

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



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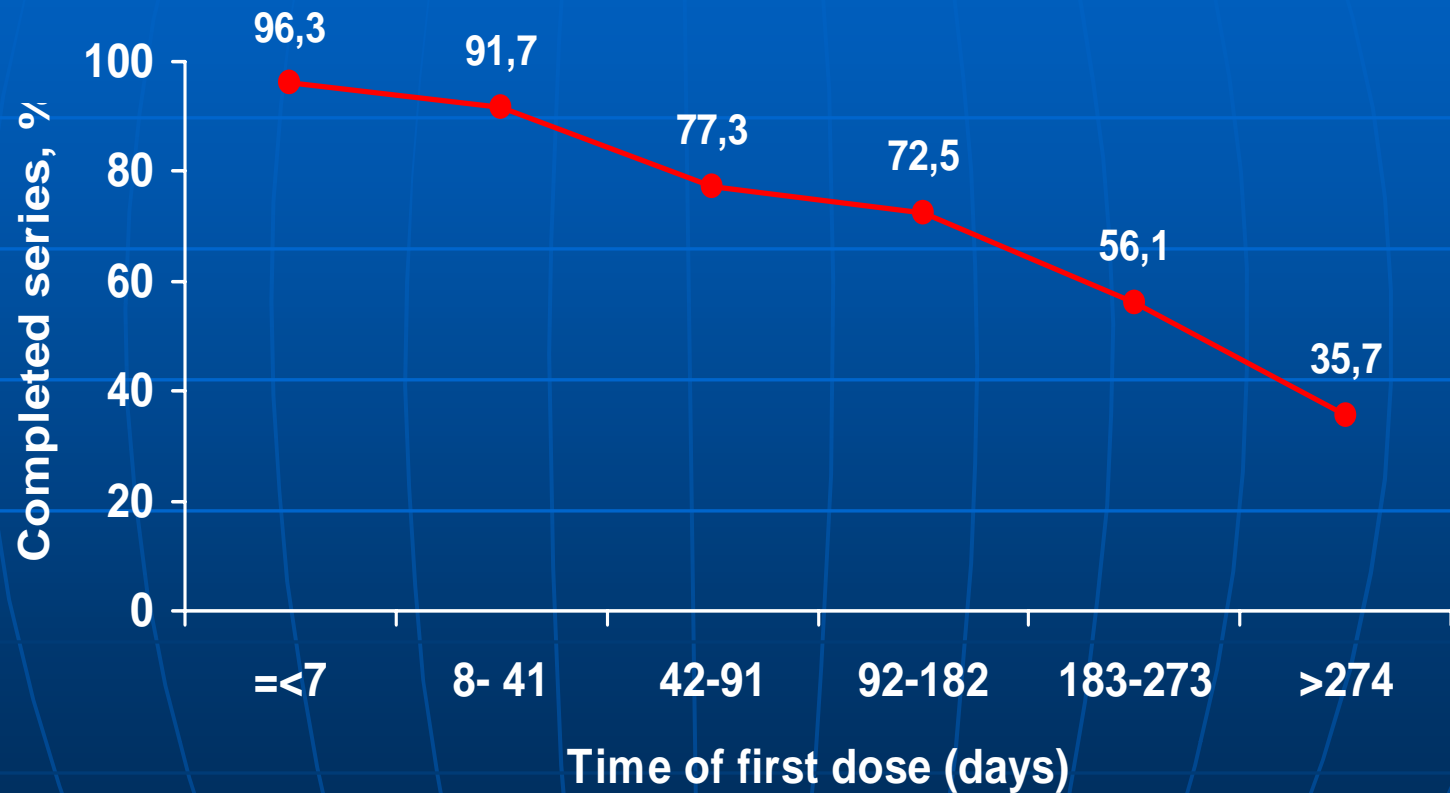
# Immunization of preterm and low birth weight infants

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Source: Yusuf H, et al, unpublished data, National Immunization Survey, 1998

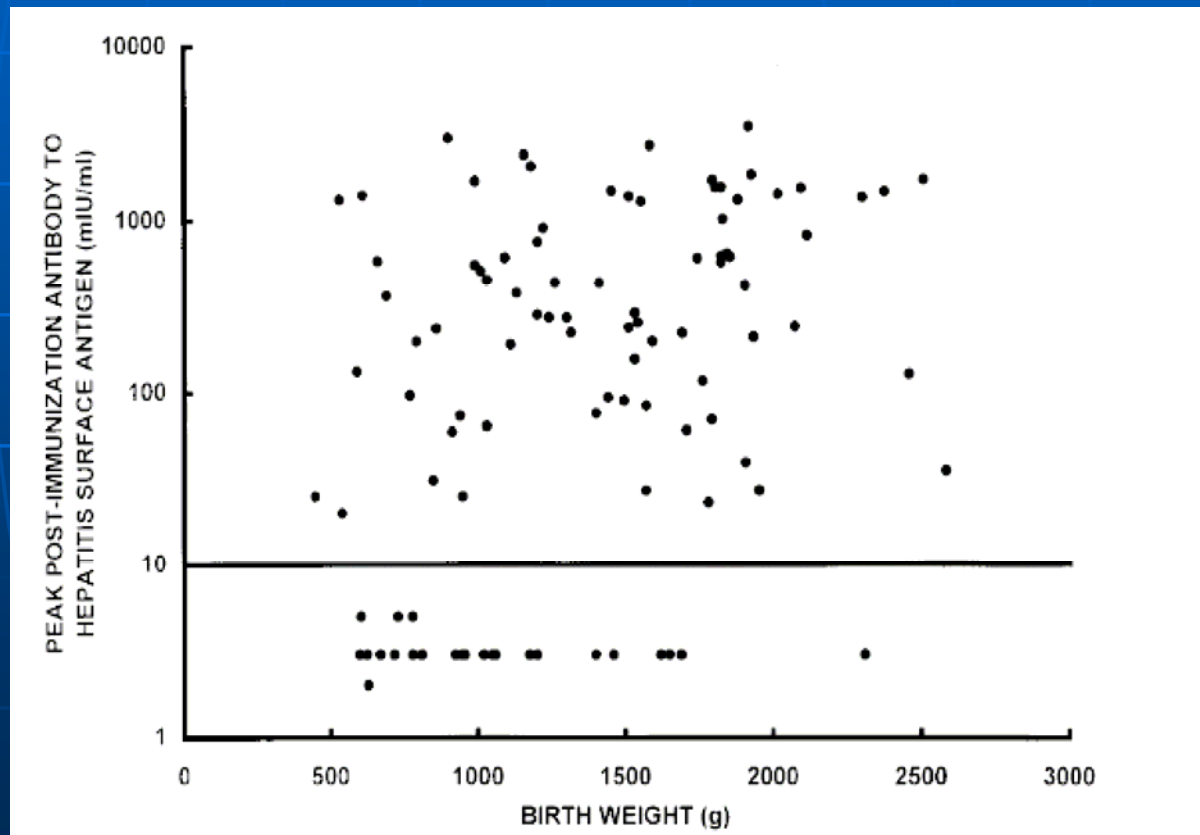
# Seroconversion rates in PT and LBW infants after HBV vaccine at birth (I)

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

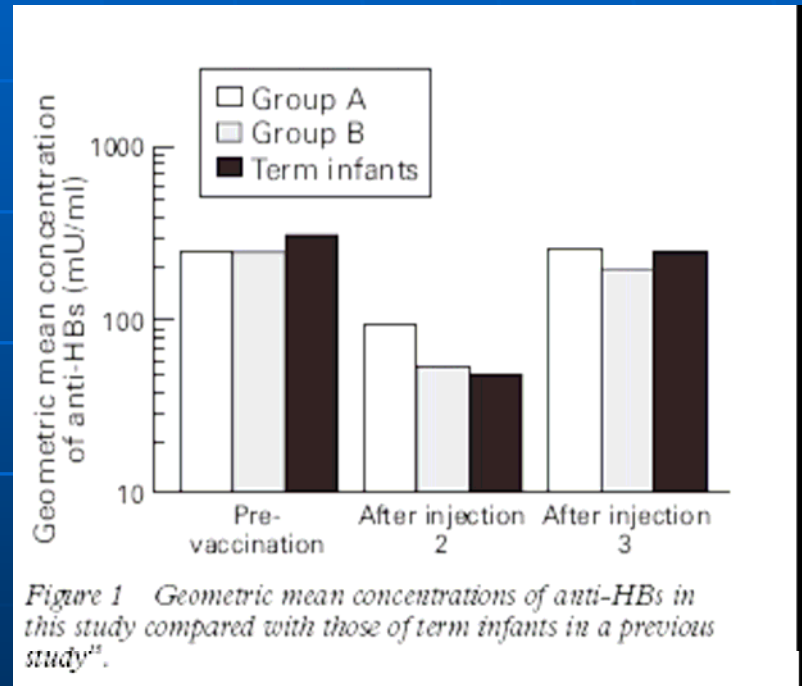
# Peak HBs-antibody titers after 3 doses of hepB vaccine in PT infants

All infants vaccinated within first 7 days of life and tested 1 month post 3<sup>rd</sup> 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<br>Premature | P-value<br>(1 vs 2) | Group 2<br>Premature  | P-value<br>(2 vs 3) | Group 3<br>Full term |
|-----------------------------------|----------------------|---------------------|-----------------------|---------------------|----------------------|
| Initial vaccination               | At birth<br>(n = 57) |                     | At 2,000g<br>(n = 40) |                     | At birth<br>(n = 39) |
| Positive AntiHBs (%) <sup>a</sup> | 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)           |

<sup>a</sup> positive AntiHBs defined as  $\geq 10$  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<sup>\*</sup>. 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<sup>\*</sup> (0,1,2-3,6-7mos) if  $BW < 2,000g$ . If limited resources available 3 vaccine doses should be given?

<sup>\*</sup> 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<br>( <i>n</i> = 38)<br>(%) | BCG<br>( <i>n</i> = 40)<br>(%) |
|----------------------------|-----------------------------|-------------------------------------|--------------------------------|
| 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<br>mIU ml <sup>-1</sup><br>No. (%) | Geometric<br>mean<br>(mIU ml <sup>-1</sup> ) | 95%<br>confidence<br>limits<br>(mIU ml <sup>-1</sup> ) |
| 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

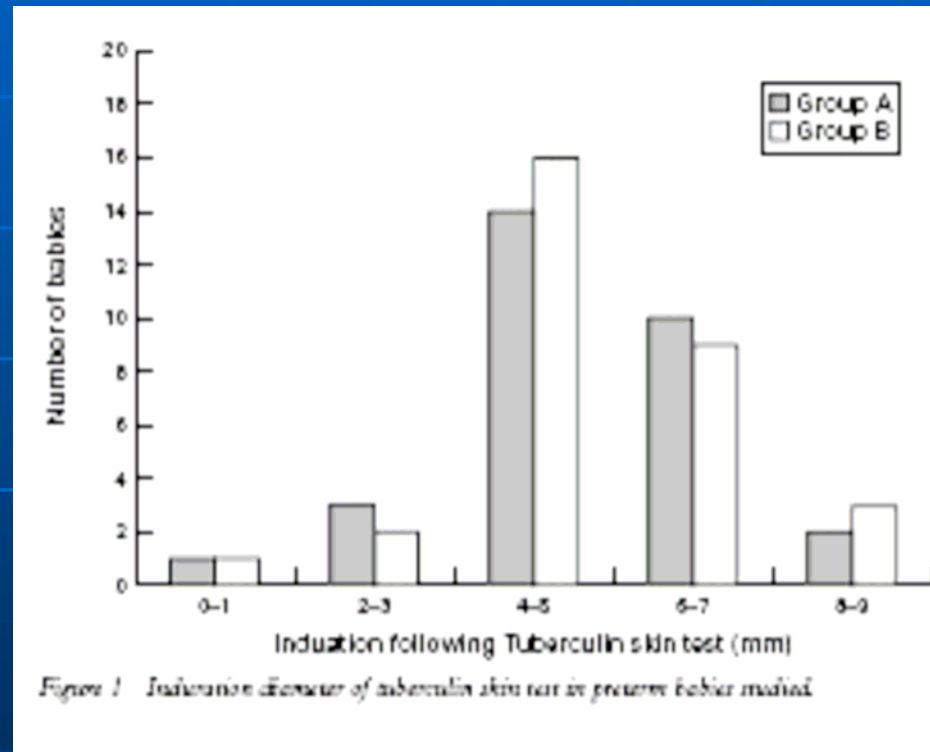
- BCG induces potent Th1 response to mycobacterial antigens in newborns.
- When BCG was administered at birth together with OPV and HepB vaccine in 35 newborns it increased cellular and Ab responses to HBV and Ab response to oral polio vaccine.
- Promoted Th1 and Th2 response to unrelated vaccines through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