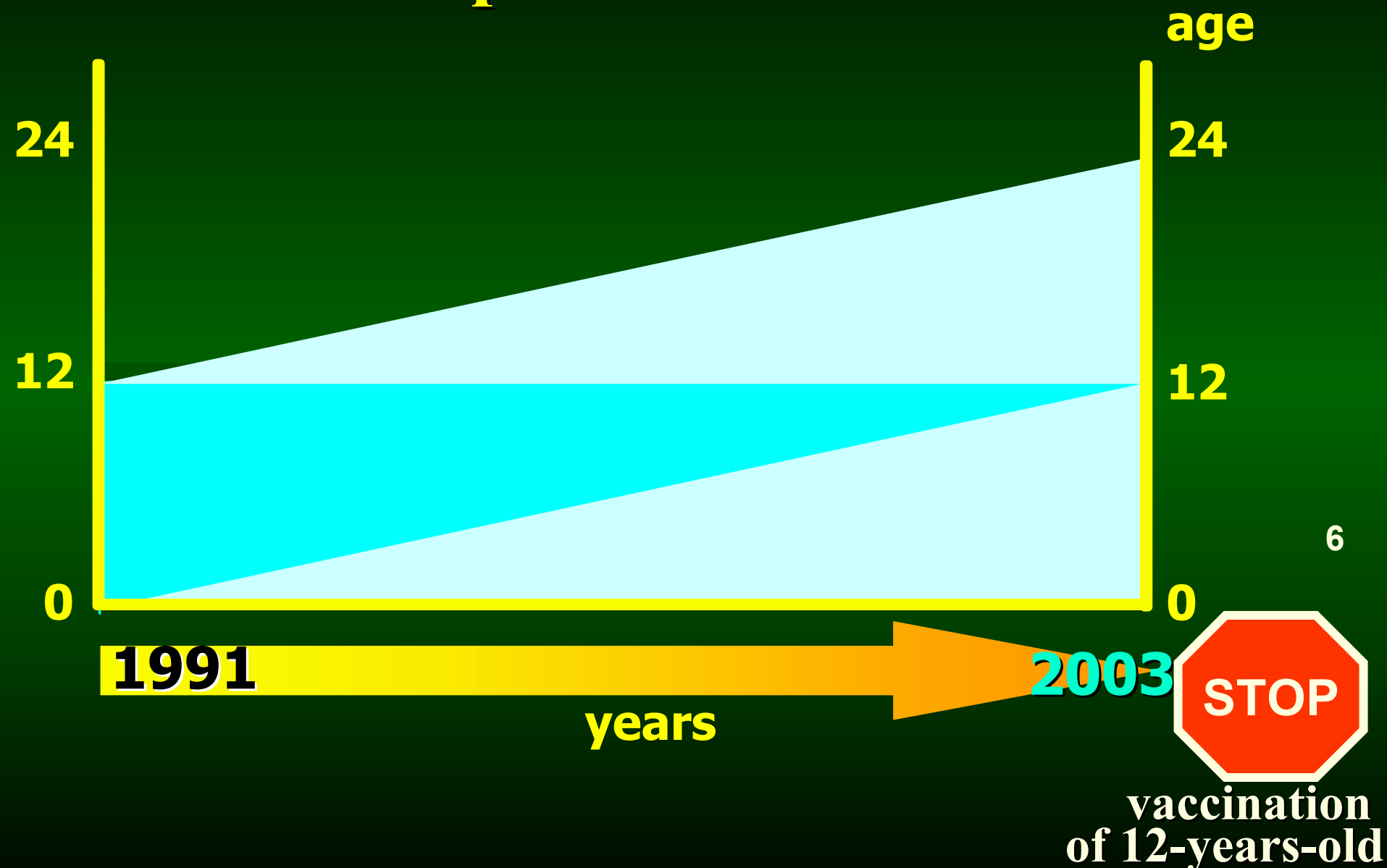
- **To protect children from HBV infection which can result in high rates of carrier state and CLD**
- **To protect adolescents prior to the exposure to HBV by the sexual route or through drug use**
- **To control the disease within a short period of time**
- **To control and prevent hepatitis Delta**

Universal hepatitis B vaccination programme in Italy

Law n° 165 of May 27, 1991 established:

- Compulsory vaccination of infants and of adolescents during their 12th year of age (end of adolescent programme: 2003)
- Mandatory HBsAg screening for all pregnant women during the last 3 months of pregnancy
- Active offer of free-of-charge vaccination to subjects belonging to categories at risk

Italian strategy for hepatitis B vaccination



Coverage with 3 doses of hepatitis B vaccine (95%confidence intervals) at 24 months of age in 20 Italian Regions, 1998

(Salmaso S. et al., Bull. WHO, 1999)

Abruzzo 94.8% (91.4-98.2)	Basilicata 99.1% (97.8-100)	Calabria 94.8% (91.7-97.9)
Campania 97.6% (81.3-93.9)	Emilia R. 97.6% (95.7-99.6)	Friuli V.G 97.6% (95.7-99.6)
Liguria 97.6% (95.3-100)	Lombardia 97.6%(95.7-99.6)	Marche 94.8% (90.4-99.1)
Molise 89.1% (82.0-96.3)	Bolzano 85.6% (80.6-90.7)	Trento 98.1% (96.3-99.9)
Piemonte 98.6% (95.8-100)	Puglia 93.0% (89.1-96.9)	Sardegna 95.2% (92.4-98.0)
Sicilia 91.1% (86.1-96.1)	Toscana 95.2% (92.4-98.0)	Umbria 98.6% (97.0-100)
Val d'Aosta 100	Veneto 97.6% (95.7-99.6)	

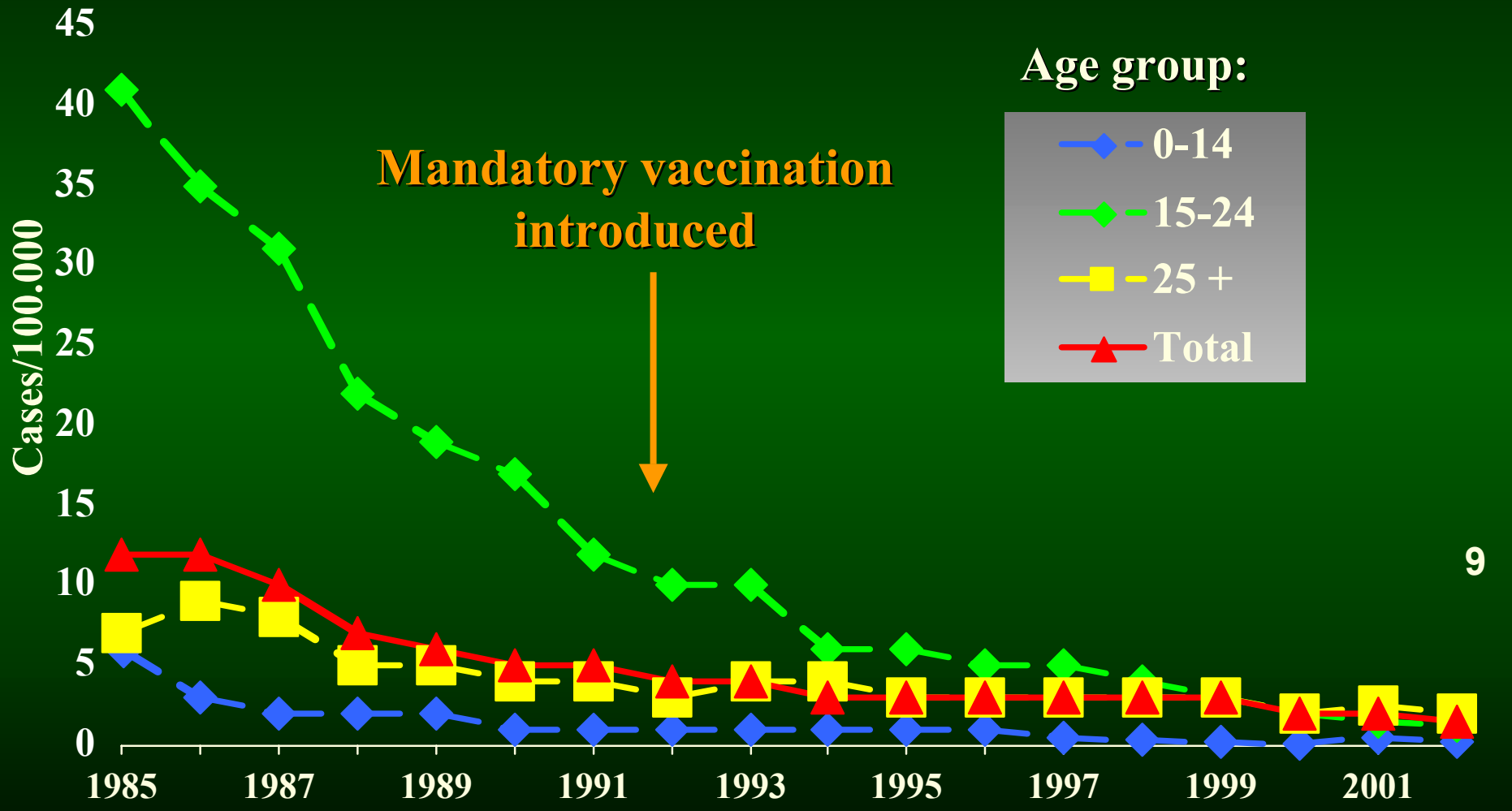
Coverage of infants and adolescents with 3 doses of hepatitis B vaccine in Tuscany, central Italy

(3.5 million inhabitants)

(Bonanni P. et al, Pediatr Infect Dis J 1999; 18: 677-82)

	Infants			Adolescents		
Year	Eligible	Vaccinated	%	Eligible	Vaccinated	%
1992	1111	1061	95.5	1560	1540	98.7
1993	2122	1922	90.5	1594	1512	94.8
1994	2109	2053	97.3	1932	1812	93.7
1995	1995	1935	97.0	2055	1968	95.7
1996	2060	1943	94.3	2166	2065	95.3
1997	1767	1692	95.8	1793	1702	94.9
TOTAL	11164	10606	95.0	11100	10599	95.4

Morbidity rate (x 10^5 inhabitants) of hepatitis B in Italy, by age (1985-2002)



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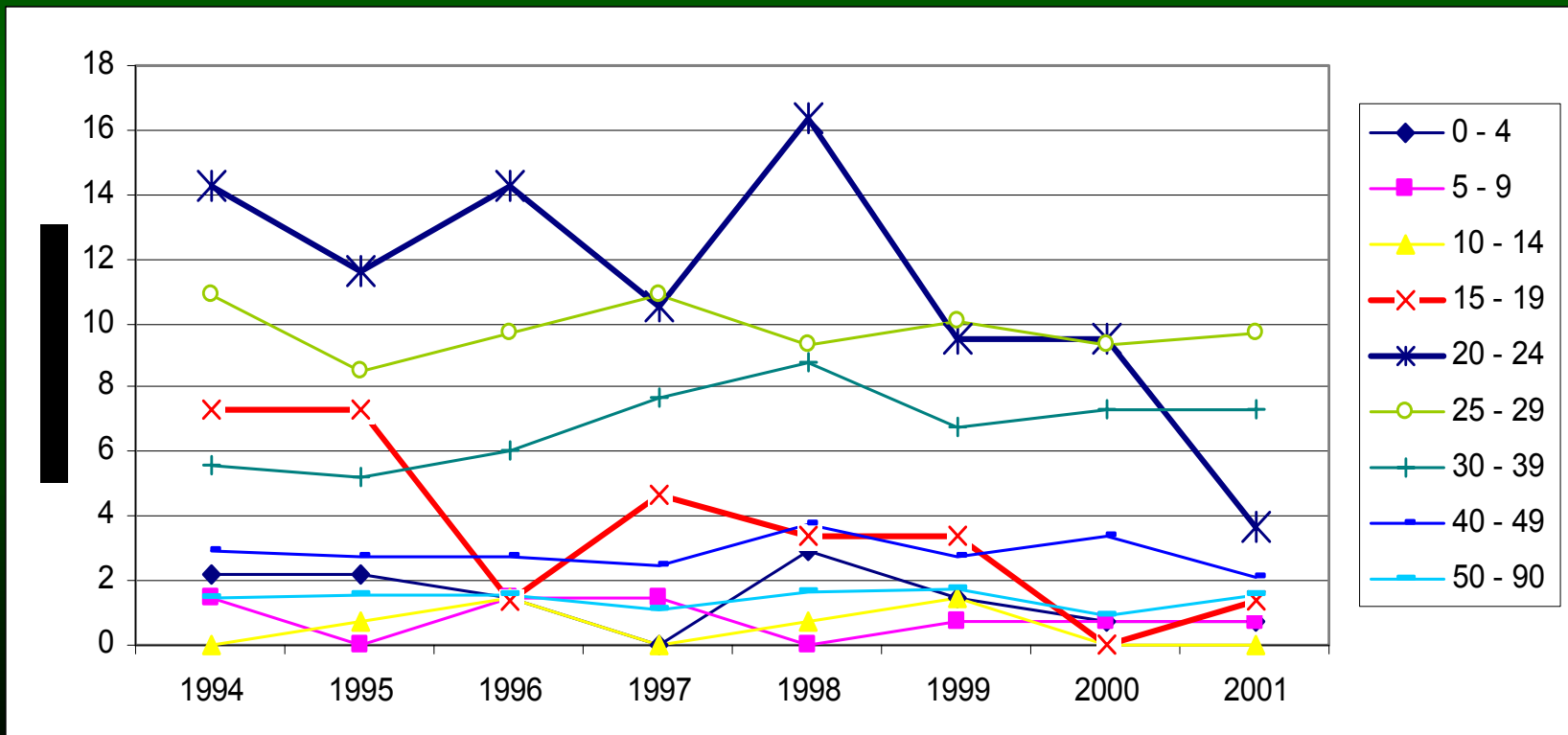
Study on the incidence of hepatitis B in Tuscany, Central Italy, 1994-2001

- Data on notifications of acute hepatitis B and information on disease cases were collected thanks to the collaboration of Regional Health Authorities
- Vaccination status, number and time of possible doses administered were collected for each notified case of acute disease
- Modifications of incidence were calculated by 5-year age groups between 0 and 29 years, 10-year age groups between 30 and 49 years, and globally over 50 years of age

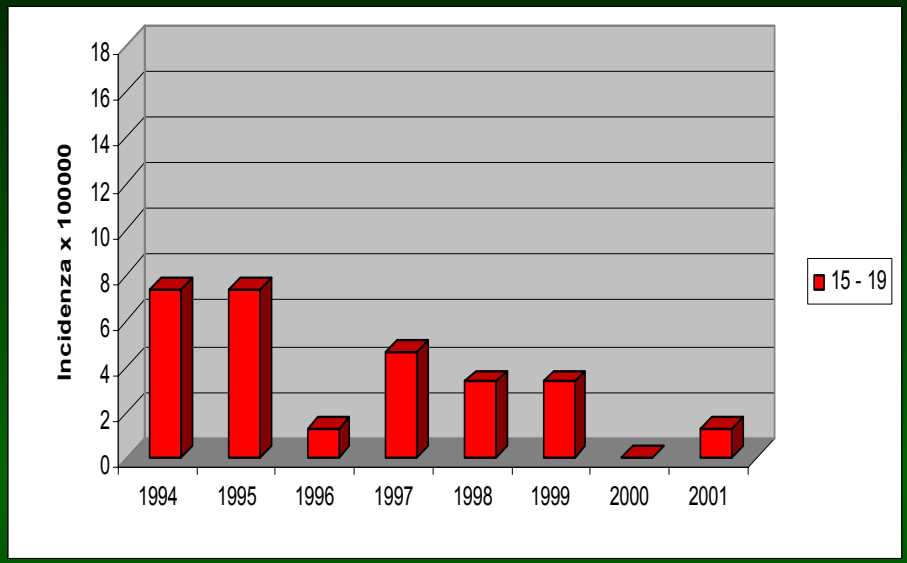
Results

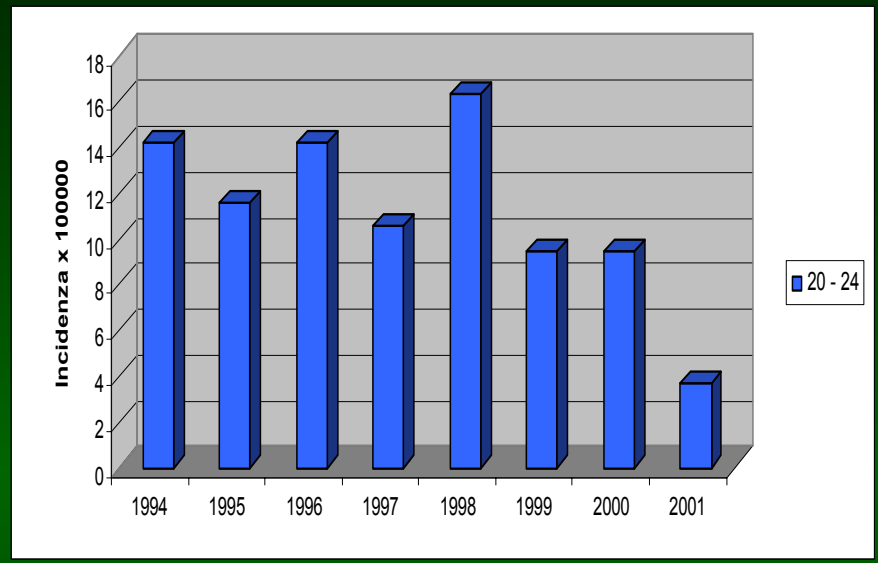
- 1032 cases of acute hepatitis B were notified in Tuscany from 1994 to 2001 (average yearly incidence: 3,7/100000)
- From 1994 to 2001, the incidence in the 20-24 year age group turned from 14,3 to 3,7/100000; in the 15-19 year age group it declined from 7,3 to 1,3/100000

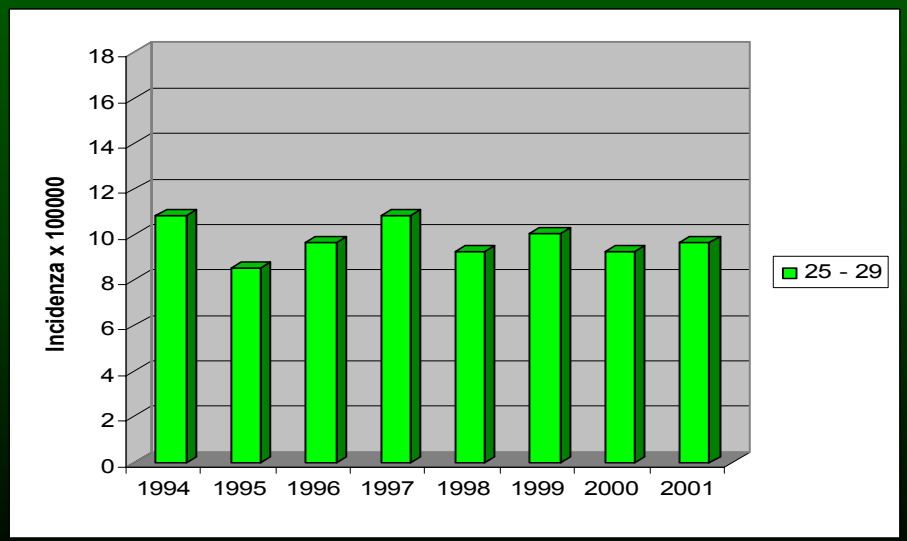


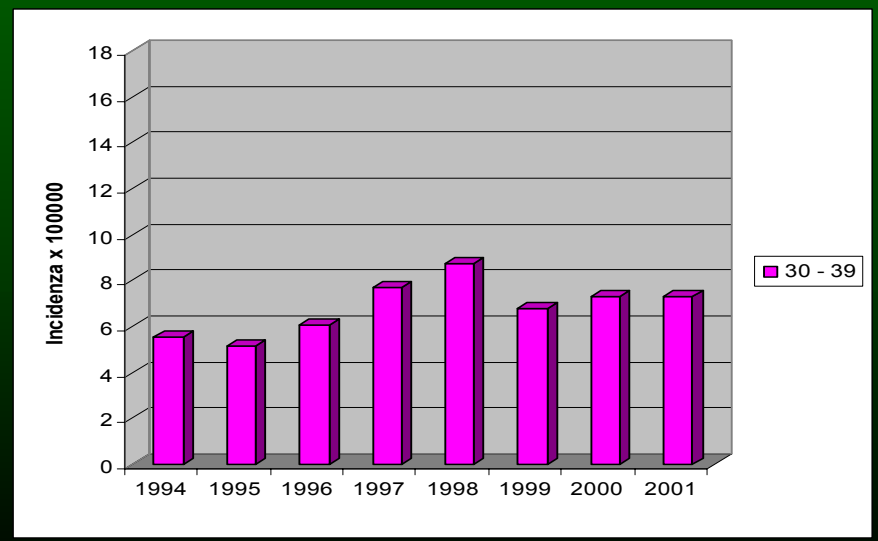
Incidence of acute hepatitis B in selected age groups in Tuscany, Central Italy (1994-2001)

(Bonanni et al., Vaccine 2003; 21:685-691)









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Vaccine 21 (2003) 685–691

Vaccine

www.elsevier.com/locate/vaccine

Impact of universal vaccination programmes on the epidemiology of hepatitis B: 10 years of experience in Italy

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A seroepidemiological study on 394 blood samples collected in Tuscany showed:

- **The absence of HBsAg positive subjects up to 22 years of age**
- **A prevalence of anti-HBc positive subjects of 0.3% in cohorts interested by mandatory vaccination and of 6.6% in those not included in the programme (statistically significant difference $\chi^2 = 15,2$ p=0,0001).**

Epidemiological impact of universal hepatitis B vaccination in a hyperendemic area (Afragola, southern Italy)

(Da Villa G. et al., Res Virol 1998)

- Pilot project of universal hepatitis B vaccination introduced in 1983
- Incidence of acute hepatitis B before vaccination: 63/100,000
- Anti-HBc and HBsAg prevalence rates: 66.9% and 13.4%
- In 1997 (after 15 years of universal infant immunization), the incidence had dropped to 3/1000□,000 population
- Anti-HBc in 1997: 34.2%; HBsAg in 1997: 3.7% (change from 6.8% to 0.7% in young children and adolescents)
- HBV was involved in 48% of chronic liver pathologies in 1982, but only in 18% in 1997

Hepatitis B: the current epidemiological situation in Italy

- about 500.000 HBsAg carriers
- HBV infections still occur in unvaccinated people

due to: injecting drugs

sexual exposure

nosocomial

transfusion
(risk extremely low)

Hepatitis B vaccination: persistence of immunity

- How long does immunity last?
- Will vaccinated babies maintain immunity until the time when risk behaviour may be expected?
- Is there a need for booster vaccination(s) to sustain immunity?

Study population (1)

1212 children* **(50.5%M, 49.5%F)**
vaccinated when infants

Year of vaccination:
1992 (69.9%) 1993 (30.1%)
Mean age (at enrollement):
10.9 years
North **30.7%** ***South*** **69.3%**

* **all born to HBsAg - mother**

Study population (2)

521 Italian recruits

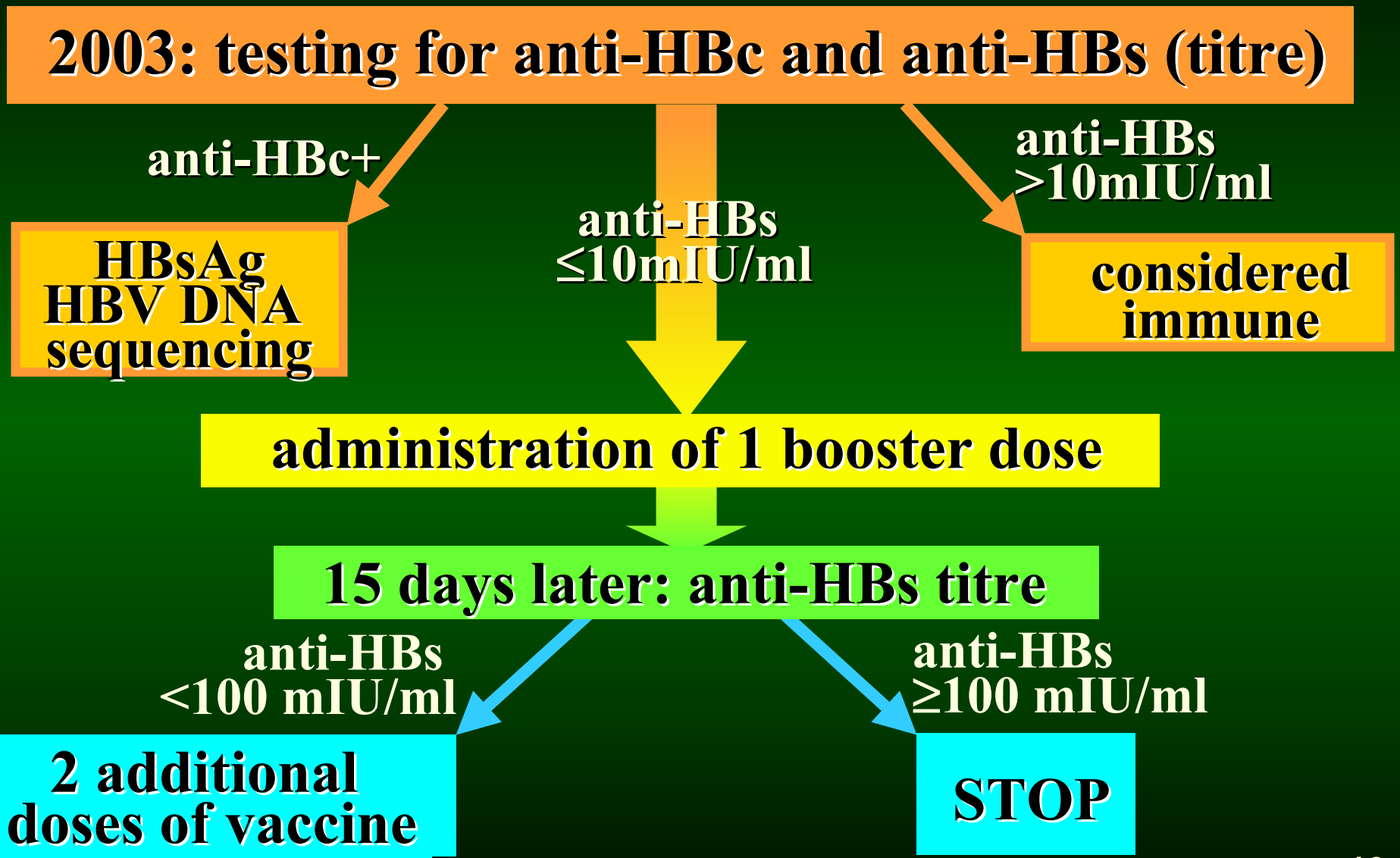
vaccinated at 12 years of age

Years of vaccination: **1992-93**

Mean age (at enrollment): **21.6 years**

North **25.5%** ***South*** **74.5%**

Methodology



Conclusions (1)

- Coverage with hepatitis B vaccination in infants and adolescents is on average >90%, and exceeds 95% in many areas of Italy
- Surveillance on acute hepatitis B cases consistently shows a decline of notifications, especially in the 15-24 years age group
- Data from Tuscany and from the rest of Italy show the virtual absence of acute HB cases in subjects belonging to compulsorily vaccinated cohorts who completed the immunization course
- Long-term surveillance on children born to HBsAg positive mothers shows the occurrence of a very limited number of asymptomatic infections in vaccinees. At present, mutant viruses do not pose a threat to universal vaccination programmes in the country

Conclusions (2)

- Sero-epidemiological data on anonymous sera confirm the high level of protection in the cohorts subject to mandatory vaccination
- The steady incidence in older age groups, and the demonstration of the role of sexual and iatrogenic exposures (Stroffolini et al., J Hepatol 2000; 33: 980-985) stress the importance to complement routine immunization with non-immunological preventive measures
- A study on persistence of immunity 12 years after implementation of universal vaccination indicates that up to now no booster dose is needed to reinforce protection
- The results presented here consistently demonstrate the deep impact 'on the field' of the first universal hepatitis B vaccination programme implemented in an industrialized country