Scale Up Birth Dose of HBV Vaccination
-Experience from China

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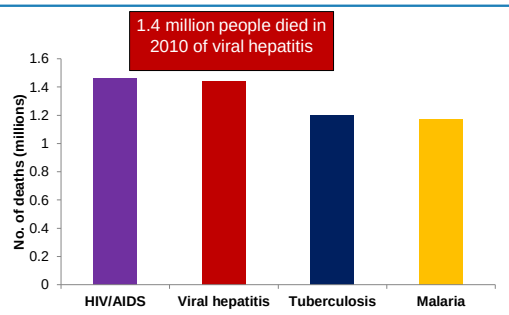
Conflict of Interest

Nothing to declare

Outline

1. **Viral hepatitis B is a leading cause of death in AP**
2. **HBV Immuniztion is the best way to control HBV infection**
3. **Birth dose is the key to prevent MTCT**
4. **Experience of China to promote the birth dose of HBV vaccination**

Number of deaths/year from selected conditions, 2010



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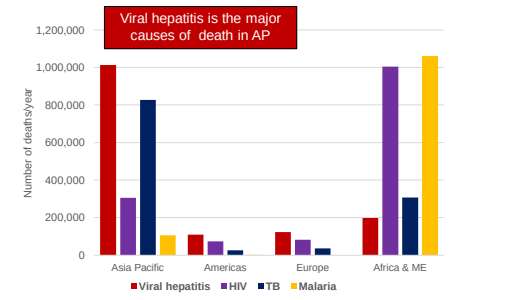
Source: Global Burden of Disease Study 2010 Lozano et al, Lancet 2012

Estimated annual deaths from selected causes by region, 2010



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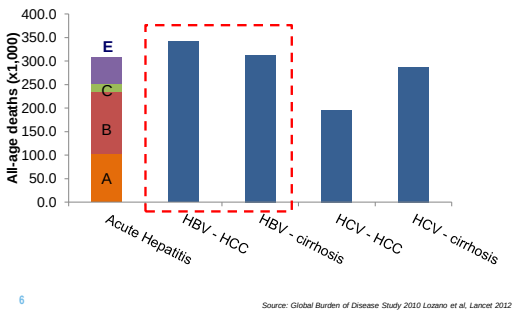
Source: Courtesy of IHME – Global Burden of Disease Study

Number of hepatitis deaths by virus type and disease outcome, 2010



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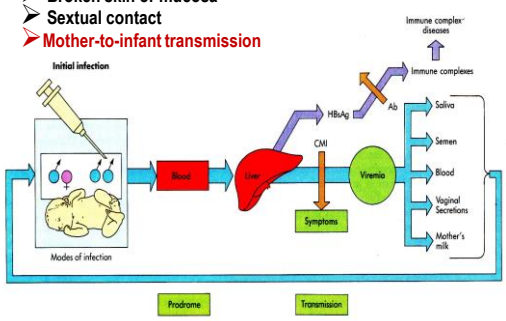
Source: Global Burden of Disease Study 2010 Lozano et al, Lancet 2012

Mode of HBV transmission

- Blood or blood products
- Broken skin or mucosa
- Sextual contact
- Mother-to-infant transmission



WHO Position Paper. Heptitis B Vaccine . Weekly Epidemiological Record. 2009,84,405-420.

Outline

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2. HBV Immuniztion is the best way to control HBV infection
3. Birth dose is the key to prevent MTCT
4. Experience of China to promote the birth dose of HBV vaccination

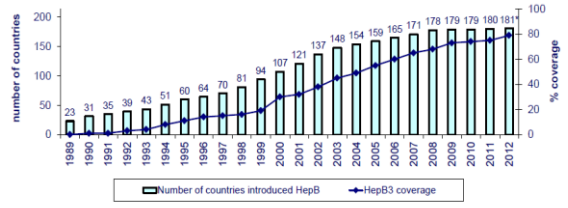
Prophylaxis Recommendation by WHO Guidelines

- For infants born to HBsAg negative mothers
  - HBV vaccine at 0, 1 and 6 months of age
- For infants born to HBsAg positive mothers
  - Birth dose of HBIG
  - HBV vaccine at 0, 1 and 6 months of age

However, even with passive-active immunoprophylaxis, 5%~15% newborns still get chronic HBV infection

NEJM 2012.

Number of countries having introduced HepB vaccine* and global infant HepB3 coverage, 1989-2012

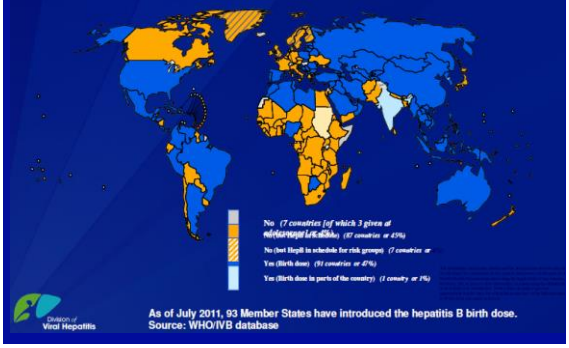


Source: WHO/UNICEF coverage estimates 2012 revision, July 2013
Immunization Vaccines and Biologicals, (IVB), World Health Organization.
194 WHO Member States, Date of slide: 22 July 2013.

*excluding 3 countries where HepB administered for adolescence

unicef World Health Organization

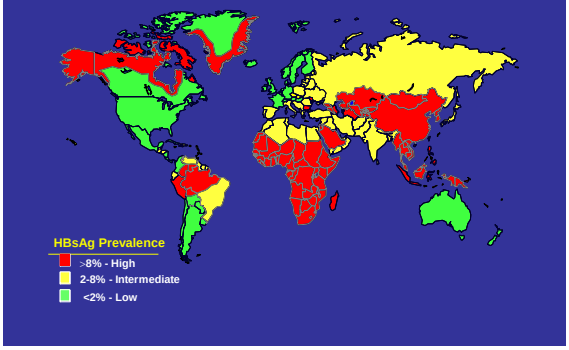
Countries Using HepB Birth Dose Vaccine in National Immunization Schedule, 2010



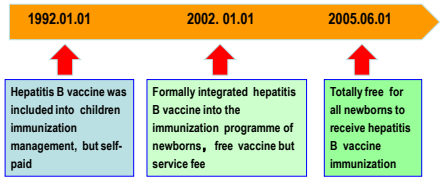
Division of Viral Hepatitis

As of July 2011, 93 Member States have introduced the hepatitis B birth dose.
Source: WHO/IVB database

China was highly endemic for Chronic Hepatitis B (1992)



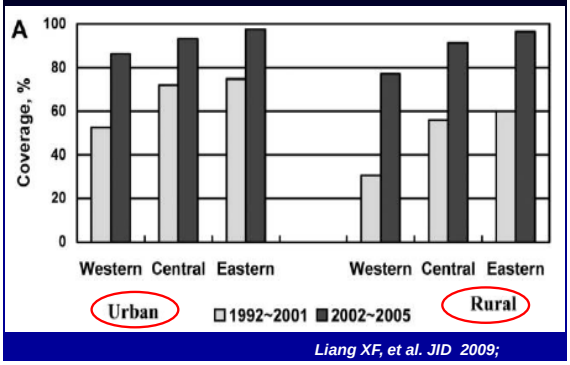
Universal immunization program for newborns against HBV in China



5μg yeast-derived / 10μg CHO hepatitis B vaccine

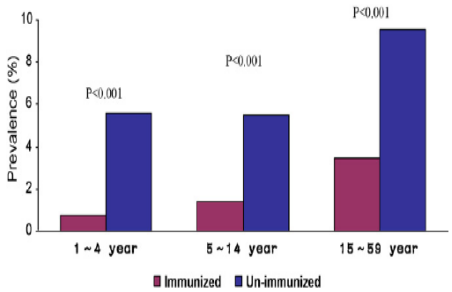
Zhuang H. Basic Med Sci Clin 2014; 24:136-40 [13]

Hepatitis B immunization Coverage of 3 Doses



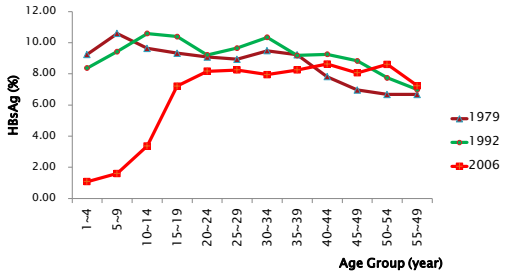
Liang XF, et al. JID 2009;

Relationship between Immunization and Prevalence of HBsAg in Different Age Groups



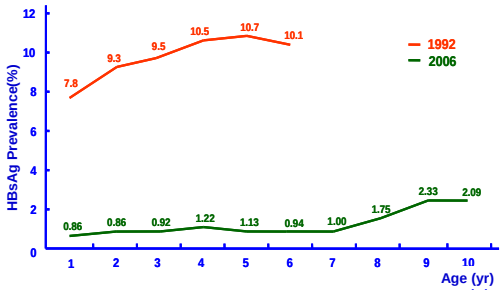
Liang XF, et al. Vaccine 2009; *27 : 6550–*

Comparison of HBsAg prevalences in 1979,1992 and2006, in China



Sources – China National Serosurveys 1979, 1992, 2006

Perinatal and Early Infant Transmission of HBV Decreased in China



Data from National Surveys on Seroprevalence of Viral Hepatitis

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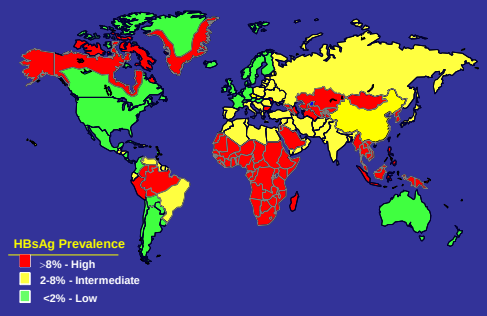
HBV infection among children born between 1992–2005

Year	No. investigated	Weighted prevalence, % (95% CI) HBsAg	Anti-HBc	Anti-HBs
1992	1724	5.5 (3.7–7.4)	16.5 (13.7–19.2)	50.5 (46.8–54.1)
1993	2285	3.4 (2.5–4.2)	13.3 (10.8–15.7)	57.9 (54.2–61.7)
1994	2415	2.9 (1.9–4.0)	10.5 (8.3–12.7)	53.4 (46.1–60.8)
1995	2773	3.0 (1.8–4.1)	8.7 (6.6–10.9)	61.6 (56.4–66.9)
1996	2647	2.1 (1.1–3.1)	7.1 (5.4–8.7)	60.5 (57.1–63.9)
1997	2578	2.3 (1.8–2.9)	7.5 (5.9–9.1)	55.7 (50.8–60.5)
1998	2434	1.8 (1.4–2.1)	6.1 (4.8–7.5)	54.2 (49.8–58.6)
1999	2326	1.0 (0.4–1.6)	5.3 (3.5–7.1)	54.8 (51.0–58.5)
2000	2356	0.9 (0.4–1.5)	3.7 (2.0–5.4)	56.9 (50.4–63.5)
2001	2215	1.1 (0.4–1.8)	4.8 (3.3–6.4)	55.8 (45.6–65.9)
2002	4175	1.2 (0.8–1.6)	4.2 (3.3–5.1)	63.5 (60.9–66.0)
2003	4412	0.9 (0.5–1.3)	4.5 (3.4–5.6)	65.7 (63.4–67.9)
2004	4153	0.9 (0.4–1.3)	4.2 (3.1–5.4)	72.9 (70.6–75.1)
2005	3636	0.9 (0.4–1.3)	3.3 (2.3–4.4)	84.5 (82.4–86.7)
Total	40,129	2.1 (1.78–2.38)	7.4 (6.8–8.0)	60.0 (58.4–61.5)

Liang XF, et al. JID 2009; 200:39–47

China is intermediate of Chronic Hepatitis B (2006)



Outline

1. Viral hepatitis B is a leading cause of death in AP
2. HBV Immuniztion is the best way to control HBV infection
3. Birth dose is the key to prevent MTCT
4. Experience of China to promote the birth dose of HBV vaccination

Different modes of HBV infection

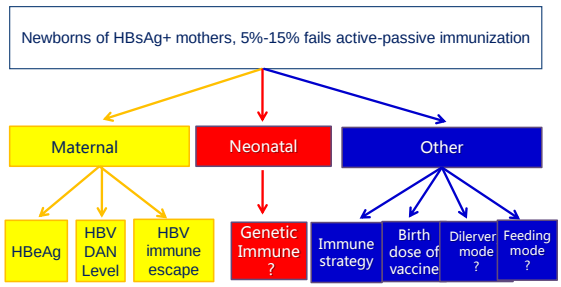
- In low endemic area(NA &EU):
  - adulthood- low rate of chronicity
- In high endemic area(AP):
  - perinatal & early childhood- high rate of chronicity

➢For infants born to mothers with HBsAg-positive and HBeAg-positive, 85%~90% of them would become chronic HBV infection.

➢For infants born to mothers with HBsAg-positive only, 30%~40% of them would become chronic HBV infection.

Immunization Practices Advisory Committee (ACIP), CDC. MMWR, 1991, 40: 1-25.

Factors associated with failure to interrupt HBV MTCT



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Timely birth dose and the HBsAg status 1~4 yr Children

Birth dose	N	HBsAg (+) 数	% HBsAg⁺ (95% CI)	P 值
Timely	12,191	93	0.67 (0.46~0.77)	
Delayed	3,284	50	1.13 (0.78~1.56)	P<0.005
Missed	481	20	5.57 (3.54~7.61)	P<0.005
Unknown	420	14	3.22 (1.60~4.84)	P>0.25
Total	16,376	177	0.96 (0.75~1.17)	

Data from National Surveys on Seroprevalence of Viral Hepatitis 2006

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Prevalence of HBsAg according to the timing of the first dose in 1992–2005 birth cohorts, China

First dose of hepatitis B vaccine	HBsAg un-weighted	
	No. positive	%
Within 1 day	193	0.90
1–7 days	8	0.58
8–14 days	10	1.83
15–27 days	12	1.66
28–180 days	57	1.77
181 days+	49	2.53
Total	329	1.12

Cui FQ, et al. Vaccine 2010; 28 : 5973–8

Multivariate analysis of risk factors for HBV MTCT

Variables	OR (95% CI)	*p*
Maternal HBV DNA	4.83 (1.38–16.98)	0.0140
The delayed injection of 1st dose of HBV vaccine	9.73 (1.78–53.21)	0.0087
The missing use of HBV vaccine after birth	8.29 (1.42–48.23)	0.0186

Li F, et al. Vaccine2012; 30:7118–22

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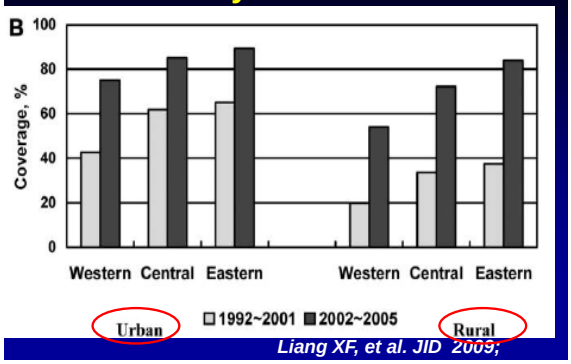
HBV Immunization Coverage of a Timely Birth Dose



Liang XF, et al. JID 2009;

Strategy to improve timely birth dose in China

- General approach: Build bridges between delivery service (MCH) and vaccination service (EPI)
  1. Initial assessment, with surveys
  2. Implementation
  3. Final evaluation
- Intervention strategies:
  1. Improve hospital delivery rate
  2. Training health care workers
  3. Increase awareness on importance of timely birth dose among parents
  4. Micro-plans to increase coverage among home births, including subsidy to providers

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Hepatitis B pilot projects in Western Provinces of China: Logic model

	Hospital delivery	Training- HCW	IEC- Population	Home delivery
Input	Subsidies	Material Experts	IEC Material	Posts Subsidies
Process	Promotion	Training sessions	Dissemination	Promotion
Output	Hospital delivery	Knowledge	Awareness	Vaccine delivery
Outcome	Birth dose timely administration- Completion of hepatitis B series			
Impact	Elimination of hepatitis B virus transmission			

Increasing hospital deliveries

- National policy
- Rural health insurance scheme
- Reimbursement of hospitalization expenses
- Financial incentive to pregnant women
- Other benefits:
  - Reduction of maternal mortality
  - Elimination of neonatal tetanus

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Strategies for infants born in hospitals

- Improve availability of vaccine
- Designate staff responsible to deliver birth dose
  - "Who delivers the infant should give the immunization"
- Strengthen communication between MCH and EPI
- Training for obstetric physicians and staff
- Registers to record delivery of timely birth dose
- Follow up using the triplicate-form for parents, hospital and village doctors
- Frequent monitoring of hospital performance

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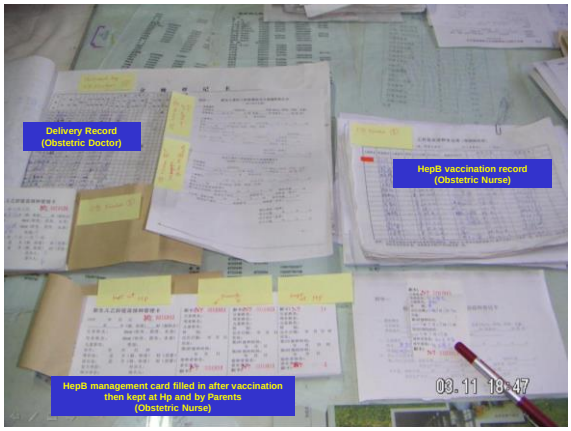

Strategies for infants born at home

- Education of health workers
- IEC for parents
- Pre-registration of pregnant women to guide timely birth dose in home births
- Timely notification of village doctors by birth attendant
- Availability of vaccine in village
- Subsidy to village doctors (only for birth dose)

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Demonstration projects for timely birth dose improvement, China, 2005-9

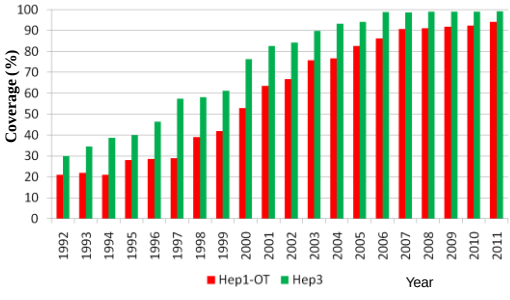
Projects	Timely birth dose coverage									Hospital deliveries		
	Hospital births			Home births			Overall					
	Initial	Final	+	Initial	Final	+	Initial	Final	+	Initial	Final	+
Qinghai 2005	95	98	3	29	70	41	51	82	31	33	43	10
Gansu2006-07	86	98	12	32	88	56	61	97	36	48	86	17
Gansu 2008-9	85	98	13	64	80	16	80	90	13	75	85	10
Ningxia 2006-07	98	100	2	9	29	20	71	88	17	67	83	16
Ningxia 2008-09	100	100	0	44	52	7	92	96	4	83	97	14

Scaled up in 13 GAVI project areas prefectures in 2008-2009 and in 29 others in 2010 (All with TBD<75%)

HBsAg prevalence according to place of birth and birth dose timing, 2006 serosurvey, China

	Timing birth dose	Specimen tested	Weighted HBsAg Prevalence	Prevalence ratio (95% CI)
County or above	Within 24 h	13,531	0.6	0.39 (0.36–0.39)
	After 24 h	2,692	1.7	Ref
Township	Within 24 h	6,381	1.2	0.73 (0.71-0.75)
	After 24 h	2,564	1.6	Ref
Home	Within 24 h	1,472	2.0	0.87 (0.75-0.95)
	After 24 h	2,482	2.3	Ref
Other	Within 24 h	141	2.3	0.84 (0.75-0.95)
	After 24 h	147	2.7	Ref
Total	Within 24 h	21,525	0.9	0.52 (0.51-0.53)
	After 24 h	7,885	1.9	Ref

Coverage of HepB Vaccine in Infants Increased 1992-2011



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WPRO HBV control goal

- In 2005 WPRO set goal of 2012: HBsAg<2% in children<5yrs
- China submitted application to WHO in March 2012

Dr Shin Young-soo, WPRO RD wrote to Dr Chen Zhu, Minister of MOH for achievement of HBV control in children, May 22, 2012,

Dr Shin Young-soo, WPRO RD presented Award to China for controlling HBV in children, Feb 24, 2014

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Conclusion: How did China managed high timely birth dose coverage?

- Full integration of hepatitis B in EPI, with GAVI support in Western Provinces
- Emphasis on institutional births where:
  - Timely birth dose is most effective
  - Coverage is easier to increase
- Initial timely birth dose demonstration projects in Western Areas to identify successful strategies
- Progressive scaling up

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Special thanks to
Dr FQ Cui from China CDC
Dr S Viktor from WHO
Prof H Zhuang, Prof J Li from Peking University

National Major Scientific Research Project- Prevention of MTCT of HBV

WHO WPRO Informal Technical Meeting
Manila, April 1-2, 2014

World Health Organization

World Hepatitis Alliance

World Hepatitis Day: July 28th, 2014