Plenary - 05 Dec. 2009; Taipei, TAIWAN, APACHE Conference

Prevention of Hepatitis B Virus Infection - the Impact and Problems

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Hepatitis B Virus Infection

- Acute / Fulminant Hepatitis
- Chronic Hepatitis
- Liver Cirrhosis
- Hepatocellular Carcinoma

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PERINATAL TRANSMISSION OF HBV FROM HBsAg POSITIVE MOTHERS

Infants of HBeAg Positive Mothers

↓

90% HBsAg Carriers

Infants of HBeAg Negative Mothers

↓

<5% HBsAg Carriers, Mostly Acute or Fulminant Hepatitis, or Uninfected

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Hepatitis B Vaccination and Control of Hepatitis B Related Diseases

- Acute /Fulminant Hepatitis
- Chronic Hepatitis
- Liver Cirrhosis ?
- Hepatocellular Carcinoma

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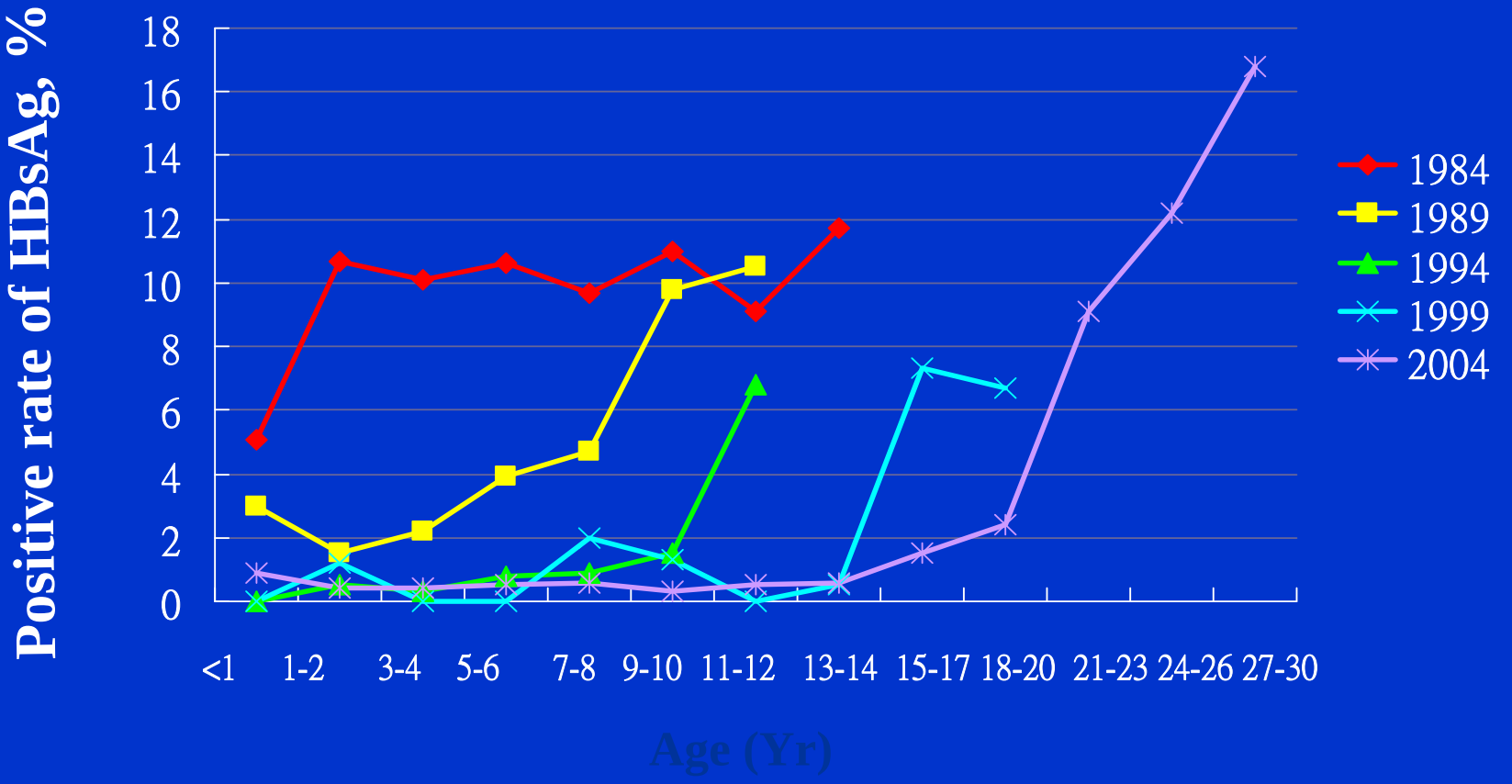
Seroprevalence of HBsAg in 1984, 1989, 1994, 1999, and 2004 in Taipei, Taiwan



Ni YH, Chang MH, et al. Gastroenterology 2007 ; 132 :1287-93. Ann Intern Med 2001;135:796-800 ; Chen HL, et al. JAMA 1996; Hsu HY, et al. J Med Virol 1986

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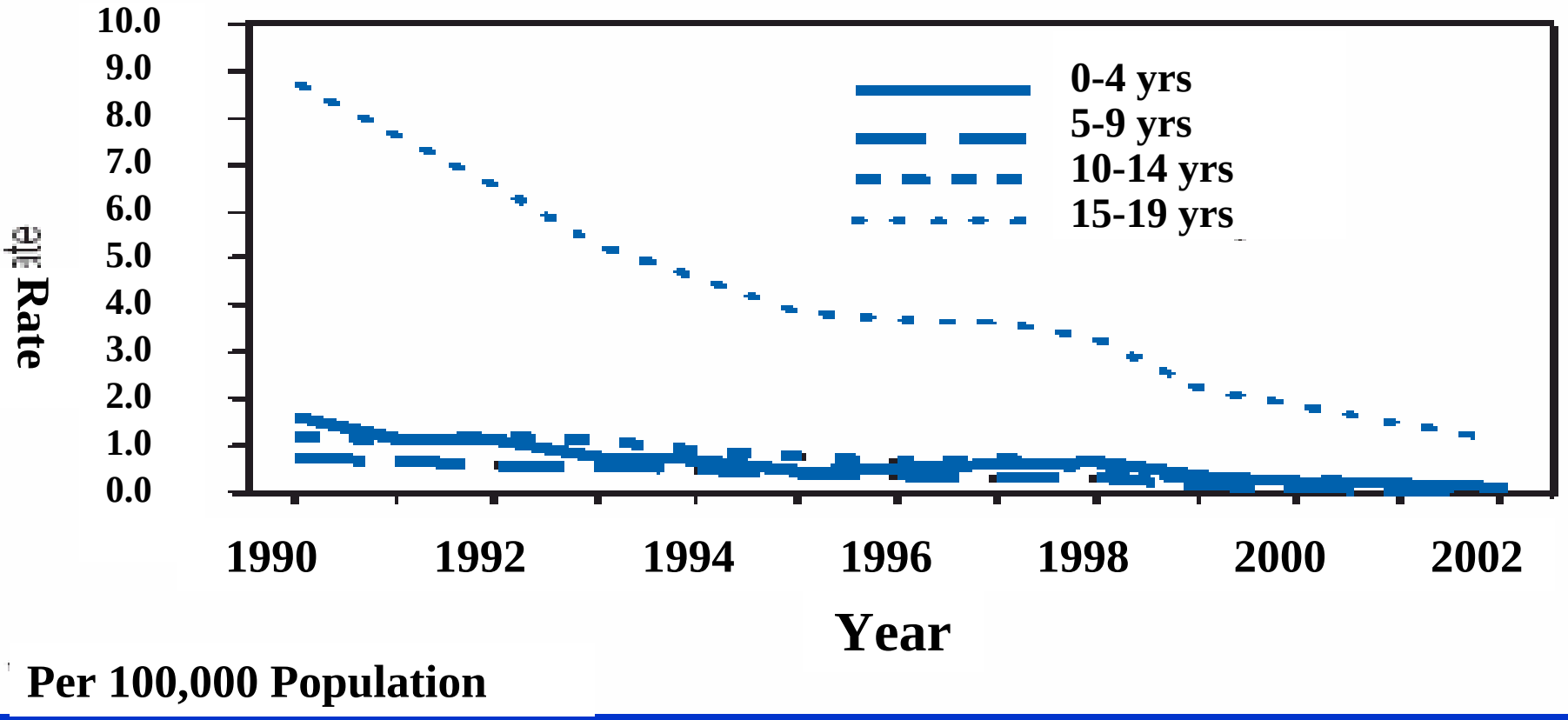
Rate of Acute Hepatitis B among Children and Adolescents, by Age Group and Year---

United States, 1990-2002



MMWR Weekly November 5, 2004 / 53(43);1015-1018

Acute Communicable Disease Control 2007 Annual Morbidity Report

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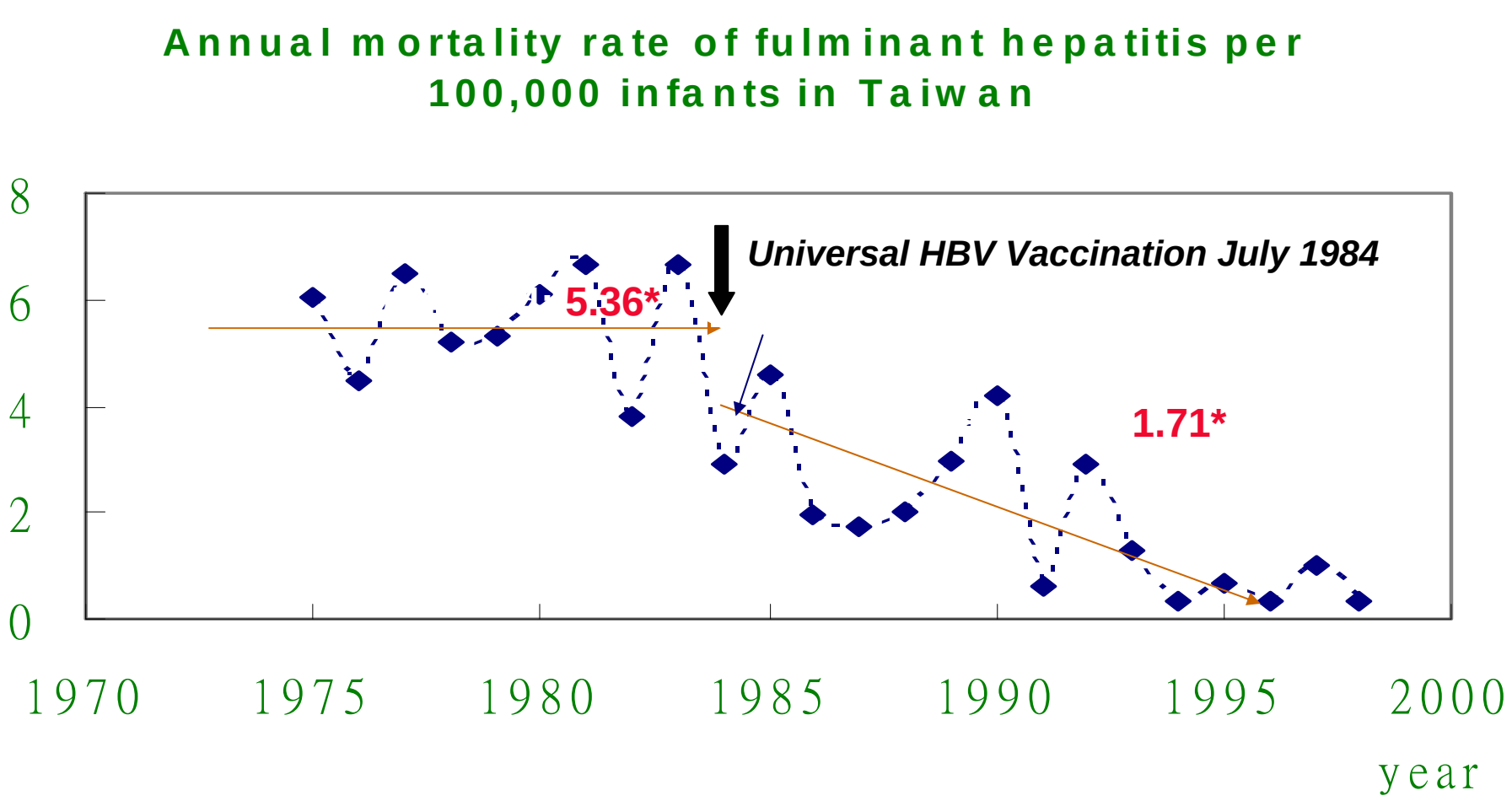
Universal HBV Vaccination and Decreased Mortality from Fulminant Hepatitis in Infants in Taiwan



***The average mortality rate per 10^5 infants Mortality Ratio: 3.2 ($p < 0.001$)**

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Kao JH, Hsu HM, Shau WY, Chang MH, Chen DS. J Pediatr. 2001;139:349-52.

Incidence of Hepatocellular Carcinoma in Children Diagnosed at Aged 6 to 14 Years from July 1981 to June 2004 According to Birth Year

Birth Year*	Incidence (per 10^5)	R.R.	95% CI
1966-84	0.52-0.54	1	
1984-94	0.13-0.20	0.25-0.36	0.26-0.52

•Birth Year was counted from July of one year to June of the next year. R.R.: risk ratio; CI: confidence interval.

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Chang MH, et al. N Engl Med 1997 ; 336:1855-9 ; Clin Cancer Res 2005;11: 7953-7.

Incidence rates of HCC diagnosed in 1983-2004 among children 6-19 years old and born before or after the launch of the Taiwanese universal HBV vaccination program in July 1984

Age at Dx	Birth year	Hepatocellular carcinoma			
		No. of HCCs	Incidence rate (per 10^5 person-years)	Rate ratio	*P*
6-9	1973-1979	36	0.51	1(referent)	
	1979-1984	38	0.47	0.93	.74
	1984-1998	26	0.15	0.30	<.001
10-14	1968-1979	102	0.60	1(referent)	
	1979-1984	50	0.50	0.84	.29
	1984-1994	28	0.19	0.32	<.001
15-19	1963-1979	138	0.52	1(referent)	
	1979-1984	80	0.80	1.55	.001
	1984-1989	10	0.16	0.30	<.001

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Chang MH, et al. J National Cancer Institute 2009; 101:1348–55.

Prenatal maternal HBsAg on risk of HCC among patients versus the vaccinated general population who were 6-19 years old during July1983 - June 2004

Risk Predictor	HCC Patients No. (%)	Vaccinated population	Odds Ratio (95% C.I.)	*P*-Value
Prenatal maternal HBsAg				
HBsAg (-)	8	3,656,182	1.00 (referent)	
HBsAg (+)	44	729,420	29.50 (13.98 to 62.60)	< .001

Chang MH, et al. J National Cancer Institute 2009; 101:1348–55.

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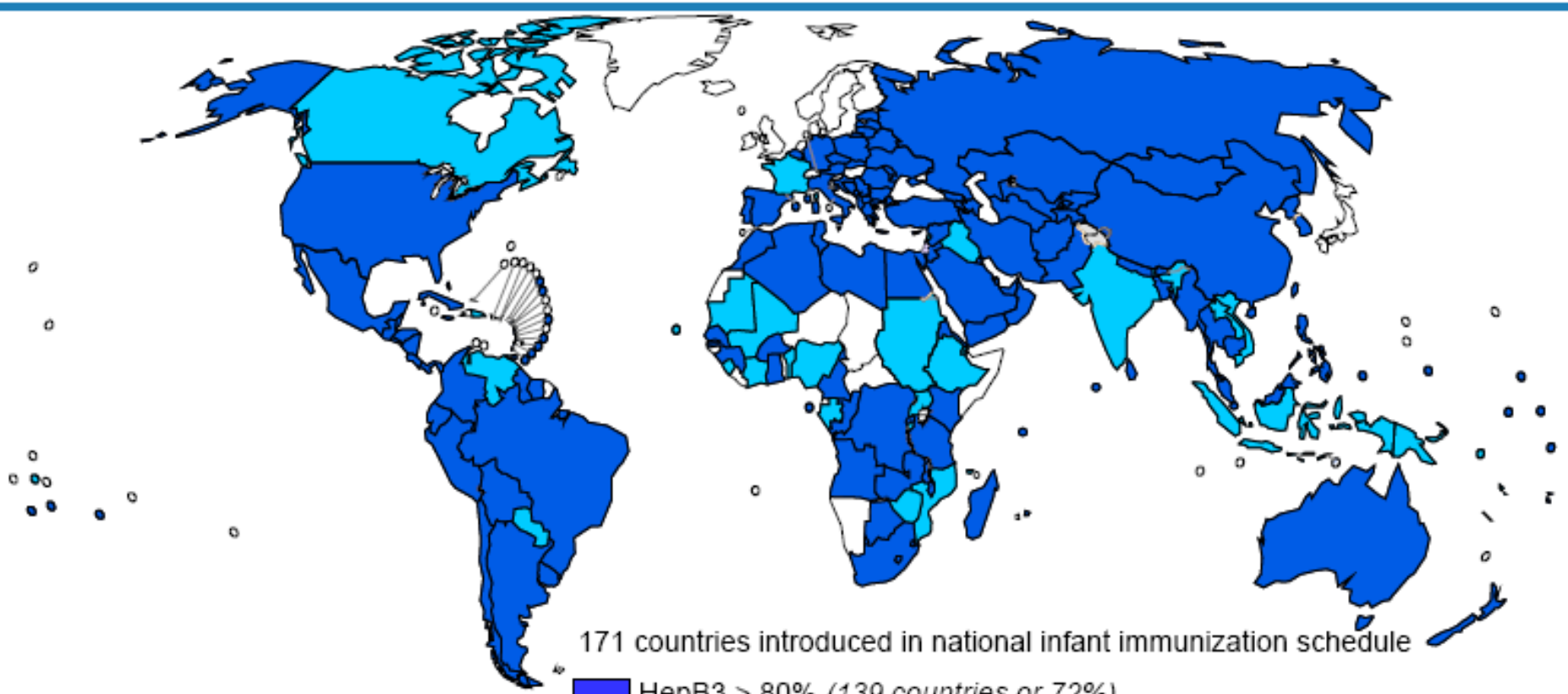
Countries having introduced HepB vaccine and infant HepB3 coverage, 2007



171 countries introduced in national infant immunization schedule

- HepB3 ≥ 80% *(139 countries or 72%)*
- HepB3 < 80% *(31 countries or 16%)*
- HepB vaccine introduced but no coverage data reported *(1 countries or 0*
- HepB* vaccine not introduced *(22 countries or 11.5%)*

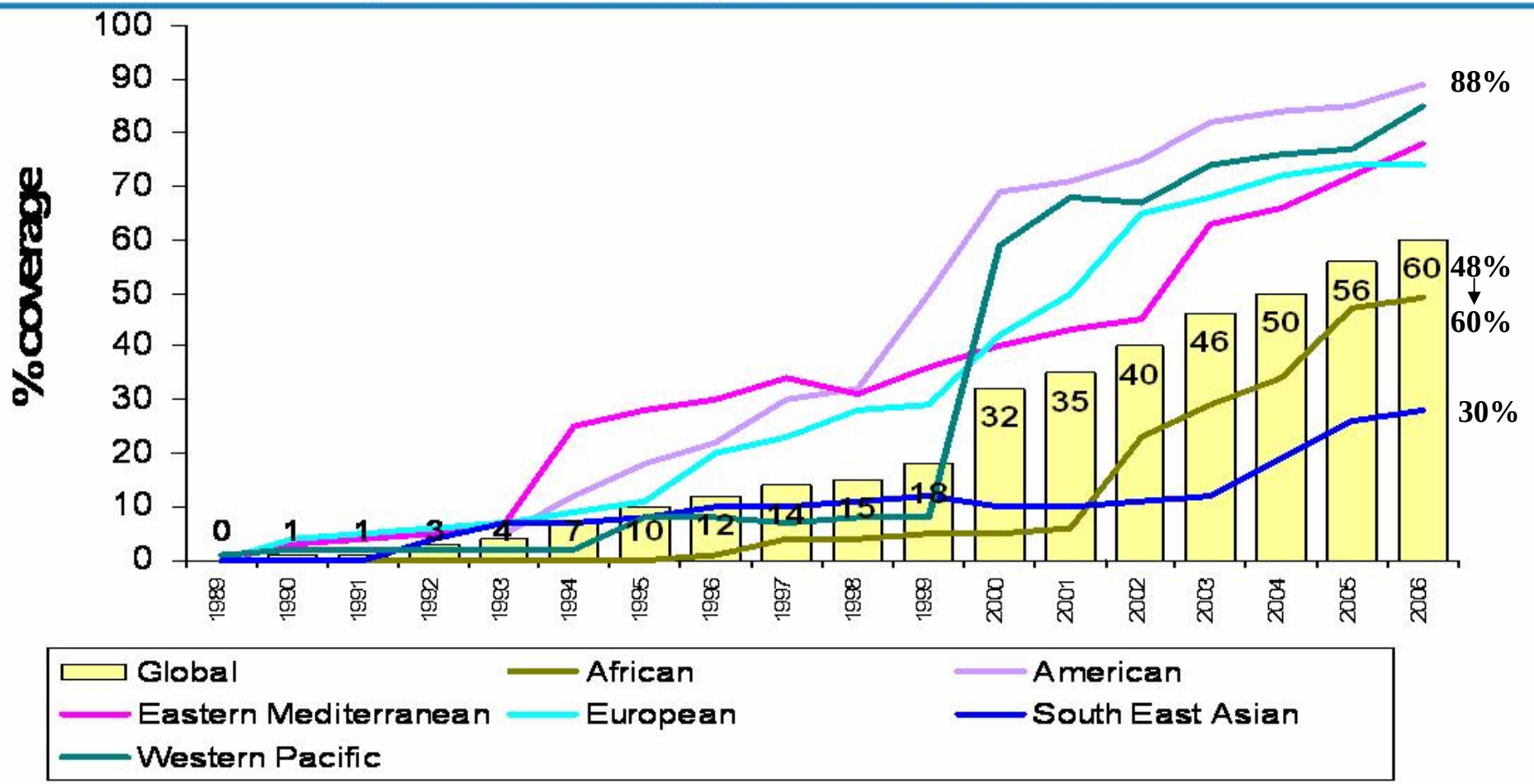
* 3 countries introduced HepB in adolescent immunization schedule

Source: WHO/UNICEF coverage estimates 1980-2007, August 2008

Date of slide: 4 September 2008

World Health Organization

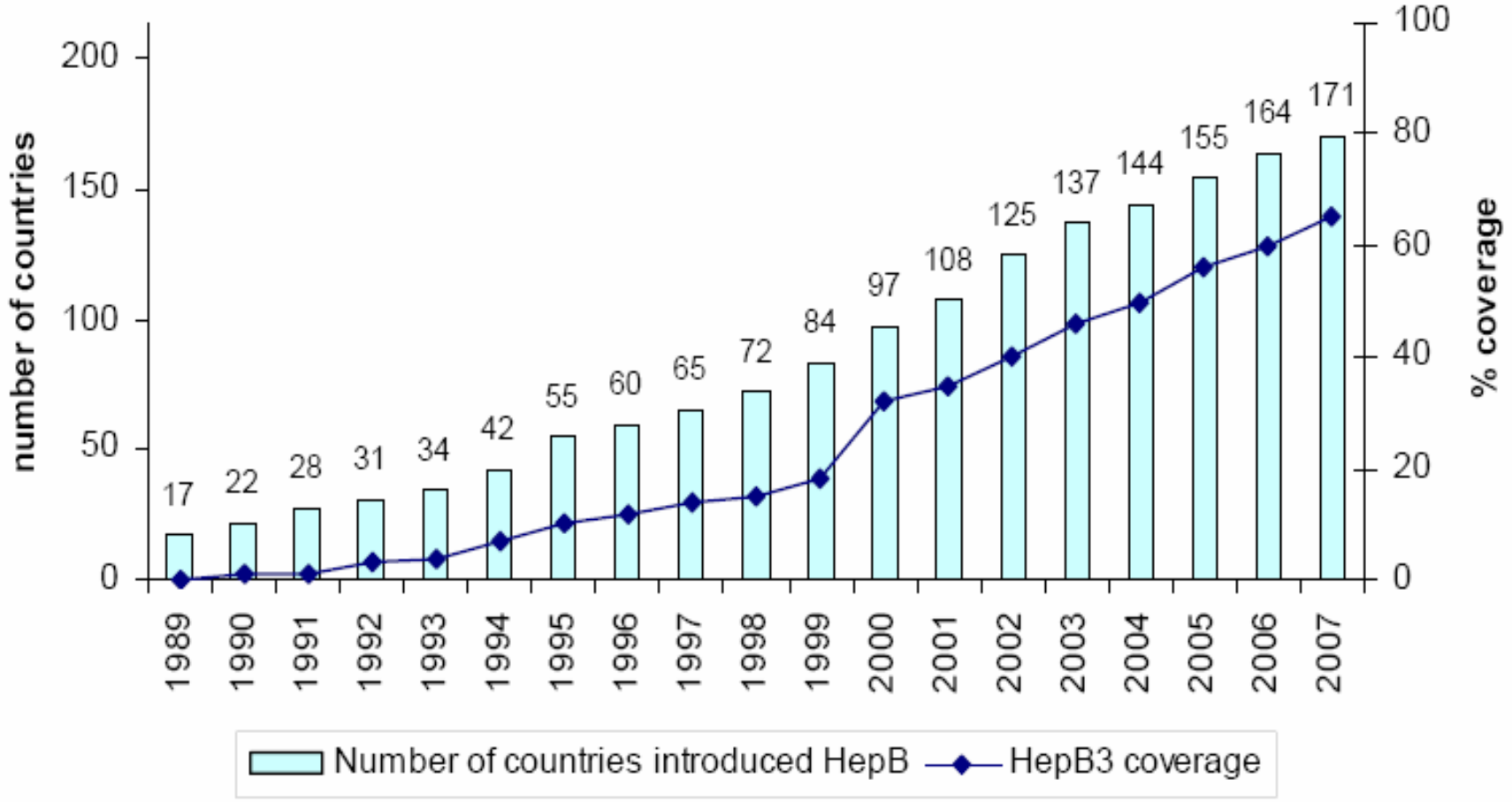
Global Immunization 1989-2006, 3rd dose of Hepatitis B coverage in infants global coverage at 60% in 2006



Source: WHO/UNICEF coverage estimates 1980-2006, August 2007 Date of slide: 17 August 2007

World Health Organization

Number of countries introduced HepB vaccine* and global infant HepB3 coverage, 1989-2007



* Includes India and Sudan where Introduction is part of the country
excluding 3 countries where HepB administered for adolescence

Source: WHO/UNICEF coverage estimates 1980-2007, August 2008,
193 WHO Member States. Date of slide: 21 August 2008

World Health Organization

CAUSES OF BREAKTHROUGH HBV INFECTION

- **Maternal Factors :**

  High Maternal Viral Load
  Intrauterine Infection

- **Viral Factors :**

  Surface Gene Mutants

- **Host Factors :**

  Genetic Hypo-responsiveness
  Immune Compromised Host

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INTRAUTERINE INFECTION OF HBV

- **HBsAg Seropositive Rate at Birth : 2.4% (16/665) Among Neonates of HBeAg Positive, HBsAg Positive Mothers**
- **Chronicity : 100%**

Tang JR et al. J Pediatr 1998 ; 133: 374

CAUSES OF BREAKTHROUGH HBV INFECTION

- **Maternal Factors :**

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  Intrauterine Infection

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  HBV Surface Gene Mutants

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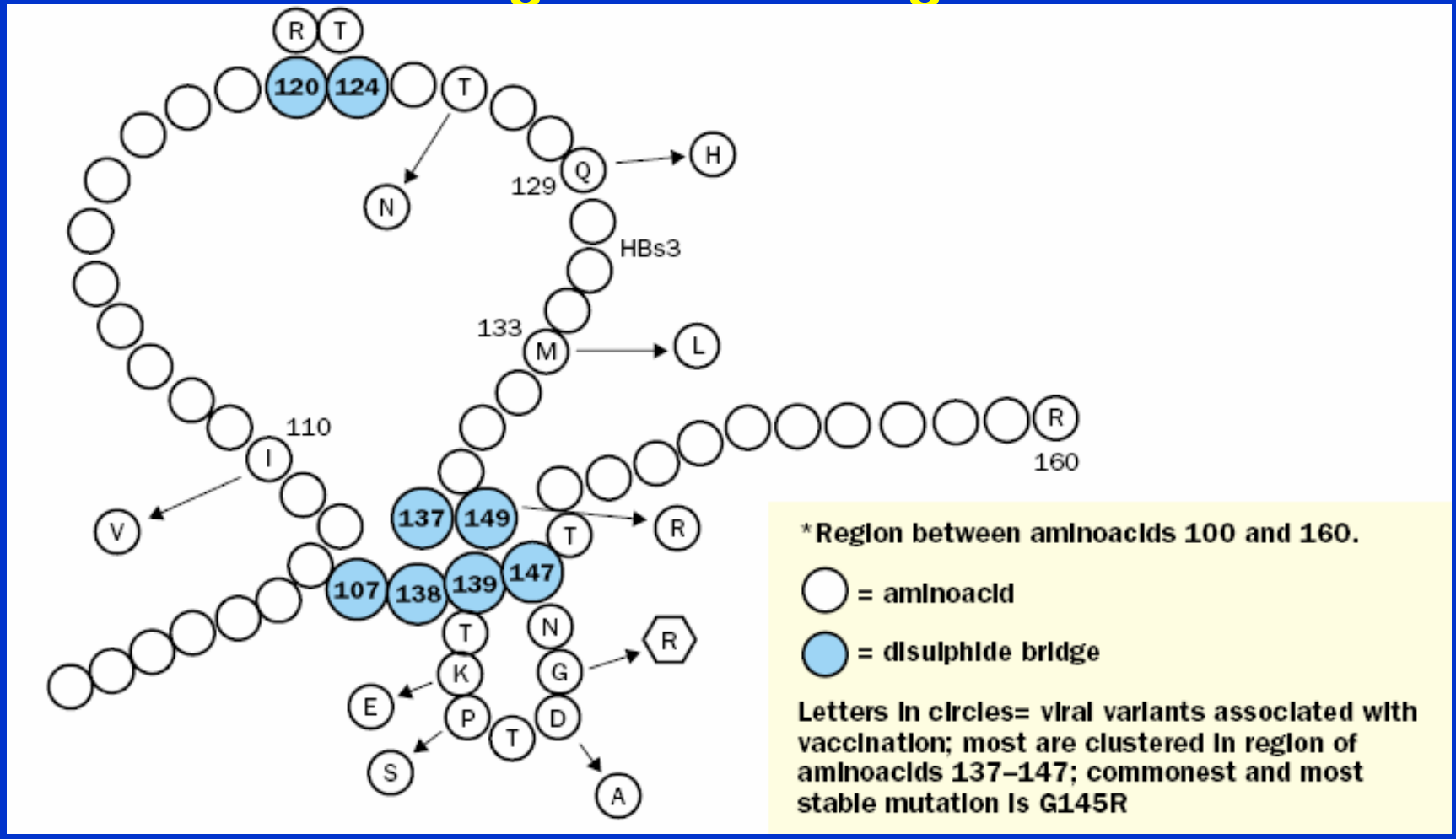
Molecular structure of major hydrophilic region of HBsAg*



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Zuckerman A. The Lancet 2000; 355 : 1382-4.

Prevalence of HBV Surface Gene *a* determinant Variants in Children <15 yrs with Positive HBsAg /or Anti-HBc Before and After HBV Vaccination in Taiwan

	1984	1989	1994	1999
No. Surveyed	1200	1134	1515	1357
No. Analyzed for HBV-DNA	148	91	65	71
No. Seropositive for HBV-DNA	103	51	32	13
No.with *a* Determin. Mutant (%) in HBV Carriers	8 (7.8%)	10 (19.6%)	9 (28.1%)	3 (23.1%)
% in Total Surveyed	0.67%	0.88%	0.58%	0.22%

Hsu HY, Chang MH, et al. GUT 2004 ; 53: 1499-1503;

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Long-Term Protection after Hepatitis B Vaccination in 1200 Children in Taiwan

- **No New HBsAg Carrier (0.7%) during Follow-up from 7 to 16 Years old**
- **Annual New Anti-HBc Seroconversion Rate* : 0.13%**
- **Annual decay of Anti-HBs from age 7 to 16 was Approximately 20% of the Titer of the Previous Year.**

** At least twice anti-HBc positive one year apart*

Lin YC, et al. J Infect Dis 2003; 187: 134-8;
Wang JW, et al. Clin Diag Lab Immunol 2005 ; 12: 1442–1447.