Hepatitis B vaccine alone or with HBIG in neonates of HBsAg+/HBeAg- mothers: a systematic review and meta-analysis.

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	Maternal screening	Infant		Cost	Efficacy	Example
		Vaccine	HBIG			
<ol> <li>Active Only</li> <li>Active + Passive</li> </ol>	No	Yes	No	Lower	Modest	Thailand
Туре І	HBsAg and HBeAg	Yes	Infants of HBeAg(+), HBsAg(+) mothers	Higher	High	Taiwan
Туре II	HBsAg only	Yes	Infants of HBsAg(+) mothers	Highest	High	USA

#### **Table 3**Different strategies for HBV immunisation, their costs and efficacy

Active immunization = hepatitis B vaccines. Passive immunization = hepatitis B immunoglobulin (HBIG). HBV, hepatitis B virus; HBeAg, hepatitis B surface antigen.

Hepatitis B vaccine alone or with HBIG in neonates of HBsAg+/HBeAg- mothers

An ongoing debate.....

### Hepatitis B vaccine alone or with HBIG in neonates of HBsAg(+)/HBeAg (-) mothers: a systematic review and meta-analysis

### HBsAg (+) in infants >1 month of age



Machaira M et al. JAC 2014

### Hepatitis B vaccine alone or with HBIG in neonates of HBsAg(+)/HBeAg (-) mothers: a systematic review and meta-analysis

### Seroprotection rate (anti-HBsAg ≥10 IU/L)



Machaira M et al. JAC 2014

# Other studies/meta-analysis

### • 29 studies; only 3 included infants of HBeAg(-) mothers

- Compared with vaccine alone, vaccine + HBIG reduced hepatitis B occurrence (0.54, 95%CI= 0.41 to 0.73; 10 trials).
- **Concluded**: Evidence on immunization for infants of mothers HBsAg(+)/HBeAg(-) is weak.
- Retrospective study of 2356 infants born to HBsAg(+) women.
  - HBIG did not appear to reduce the rate of chronic HBV infection (0.29% versus 0.14%; p=0.65) in infants born to HBeAg(-)mothers, but might prevent infantile fulminant hepatitis.

Lee et al BMJ 2006 Chen et al Gastrenterology 2012

# Most recent studies (I)

### • Multicenter prospective study in China (2008-2013)

#### Table 2

HBIG to neonates on preventing HBV mother-to-infant transmission (n = 1202).

Neonate	Mother HBeAg(+	-)	Mother HBeAg(–)		
	n	Infant infected HBV n(%)	n	Infant infected HBV n(%)	
Vac	65	11(16.9%) <sup>c</sup>	123	0	
Vac + HBIG	367	<b>29</b> (7.9%) <sup>d</sup>	647	0	

Vac: HB vaccine; comparison between c and d,  $^2 = 5.349$ , p = 0.021.

• The anti-HBs positive rate was 83.6% in infants given HBV vaccine only and 84.7% in infants who received HBIG plus HBV vaccine, p = 0.721.

# Most recent studies(II)

- Comparison between two regions where # policies exist (>880 babies born to HBeAg(-) mothers).
- No differences were revealed regarding the occurrence of perinatal HBV transmission with (0.1%) or without HBIG at birth (0%)
- At 7 months of age, the anti-HBs response rates were 97.7% and 98.5% for the neonates with vaccine alone and with HBIG (p=0.758), respectively.
- At 12months of age, protective levels of anti-HBs remained in 97.4% and 98.3% of the neonates receiving or not receiving HBIG, respectively (p=0.771).
- Moreover, the neonates receiving combined prophylaxis had a markedly lower anti-HBs GMC (210.7mIU/mL vs. 297.0mIU/mL, p=0.011).
- Vaccine alone may be enough for preventing HBV transmission in neonates of HBsAg (+)/HBeAg (-) mothers.

# Conclusions

Although there is evidence indicating that combined active-passive immunoprophylaxis is of limited benefit to infants born to HBsAg(+)/HBeAg(-) mothers.....

Most experts are supporting current guidelines of combined immunoprophylaxis due to:

- Additional screening for HBeAg might be difficult to implement and might cause missed opportunities to provide appropriate prophylaxis
- Low but existing risk of fulminant hepatitis in these infants
- More data will be available if extended screening of VL is implemented

Adherence to perinatal hepatitis B prevention programmes

Adherence to perinatal hepatitis B prevention programme in Greece

- 1.1.1998: Universal screening of pregnant women and administration of passive-active immunoprophylaxis to newborns of HBsAg(+) mothers.
- 5 years later (17-30 March 2003) we conducted a National observational study to assess adherence to guidelines.
- One contact person/ maternity clinic responsible for collection of:
  - Demographic data
  - Prenatal care prenatal HBsAg screening
  - Screening in delivery room
  - Timely administration of immunoprophylaxis

### Adherence to perinatal hepatitis B prevention programme in Greece

ORIGIN	No (%)	Prevalence of HBsAg(+)**	Prenatal screening for HBsAg
GREEK	3007 (79.97%)	46/2705(1.7%)***	2467/2641(93.4%)***
ALBANIAN	409 (10.88%)	36/368(9.8%)	227/288 (78.8%)
IMMIGRANT*	258 (6.86%)	l 3/228(5.7%)	104/119 (87.4%)
ROMA	86 (2.28%)	3/ <u>83(3.6%)</u>	31/43 (72.1%)
TOTAL	3760	98/3384(2.89%)	2856/3128 (91.3%)

#### Table I: Study population, prevalence of HBsAg(+) and prenatal screening for HBsAg by origin.

 $^{*}$  other than Albanian

\*\* Total prevalence in women tested either prenatally or perinatally

\*\*\* Statistically significant difference among Greek women versus non-Greek in HBsAg (+) prevalence and in prenatal screening was p < 0.001.

- Women tested in delivery room with higher HBsAg(+) prevalence (4.2% vs 2.3%, p=0.1)
- 122 women (3.2%) never tested.
  - Delivery in public hospital
  - Maternal illiteracy
  - No association with ethnicity or maternal age

Papaevangelou V et al. BMC ID 2006 Stroffolini T et al Vaccine 2003

### Other EU studies

- **Denmark:** Retrospective study of 700 children born to HBsAg(+). Guidelines issued in 2005
  - 93% of the children were vaccinated within 48 hours of birth.
  - 64% of the children fully vaccinated at the age of two years, and
  - 10% of the children had received **no** hepatitis B vaccinations at all.
  - No or few prenatal examinations was a risk factor for incomplete vaccination.

# Migrants in Europe

- NHS data and online questionnaire for GPs were used
  - **12%** of migrants for whom HBV testing was recommended were 'HBV- tested'.
  - HBV testing coverage was: Eastern Africa 20%; Western Africa 15%; South Eastern Asia 9%; Eastern Asia 5%.
  - Most GPs stated that workload and lack of human, and financial resources were the most significant barriers to increased testing.
- Online survey was sent to experts in health care services involved in screening or treating viral hepatitis in: Germany, Hungary, Italy, the Netherlands, Spain and the United Kingdom (UK).
  - Pronounced differences in availability of interpreters and translated materials
  - Improved language support is needed given the complex natural history of hepatitis B/C, the recognized barriers to screening and care, and the large undiagnosed burden among (potentially) linguistic minority migrant groups.

Evlambidou et al. British Journal of General Practice 2016 Falla et al. BMC Health Services Research 2017 Antenatal maternal Hepatitis B care is a predictor of timely perinatal administration of Hepatitis B immunoglobulin.

- Retrospective cohort study (Australia) to assess adherence to universal guidelines.
- 451 CHB mothers delivered 454 live births.
- HBV immunoglobulin (HBIg) was dispensed within 12 hours in **79.5%** of births. HBIg was not administered to 8 neonates.
- 125/451 women were interviewed: **88.8%** of babies completed the vaccine schedule and **19.2%** of infants had post-vaccination testing.
- Antenatal HBV care was independently associated with a greater likelihood of timely HBIg administration (odds ratio 1.64, p=0.04, 95% CI:1.03-2.61).

## Endemic areas ?

- China: retrospective study on 300 infants born to HBsAg(+) mothers
  - HBsAg screening was performed only in 156 (52.3%) of the carrier mothers.
  - Only 112 (37.6%) of HBV-exposed infants received HBIG after birth.
  - 15.1% of HBV-exposed infants did not receive the timely birth dose.
  - In **10/11 HBV infected children**: delayed vaccination and no HBIG noted
  - Good vaccine coverage overall (>94%)



# Thank you for your attention