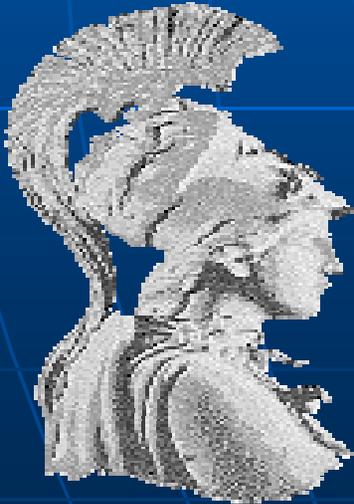


Hepatitis B vaccination and HBIG
administration policies implemented for
premature babies;
Vaccines concurrently administered with
the hepatitis B vaccine birth dose



Vana Papaevangelou
Pediatric ID specialist
Athens, Greece

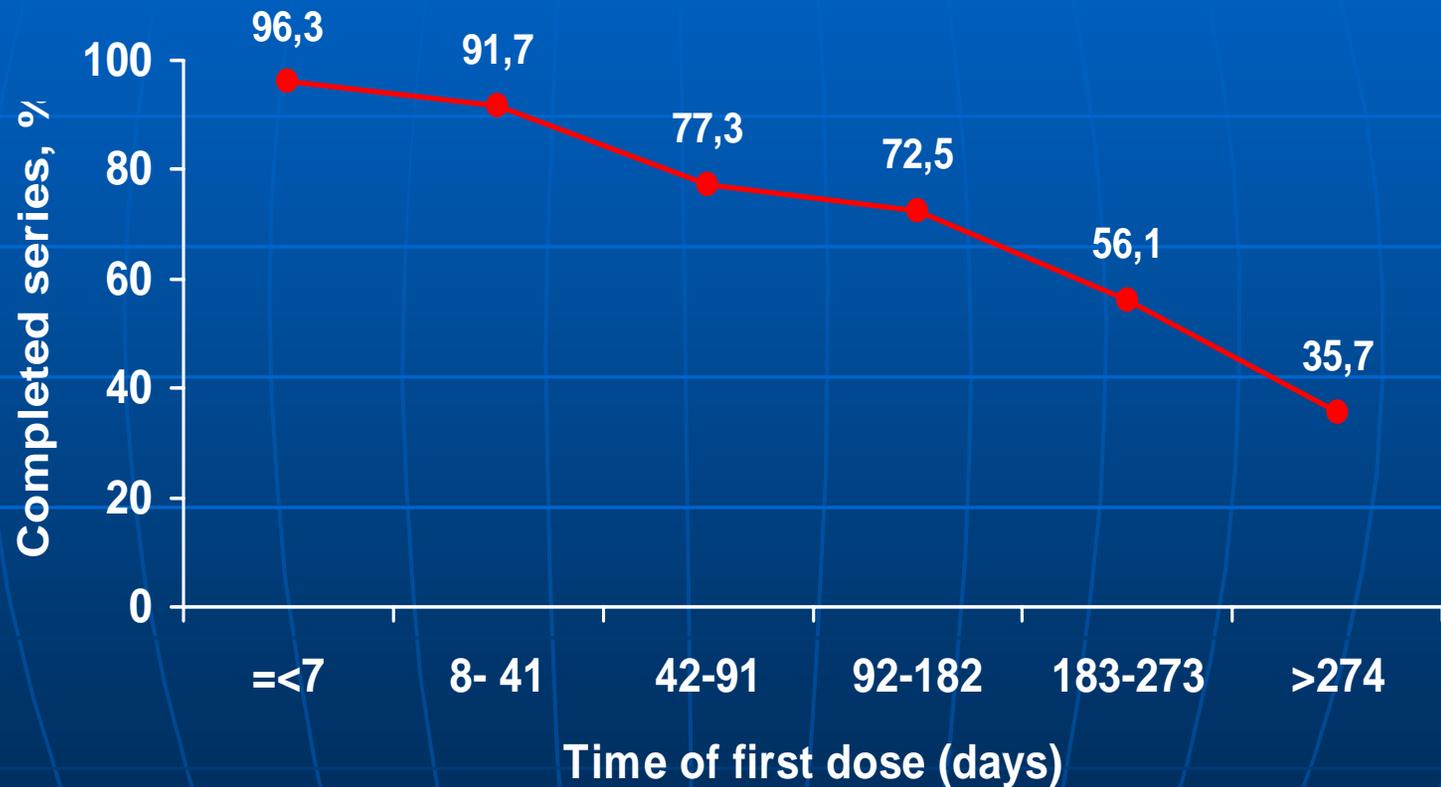
Immunization of preterm and low birth weight infants

- Preterm (PT, <37wks) and low birth weight (LBW, <2,500gm) infants are at greater risk of morbidity from vaccine preventable diseases.
- Gestational age (GA) and birth weight (BW) should not be limiting factors in delaying vaccination in clinically stable infants.
- Reduced or divided doses are not recommended and vaccines are generally well tolerated.

Hepatitis B vaccine

- The only vaccine recommended for administration at birth in developed countries:
- Although HBsAg screening of pregnant women is recommended, women without prenatal care have higher HBsAg seropositivity rates.
- Provides early protection in infants at risk for postnatal HBV transmission.
- HBV vaccine given closer to birth increases the likelihood of vaccination completion on time.

Completion of Hepatitis B Vaccine Series by Time of First Dose



Source: Yusuf H, et al, unpublished data, National Immunization Survey, 1998

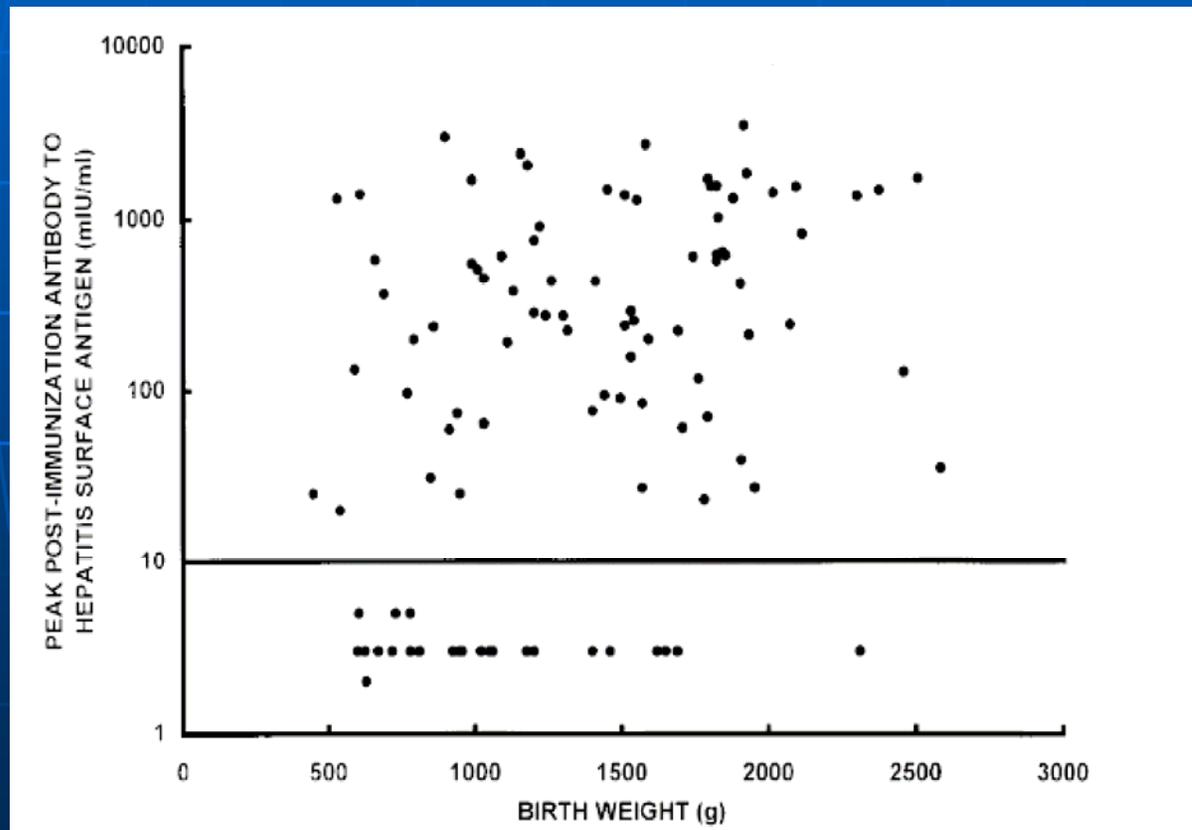
Seroconversion rates in PT and LBW infants after HBV vaccine at birth (I)

- In 1994 AAP recommended that in PT < 2,000g first dose is deferred if born to HBsAg(-) mothers based on:
- Lau et al: 99 PT with BW < 1,750g. vaccinated at birth

	<2,000g (N=57)	>2,000g (N=42)	Full Term (N=43)
Seroconversion rate (%) (95%CI)	78.9 (66.1-78.9)	90.5 (77.4-97.3)	100 (91.7-100)
HBsAb titer (miu/ml) (95%CI)	61 (27,138)	262 (101,680)	679 (265,1742)

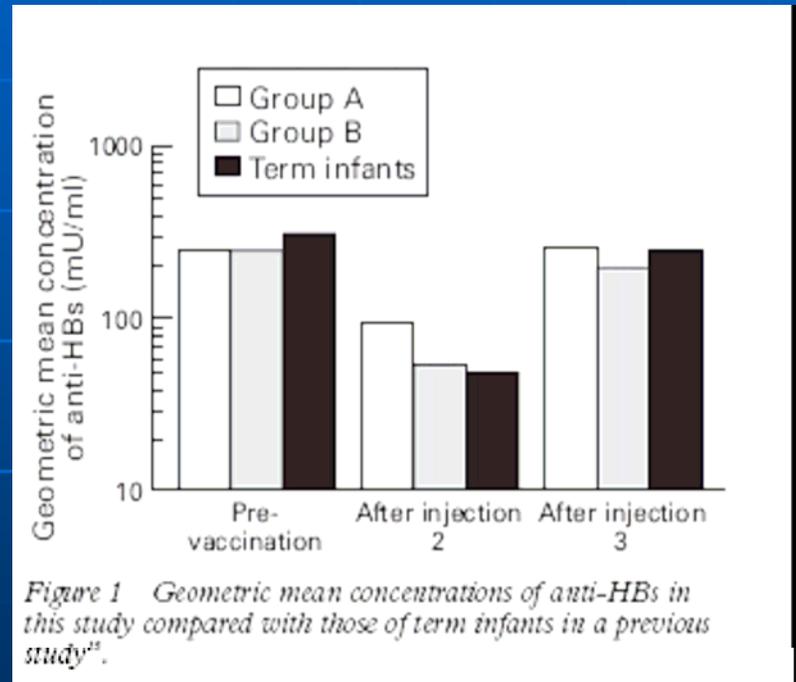
Peak HBs-antibody titers after 3 doses of hepB vaccine in PT infants

All infants vaccinated within first 7 days of life and tested 1 month post 3rd dose.



Deferring birth dose in low risk PT infants with $BW < 2,000g$

- Group A: $BW < 2,000g$ vaccinated at 1,2,7 months
- Group B: $BW > 2,000g$ vaccinated at 0,1,6 months



Hepatitis B vaccine: Follow up of PT infants at 3-3.5 yrs

Table 2

Percentage of children with positive antibody levels and GMC at 3-3.5 years of age.

Group	Group 1 Premature	P-value (1 vs 2)	Group 2 Premature	P-value (2 vs 3)	Group 3 Full term
Initial vaccination	At birth (n = 57)		At 2,000g (n = 40)		At birth (n = 39)
Positive AntiHBs (%) ^a	54.4	< 0.001	92.5	< 0.05	71.8
GMC (IU/l) mean (SD)	14.2 (11.1)	< 0.001	119 (4.8)	< 0.005	32.7 (9.2)

^a positive AntiHBs defined as ≥ 10 IU/l; AntiHBs: hepatitis B surface antibody; GMC: geometric mean concentration

Seroconversion rates in PT and LBW infants after HBV vaccine at birth (II)

- Many other studies (1997-1999) supported AAP recommendation for postponing birth dose of HBV vaccine in PT/LBW infants (<2,000g) born to HBsAg (-) mothers.
- Additional risk factors identified for inadequate immunogenic response:
 - Poor weight gain
 - Steroid use
- All studies showed good immunologic response when first dose administered at 1 month regardless of GA or BW.
- Need to protect infants exposed to multiple blood products and surgical interventions.

Recommendations for hepatitis prophylaxis in PT and LBW infants born to HBsAg (-) mothers

Infants with BW < 2,000g

- Dose 1 at 30 days of age or before discharge if earlier.
- Total of 3 doses at 1-2, 2-4, and 6-18 mos.
- May use combination vaccines
- No need for post – vaccination testing.

Infants with BW > 2,000g

- Dose 1 at birth or when medically stable.
- Total of 3 doses at 1-2, 2-4, and 6-18 mos.
- May use combination vaccines
- No need for post – vaccination testing.

Recommendations for hepatitis prophylaxis in PT and LBW infants born to HBsAg (+) mothers

Infants with BW < 2,000g

- HBIG + HepB vaccine within 12h of birth.
- Immunize with 4 doses: 0, 1, 2-3, 6-7 mos
- Check HBsAg and anti-HBs at 9-15 mos
- If negative re-immunize with 3 doses at 2 mos intervals and retest.

Infants with BW > 2,000g

- HBIG + HepB vaccine within 12h of birth.
- Immunize with 3 doses: 0, 1, 6 mos
- Check HBsAg and anti-HBs at 9-15 mos.
- If negative re-immunize with 3 doses at 2 mos intervals and retest.

Recommendations for hepatitis prophylaxis in PT and LBW infants born to a mother with **unknown HBsAg status**

Infants with BW < 2,000g

- HepB vaccine (by 12h)
- If mother's HBsAg not available by 12h give also HBIG.
- Vaccinate with 4 doses total.

Infants with BW > 2,000g

- HepB vaccine (by 12h)
- Can wait for mother's HBsAg status up to 7 days.
- Vaccinate with 3 doses total.

Hepatitis B prophylaxis in PT and LBW infants

CONCLUSIONS (I)

- Evaluating medical condition of newborn.
- Screening HBsAg status of the mother^{*}. If testing not available administer birth dose.
- May defer birth dose to 30 days of age if low risk infant with $BW < 2,000g$.
- Newborns born to mother with HBsAg (+) or unknown status, should be vaccinated at birth and receive total 4 doses^{*} (0,1,2-3,6-7mos) if $BW < 2,000g$. If limited resources available 3 vaccine doses should be given?

^{*} If resources available

Bhave S et al, Indian Pediatrics 2002,
Ballesteros-Trujillo A, et al. Amer J Perinatol 2001

Hepatitis B prophylaxis in PT and LBW infants

CONCLUSIONS (II)

- HBIG (0,5ml) IM should be administered to all newborns needing post-exposure prophylaxis irrespective of GA or BW*.
- Use of needles of 5/8 inch length.
- Alternative 4 dose schedules have been tested in PT (0,1,5,9 or 0,1,2,12)

* If resources available

Bhave S et al, Indian Pediatrics 2002,
Ballesteros-Trujillo A, et al. Amer J Perinatol 2001

Hepatitis B prophylaxis in PT infants:

Suggested recommendations for areas with limited resources

- Hepatitis B vaccine can be safely administered in PT infants at birth.
- If maternal HBsAg screening not available, hepatitis B vaccine birth dose should be administered to all PT newborns.
- If HBIG available, administer 0.5ml, irrespectively to GA and BW, to all PT needing post-exposure prophylaxis.
- In PT infants with $BW < 2,000g$, 4 doses of hepatitis B vaccine should be administered.

Vaccines concurrently administered with hepatitis B birth dose

- Data on

- BCG

- IPV

Co-administration of hepB and BCG in newborns

Table 1 Immune response to BCG: vaccinal lesions and tuberculin reactions in infants immunized at birth with BCG simultaneously or not with hepatitis B vaccine

	Months post BCG vaccination	BCG + HB (<i>n</i> = 38) (%)	BCG (<i>n</i> = 40) (%)
Vaccinal lesions	2	32 (84)	36 (90)
	3	35 (92)	35 (88)
	4	25 (66)	31 (78)
Tuberculin reaction	6		
	Size >6 mm	26 (68)	31 (77.5)
	Mean size (mm)	8.5	9.6
	95% confidence limits (mm)	6.9-10.1	7.7-11.6

Co-administration of hepB and BCG in newborns

Table 3 Anti-HBs response after primary immunization starting at birth

Group	No. of children	Vaccine	Anti-HBs antibody titres		
			> 10 mIU ml ⁻¹ No. (%)	Geometric mean (mIU ml ⁻¹)	95% confidence limits (mIU ml ⁻¹)
A	33	BCG + HB	29 (87.9)	90	46-177
B	31	HB	25 (80.6)	93	40-218

Influence of BCG on antibody and cytokine responses to neonatal vaccination

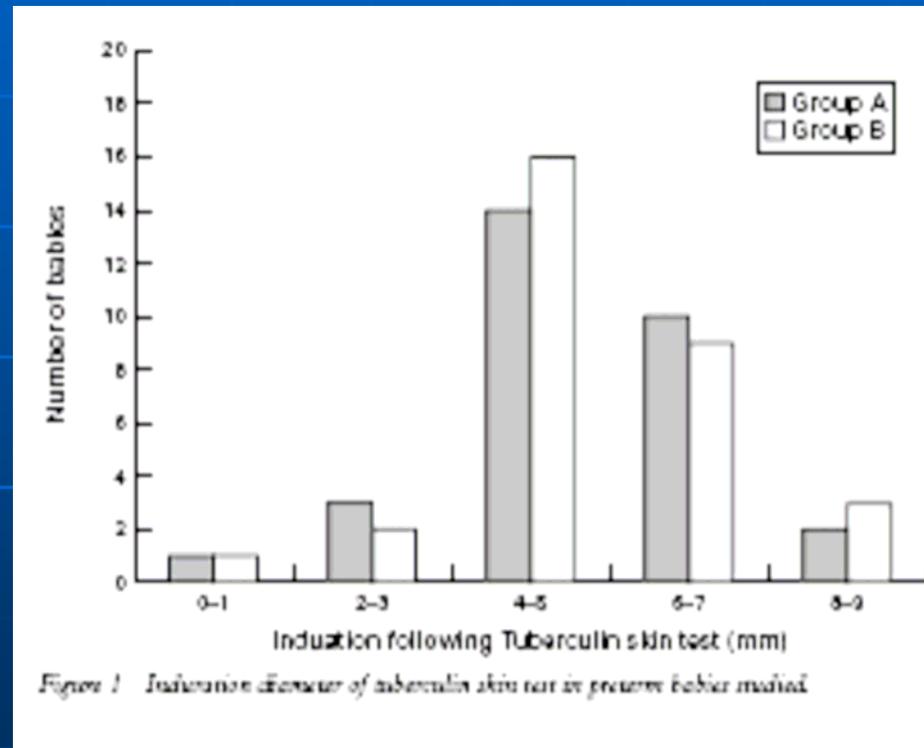
- BCG induces potent Th1 response to mycobacterial antigens in newborns.
- When BCG was administered at birth together with OPV and HepB vaccine in 35 newborns it increased cellular and Ab responses to HBV and Ab response to oral polio vaccine.
- Promoted Th1 and Th2 response to unrelated vaccines through maturation of dendritic cells.

BCG vaccination in PT infants

62 PT <35wks
vaccinated with BCG at
postconceptional age of:

- Group A: 34-35wks
- Group B: 38-40wks

Saliou P et al: BCG should
not be given at birth in
PT <33 wks GA



Co-administration of hepB and IPV in PT infants

- In Israel outbreak of polio type 1 in 1998 had as victim an unvaccinated 2mos.
- ~50% of PT <1:8 Ab titer to polio.
- 50 PT (30-35wksGA, >1,000g) received IPV+HepB vaccine at birth and compared with PT and FT infants receiving only HepB vaccine at birth and IPV at 2 mos.
- Safe and effective way providing protection from both diseases.

Vaccines concurrently administered with hepatitis B birth dose

- Both BCG and IPV can be co-administered at birth with hepatitis B vaccine with similar immune responses to those observed after separate administration of each vaccine.
- No study of co-administration of BCG and HepB in PT infants.