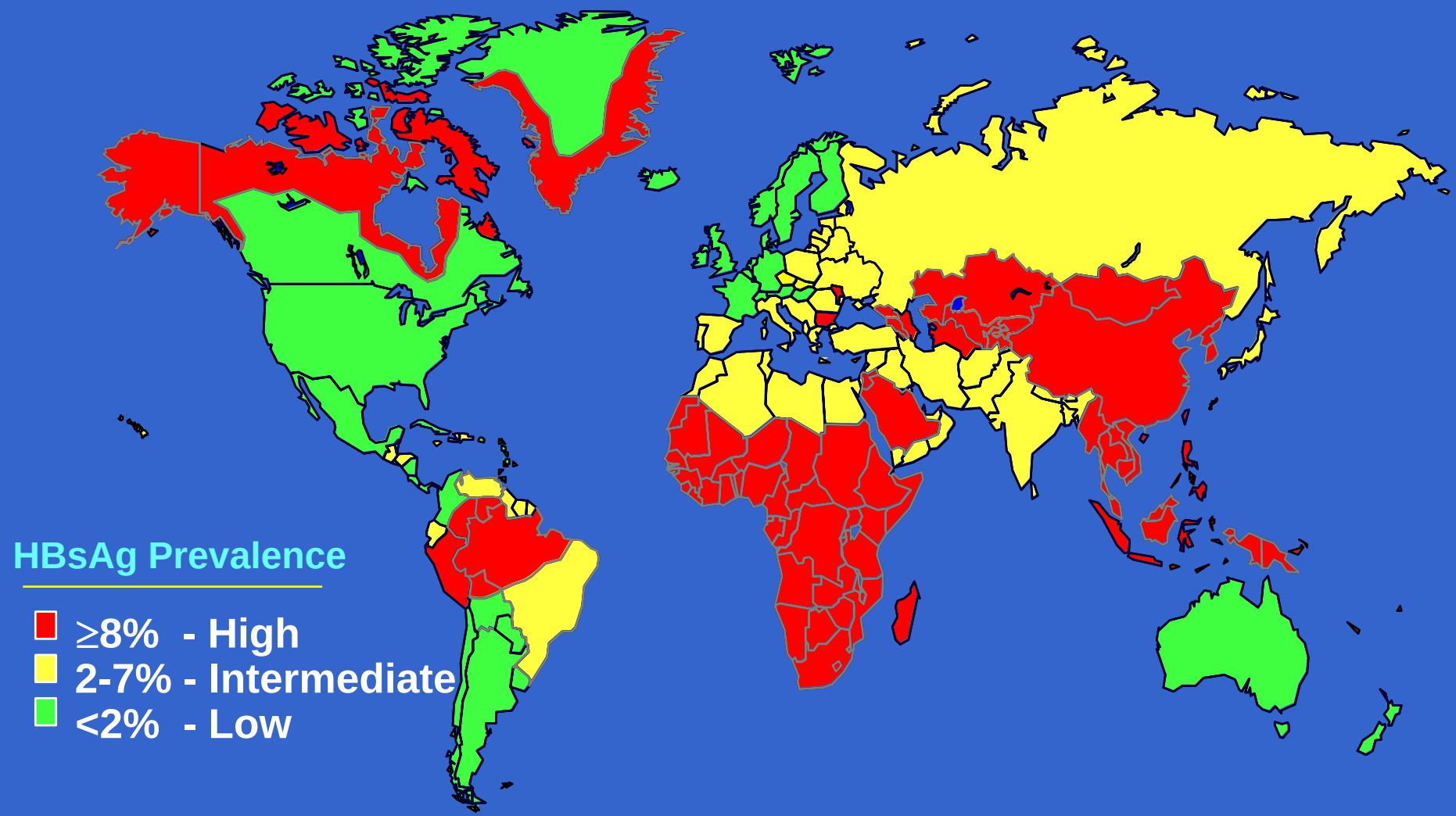
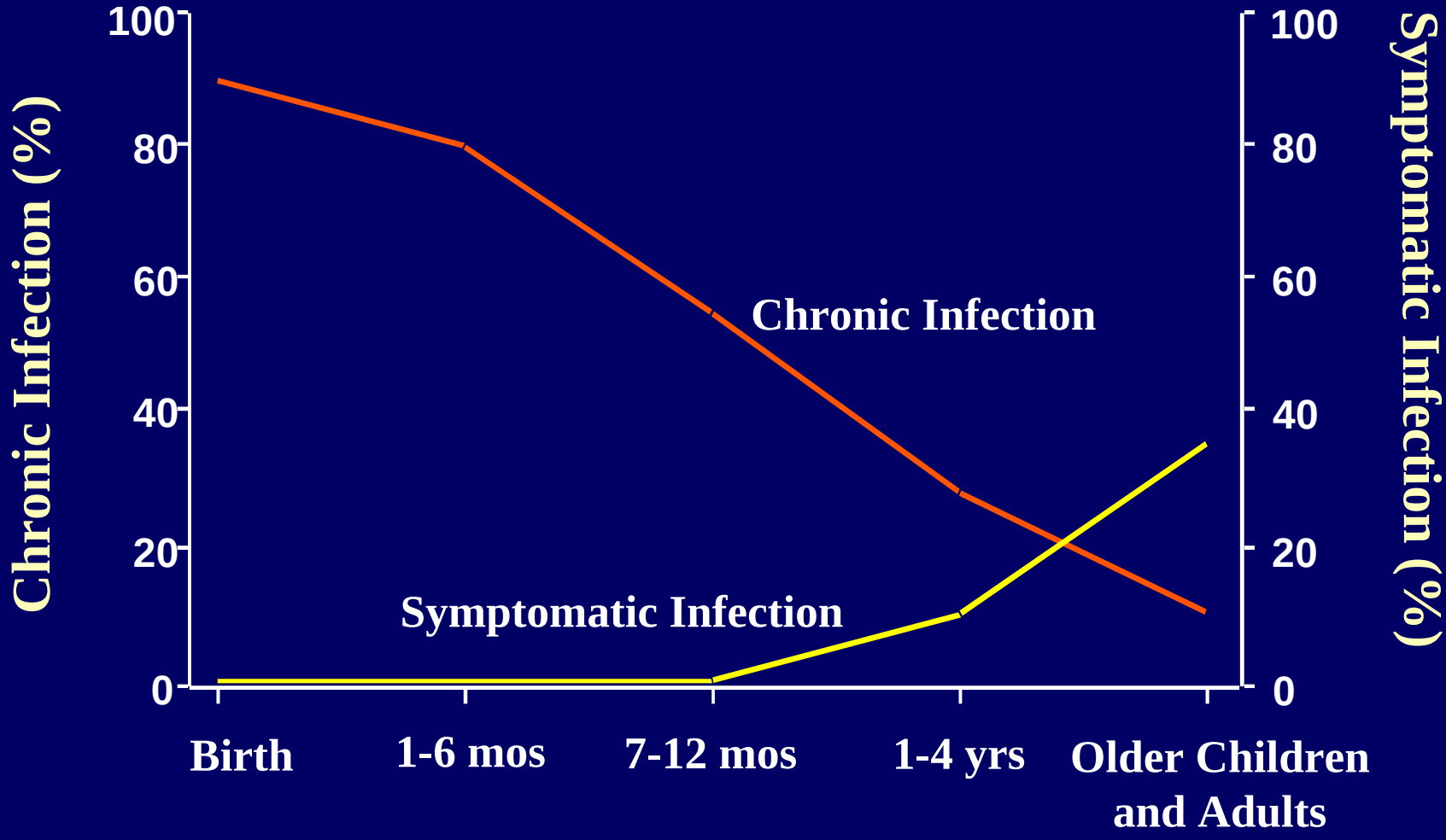
Center of Excellence in Viral Hepatitis Research

Are immunogenicity and protective efficacy of hepatitis B vaccine related to different administration schedules?

Geographic Distribution of Chronic HBV Infection



Outcome of HBV Infection by Age at Infection



Edmunds WJ, *et al*. Proc Biol Sci 1993;253:197-201.

Infant of HBsAg + /HBeAg + mother

The risk for chronic HBV infection is 70%-90% by age 6 months in the absence of postexposure immunoprophylaxis

Okada K, *et al*. N Engl J Med 1976;294:746-9.
Beasley RP, *et al*. Am J Epidemiol 1977;105:94-8.
Wong VC, *et al*. Lancet 1984;1(8383):921-6.

Infant of HBsAg + /HBeAg - mother

The risk for chronic infection is <10% in the absence of postexposure immunoprophylaxis

Stevens CE, *et al*. J Med Virol 1979;3:237-41.

Perinatal HBV transmission is responsible for 35–40% of HBV infections every year worldwide

Ghendon Y. J Virol Methods 1987;17:69-79.

Hepatitis B vaccination Thailand Experience

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Hepatitis B immunization program in Thailand

1988

- Demonstrate methods of incorporating HB vaccine into EPI

- Sites: 2 provinces

- Chiengmai

- Chonburi

1992

Universal HB vaccination

Thailand EPI

At birth	HB1, BCG
2 months	OPV1, DPT1, HB2
4 months	OPV2, DPT2
6 months	OPV3, DPT3, HB3
9-12 months	Measles or MMR
18 months	OPV4, DPT4, JE1 & 2 (2 weeks apart, booster 1 yr after)
4-6 years	OPV5, DPT5, MMR

Efficacy of HB vaccine in infants of HBeAg + mothers (n=263)

Group	Vaccine (mo)	HBIG	Protective efficacy
1	0,1,2,12	-	94.8%
2	0,1,2,12	+	97.6%
3	0,1,6	-	92.2%
4	0,1,6	+	100%

Poovorawan Y, *et al*. Pediatr Infect Dis J 1992;11:816-21.

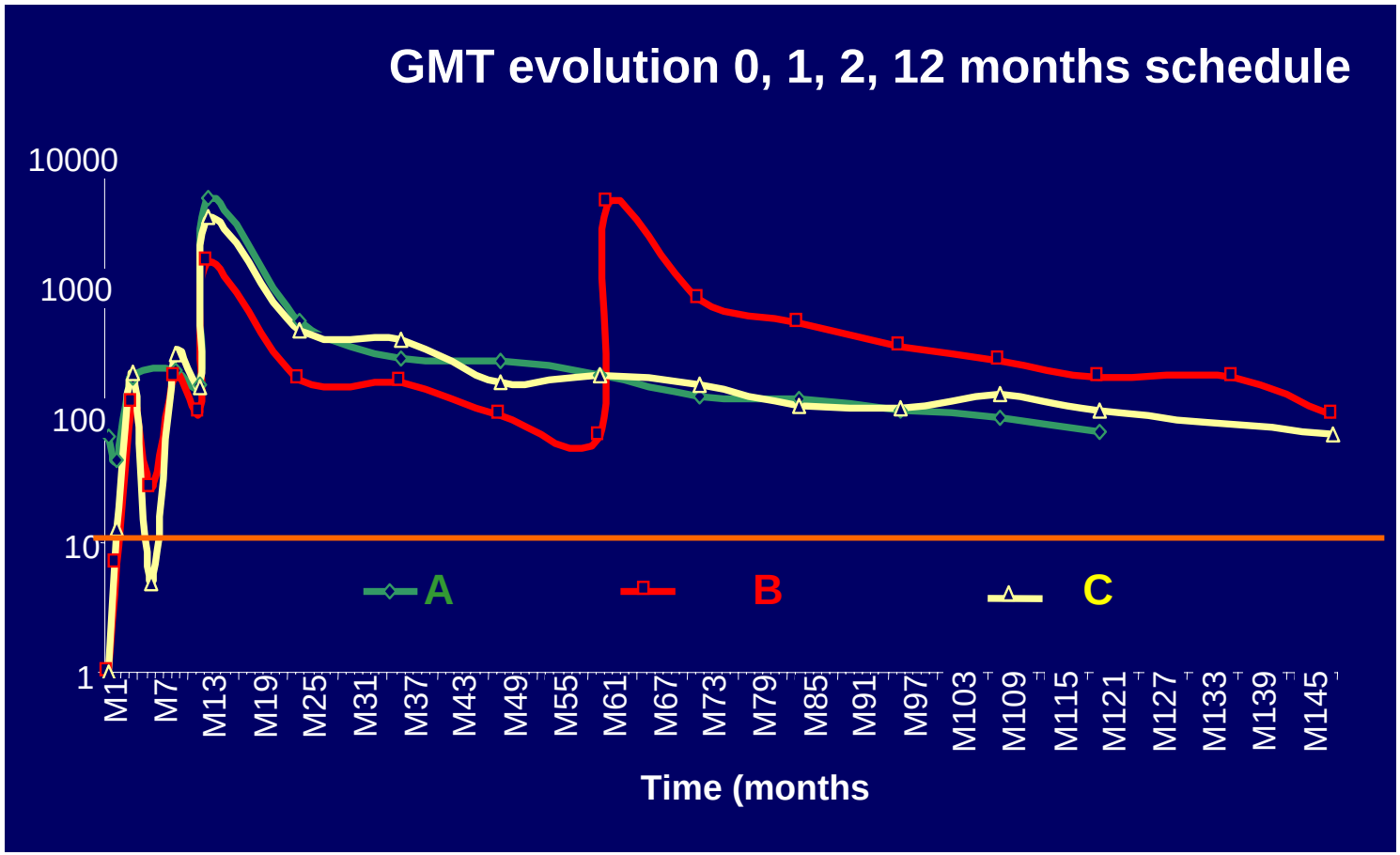
Immunogenicity of HB vaccine in infants of HBeAg + mothers (n=263)

Group	GMT (mIU/ml)		No. with anti-HBs≥10 mIU/ml	
	mo 12	mo 24	mo 12	mo 24
1	165	380	98.2%	97.9%
2	161	523	96.9%	100%
3	317	80	100%	91.4%
4	180	67	98.3%	94.9%

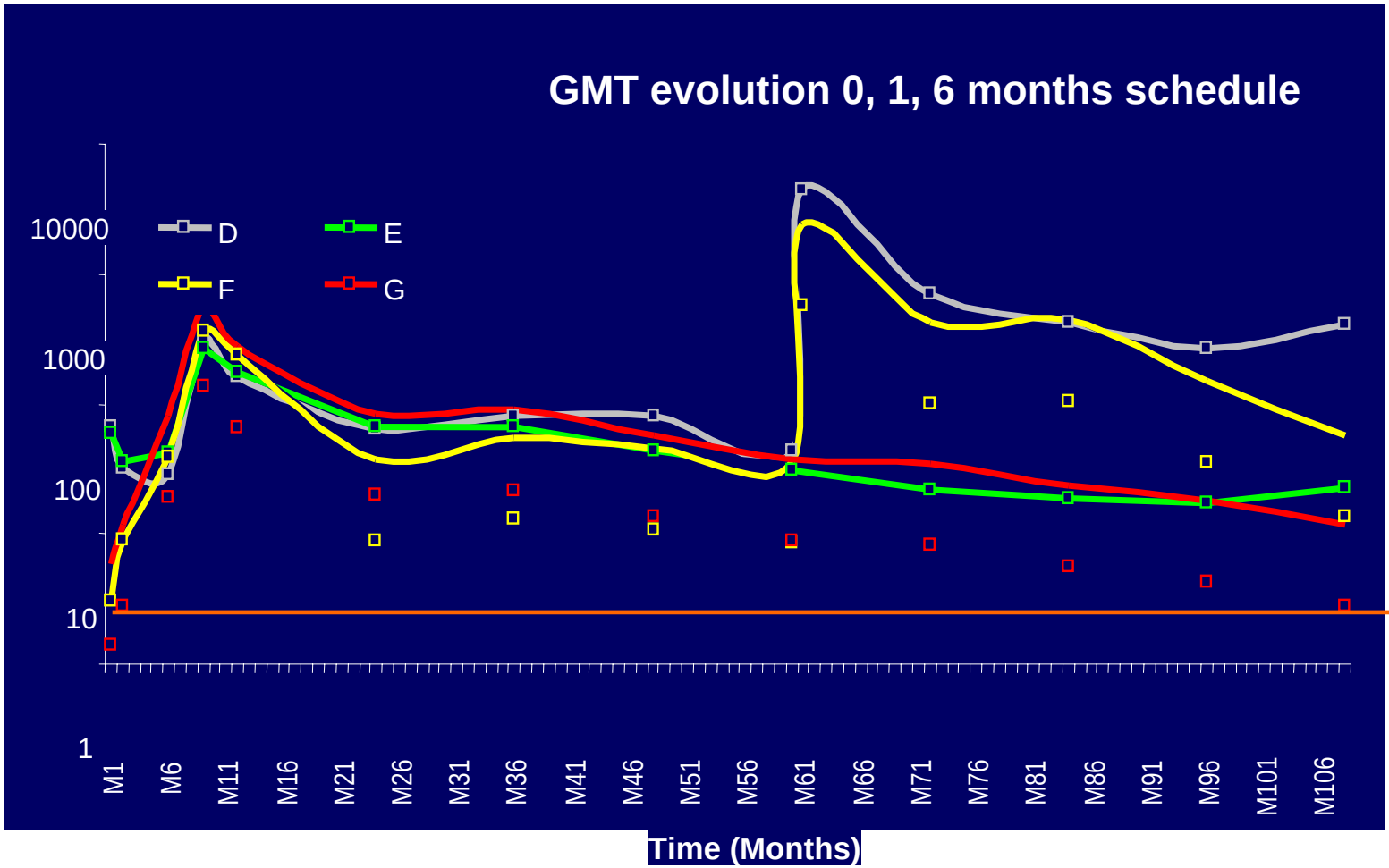
Poovorawan Y, *et al*. Pediatr Infect Dis J 1992;11:816-21.

Long term follow-up of high risk neonates vaccinated against hepatitis B vaccine in Thailand

Poovorawan Y, *et al*. Arch Dis Child 1997;77:F47–F51.



A : booster + HBIG B : booster no HBIG C: no booster no HBIG



D: booster + HBIG

E: no booster + HBIG

F: booster no HBIG

G: no booster no HBIG

Impact of Universal Hepatitis B Vaccination in Thailand in 2000

LUMPANG

UDON THANI

LOP BURI

CHON BURI

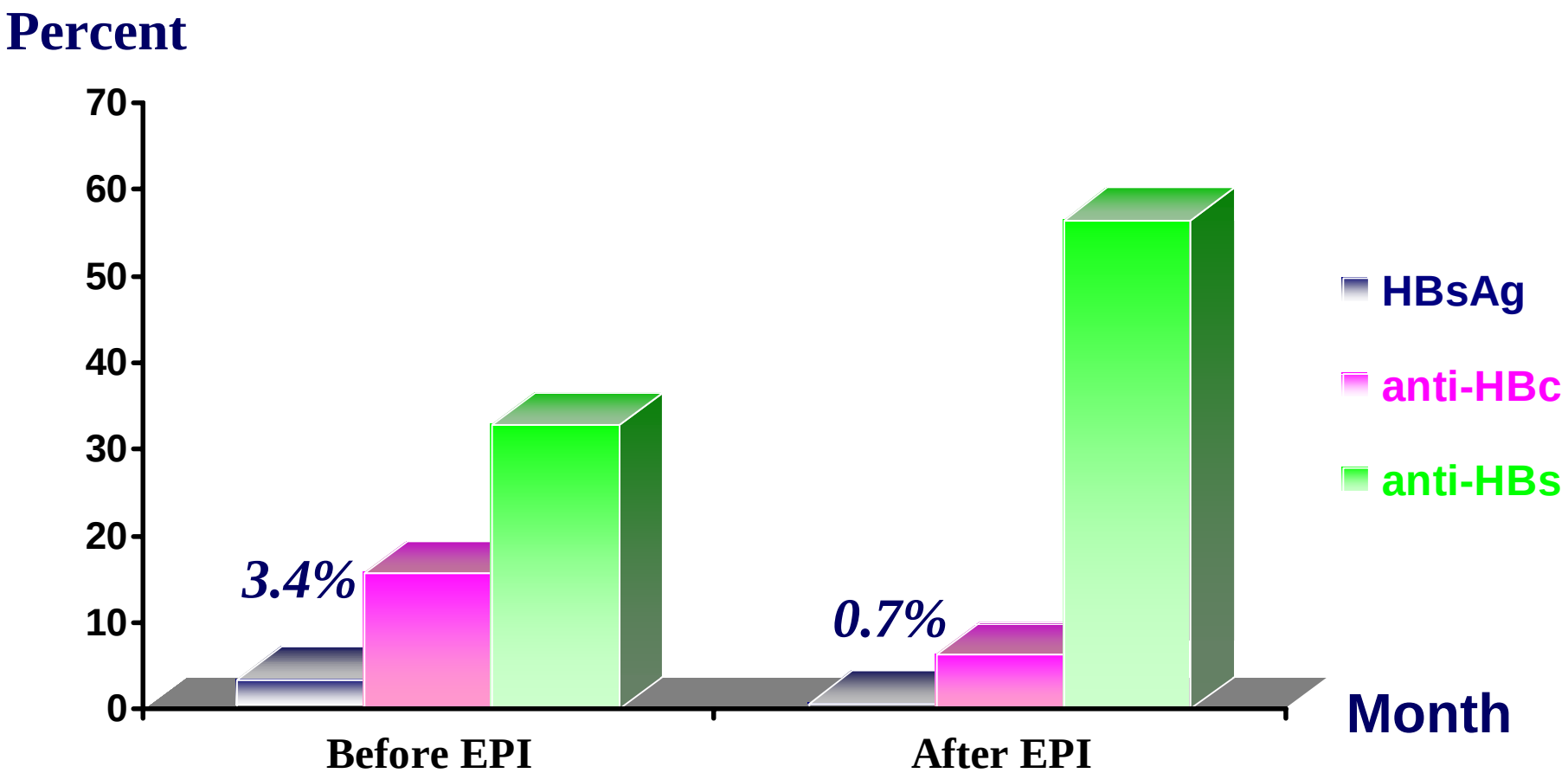
NAKHON SI THAMMARAT

Population examined for HB markers per province in relation to HB vaccine integration into EPI

Location	No. of children studied	Male	Female	Start of EPI (date)
Chonburi	458	245	213	1 Jan 1989
Lopburi	488	210	278	1 May 1992
Udon Thani	400	196	204	1 Oct 1992
Nakhon Si Thammarat	472	196	276	1 Oct 1992
Lampang	411	190	221	1 Oct 1992
Total	2229	1037	1192	

Poovorawan Y, *et al*. Vaccine 2001;19:943–9.

Hepatitis B virus markers in children under 18 years in 1999



Poovorawan Y, *et al*. Vaccine 2001;19:943–9.

Impact of universal HBV vaccination 2004

2004 survey (6200 samples)

Age: 6 mos – 60 yrs

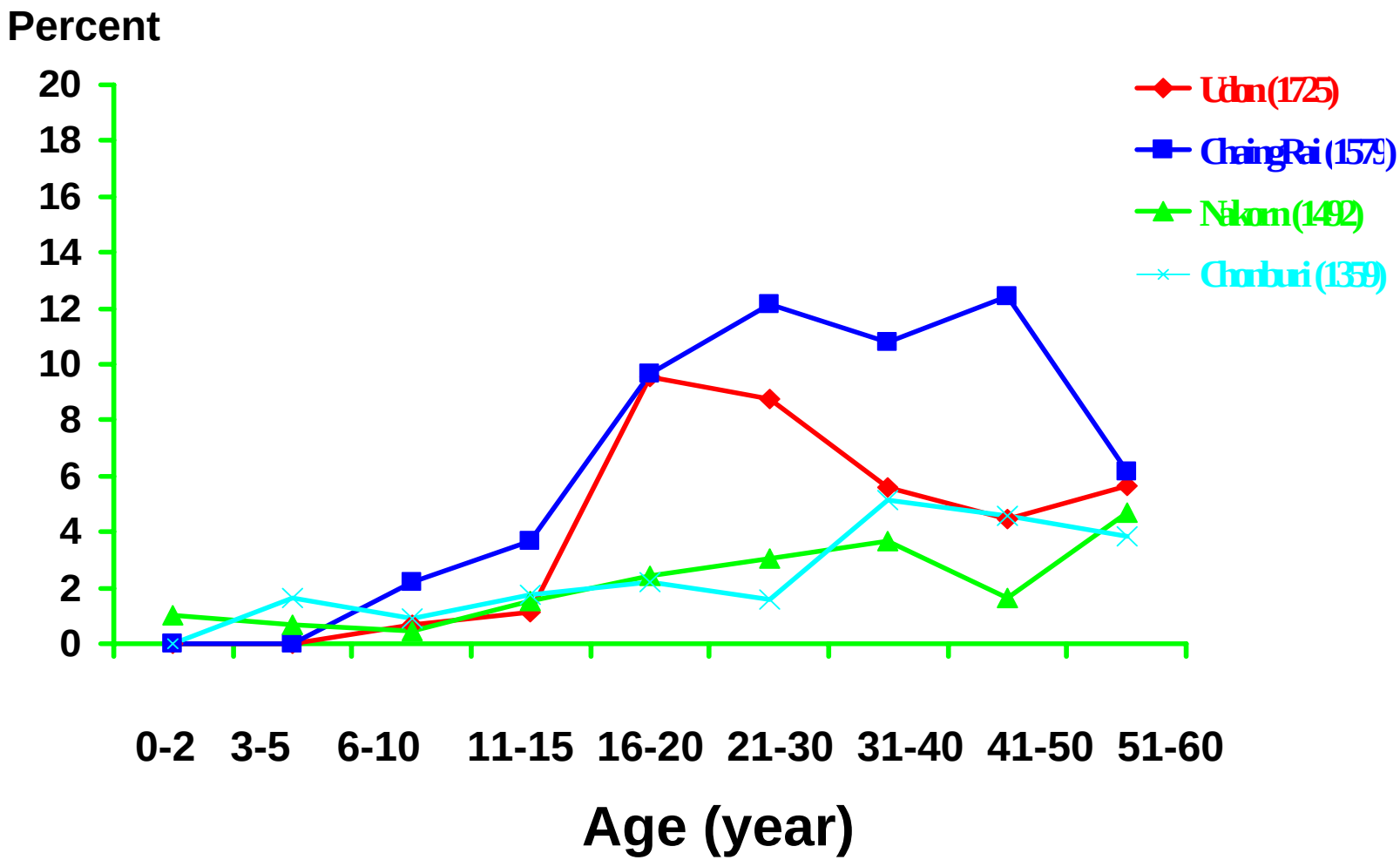
Provinces :

Geographical area

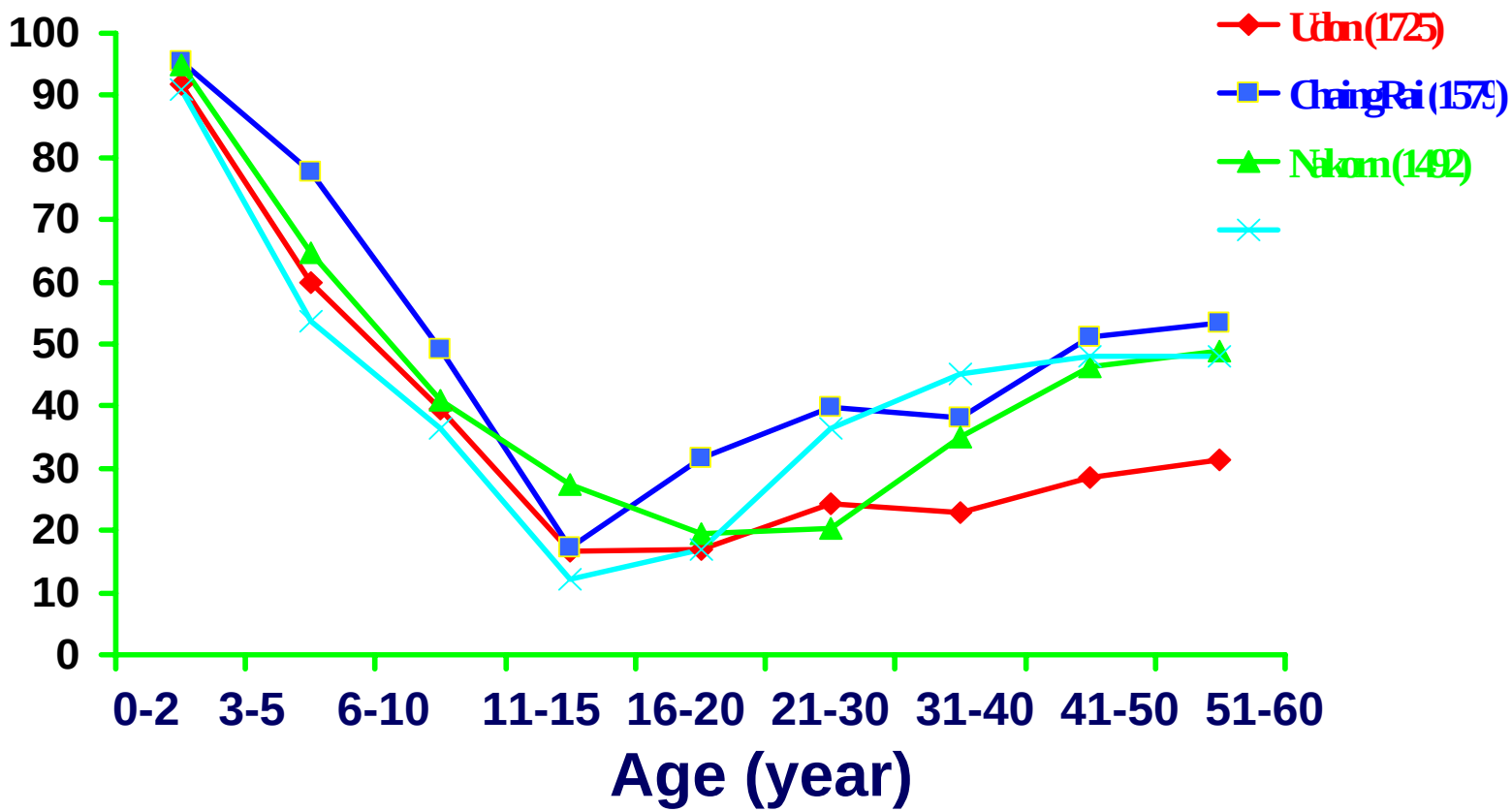
1 city hospital

2 district hospitals

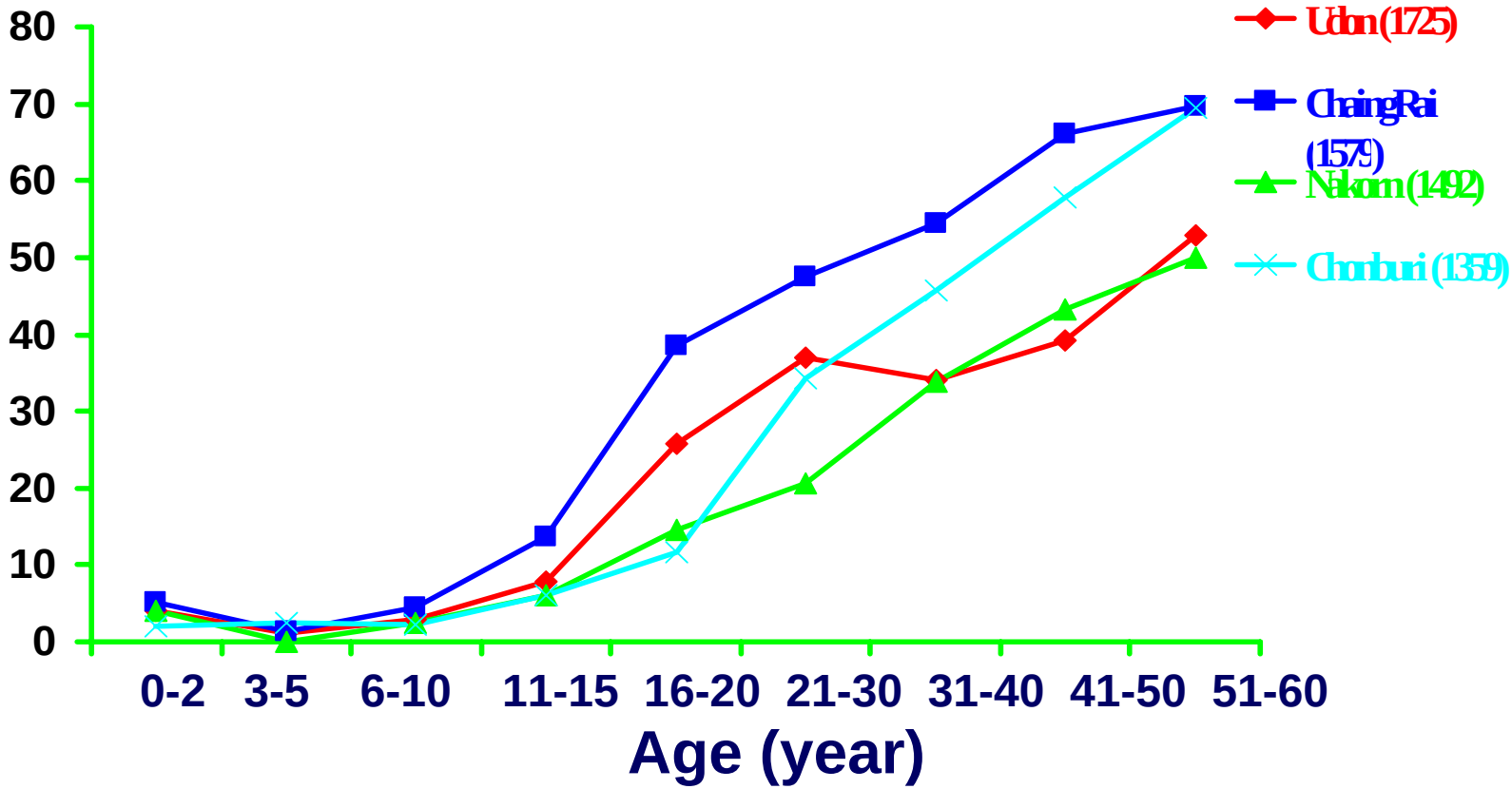
Seroprevalence of HBsAg among different age groups in Thailand



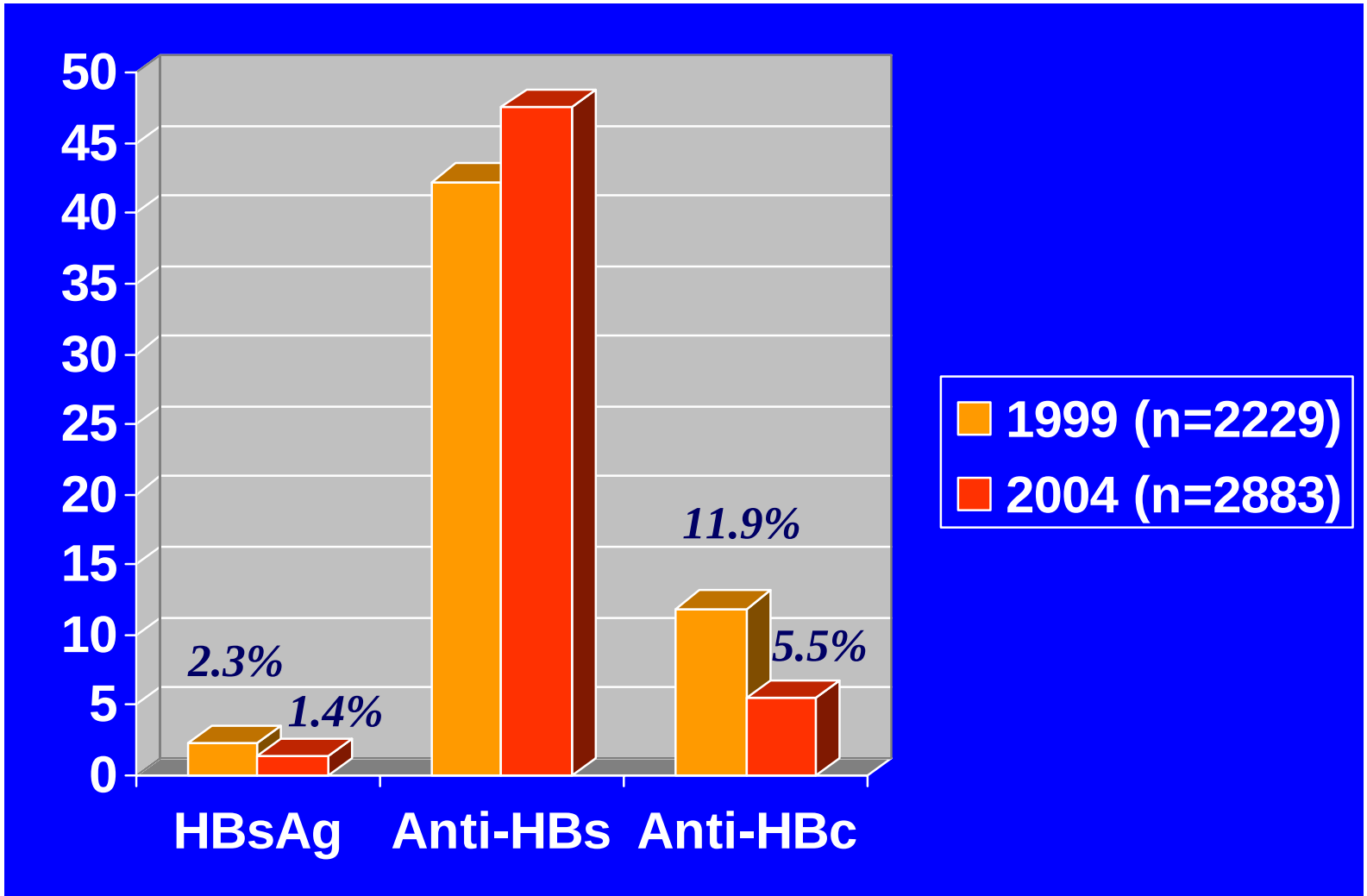
Seroprevalence of anti-HBs among different age groups in Thailand



Seroprevalence of anti-HBc among different age groups in Thailand



Prevalence of HB markers in children < 18 years



Vaccine Efficacy

HB vaccine & HBIG administered 12-24 hrs after birth, followed by completion of a 3-dose vaccine series, has been demonstrated to be 85%-95% effective in preventing acute & chronic HBV infection in high-risk infants

Andre FE, *et al*. J Med Virol 1994;44:144-51.

Vaccine Efficacy

High-risk babies

- **HBIG at birth & 2 mo**
- **vaccines at 2, 3 & 5 mo**

RESULTS: efficacy = 95.1%

Noto H, *et al.* J Gastroenterol Hepatol 2003;18:943-9.

Vaccine Efficacy

In RCTs, HB vaccine (3- or 4-dose schedule) without HBIG beginning ≤12 hours after birth has been demonstrated to prevent 70%-95% of perinatal HBV infections among high-risk infants

Poovorawan Y, *et al*. Vaccine 1990 (Suppl 8):S56-9.
Milne A, *et al*. J Med Virol 2002;67:327-33.

Spacing of vaccine

- **No apparent effect on immunogenicity when minimum spacing of doses is not achieved precisely**
- **Increasing the interval between the first 2 doses has little effect on immunogenicity or final antibody concentration**

Wistrom J, *et al*. Vaccine 1999;17:2162-5.
Halsey NA, *et al*. Pediatrics 1999;103:1243-7.

Combined DTPw-HB vaccines

- **Compare combined DTPw-HB vaccines vs separate administration of DTPw & HB vaccines in 124 children of HBsAg-negative mothers**
- **Higher anti-HBs response in combined vaccine group than in monovalent vaccine group**

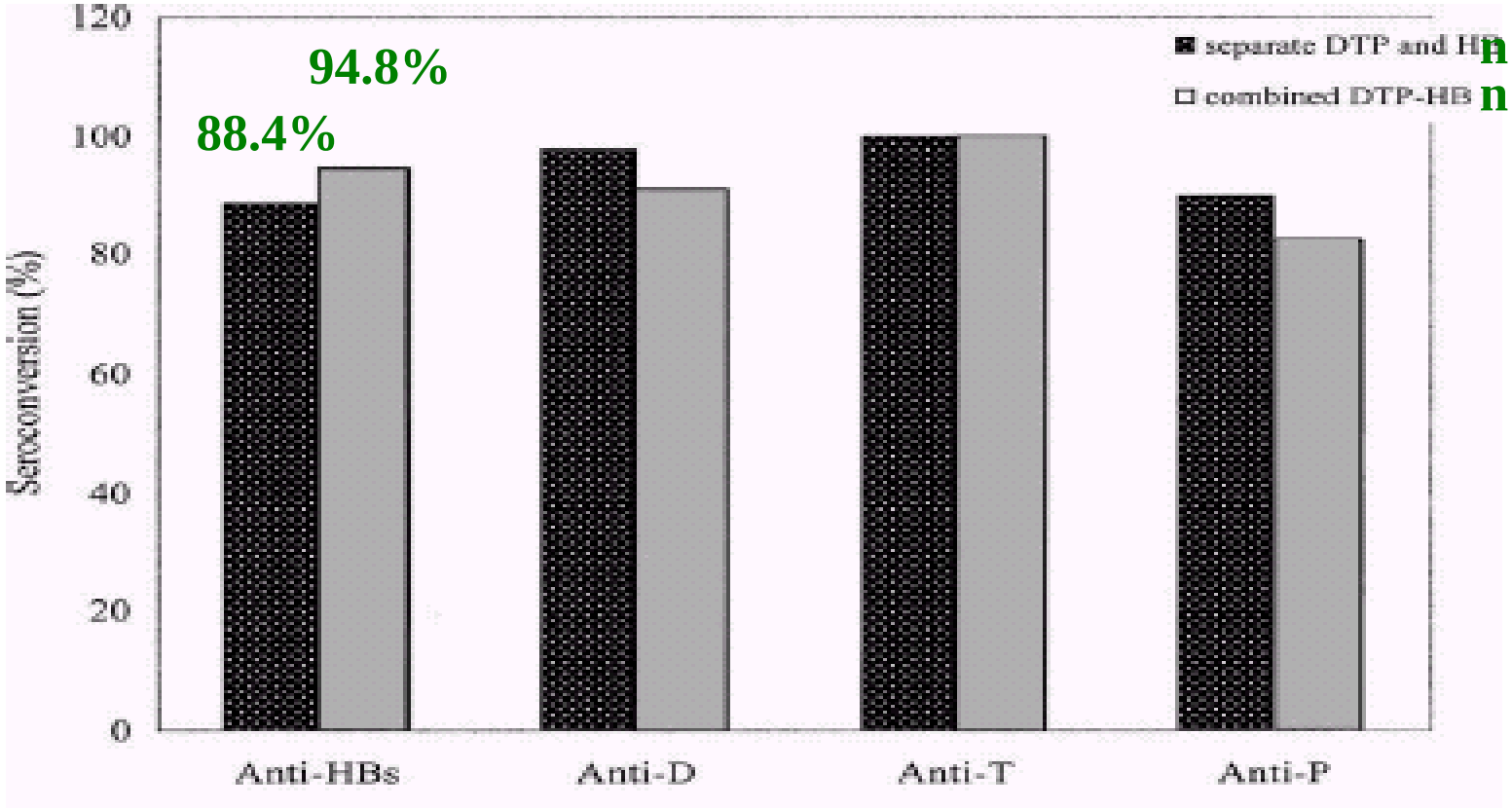
Poovorawan Y, *et al*. Asian Pac J Allergy Immunol 1999;17:113-20.

Combined DTPw-HB vaccines

- **One month after the booster dose of DTPw-HB vaccine, at least 97.8% of subjects had seroprotective anti-HBs levels**
- **One year later at least 93.9% of these subjects remained seroprotected**

Poovorawan Y, *et al*. Ann Trop Paediatr 1997;17:301-8.

Serological survey in 7-12-mo-old children



Chunsuttiwat S, *et al.* Vaccine 2002;21:188–93.

Combination vaccine

The immunogenicity of DTaP-HB-IPV/Hib (3 doses) with & without single-antigen HB vaccine at birth is comparable

Pichichero ME, *et al*. Pediatr Infect Dis J 2002;21:854-9.

Conclusion

HB vaccines with or without HBIG have comparable immunogenicity and protective efficacy in prevention of perinatal HBV transmission

Conclusion

Combined DTP-HB vaccine:

- **Good immunogenicity**
- **Replace separate vaccines in areas of high HBV endemicity in terms of clinical, economic & strategic benefits**

Acknowledgements

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Thank you for your attention