Mother-to-child transmission of hepatitis B in sub-Saharan Africa

1 June 2017
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Institut Pasteur, Paris
• Epidemiology of HBV in sub-Saharan Africa

• Why is the PMTCT of HBV important?

• Current situations and challenges in implementing PMTCT in sub-Saharan Africa
Modes of Transmission

East Asia

- Childhood (60%)
- MTCT (40%)

Sub-Saharan Africa

- Childhood (90%)
- MTCT (10%)

Edmunds WJ et al., Epidemiol Infect, 1996
Sero-prevalence in children

MTCT

Horizontal transmission

The Gambia

Anti-HBc (+) only

HBsAg(+) HBeAg(-)

HBsAg(+) HBeAg(+)

Whittle H et al., J Infect Dis, 1990
### Determinants of frequency of MTCT

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WHO, 1990  
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### Risk of MTCT from HBsAg(+) HBeAg(+) mothers

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<td>Marinier, 1985</td>
<td>3/15</td>
<td>0.20 (0.07, 0.45)</td>
</tr>
<tr>
<td>Greenfield, 1986</td>
<td>1/2</td>
<td>0.50 (0.09, 0.91)</td>
</tr>
<tr>
<td>Grathwohl, 1992</td>
<td>1/1</td>
<td>1.00 (0.21, 1.00)</td>
</tr>
<tr>
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<td>2/2</td>
<td>1.00 (0.34, 1.00)</td>
</tr>
<tr>
<td>Menendez, 1999</td>
<td>3/14</td>
<td>0.21 (0.08, 0.48)</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td></td>
<td><strong>0.38 (0.07, 0.74)</strong></td>
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### Risk of MTCT from HBsAg(+) HBeAg(-) mothers

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<tr>
<td>Marinier, 1985</td>
<td>0/62</td>
<td>0.00 (0.00, 0.06)</td>
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<td>Greenfield, 1986</td>
<td>7/49</td>
<td>0.14 (0.07, 0.27)</td>
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<td>Tsega, 1988</td>
<td>1/20</td>
<td>0.05 (0.01, 0.24)</td>
</tr>
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<td>Roingeard, 1993</td>
<td>2/19</td>
<td>0.11 (0.03, 0.31)</td>
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<td>1/34</td>
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Keane E, Funk AL, Shimakawa Y. Aliment Pharmacol Ther, 2016
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<td>70-90%</td>
<td>38%</td>
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<td>5-30%</td>
<td>5%</td>
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Keane E, Funk AL, Shimakawa Y. Aliment Pharmacol Ther, 2016
Compared to Asia, the frequency of MTCT in sub-Saharan Africa was low.

However, its prevention is still important in Africa for two reasons.
1. Risk factor for chronic infection

2. Risk factor for Liver Disease

• Longitudinal population-based study in The Gambia

• People with chronic HBV infection
  – 88 born to HBV-infected mothers
  – 165 born to non-infected mothers

• After 28 years of follow-up
Cumulative incidence of seroclearance by maternal HBsAg

HBeAg seroclearance

Born to non-infected mothers

Born to HBV-infected mothers

HBsAg seroclearance

Shimakawa Y et al., Gut, 2016
## Incidence of liver cancer

<table>
<thead>
<tr>
<th>Maternal HBV status</th>
<th>Person-years at risk</th>
<th>No. of events</th>
<th>Rate</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>4 720</td>
<td>0</td>
<td>0 / 100 000</td>
<td>N/A</td>
</tr>
<tr>
<td>Positive</td>
<td>2240</td>
<td>2</td>
<td>89 / 100 000</td>
<td>22-356</td>
</tr>
</tbody>
</table>

## Prevalence of significant liver fibrosis

<table>
<thead>
<tr>
<th>Maternal HBV status</th>
<th>Proportion</th>
<th>Adjusted OR</th>
<th>95% CI</th>
<th>p</th>
</tr>
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<tbody>
<tr>
<td>Negative</td>
<td>4%</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>15%</td>
<td>5.0</td>
<td>1.6-15.4</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Shimakawa Y et al., Gut, 2016
Chronic HBV infection and Horizontal transmission.

Horizontal transmission: 63% 
MTCT: 16%

Shimakawa Y et al., Gut, 2016
Shimakawa Y et al., Lancet Infect Dis, 2016
It is critical to prevent HBV MTCT in Africa to achieve the WHO’s global elimination strategy to reduce:

- Incidence of new chronic infection
- Mortality from chronic infection
HBV MTCT IS A NEGLECTED PROBLEM IN AFRICA
Hepatitis B vaccine

• Integrated in the national program in all the African countries
• Coverage in Africa: 76%  
  WHO, Wkly Epidemiol Rec, 2016
• As a combined vaccine: 6-10-14 wks
  – Pentavalent (DTaP-Hib-HepB)
  – Hexavalent (DTaP-Hib-IPV-HepB)
• Vaccine failure: 1%
  – Majority (60-90%) are due to MTCT before the vaccine was given
  Ekra D et al., Vaccine, 2008
  Mendy M et al., Plos One, 2013
  Shimakawa Y et al., Gut, 2016
Only 10 countries in sub-Saharan Africa adopted birth dose vaccine

Why?

• GAVI does not support monovalent hep B vaccine
• Importance of HBV PMTCT has been poorly recognized
• Logistical challenges where the majority of women deliver their children at home

Kramvis A & Clements CJ, Vaccine, 2010
Shimakawa Y et al., BMC Public Health, 2014
Shimakawa Y et al., Gut, 2016
MTCT in sub-Saharan Africa

HBV > HIV

- Estimated number of infants infected in sub-Saharan Africa each year

Keane E, Funk AL, Shimakawa Y, Aliment Pharmacol Ther, 2016
BARRIERS TO TIMELY ADMINISTRATION OF BIRTH DOSE
Birth dose vaccine coverage
The Gambia (WHO/UNICEF)
Barriers to timely administration of birth dose vaccines in The Gambia, West Africa

Reiko Miyahara\textsuperscript{a,b,c}, Momodou Jasseh\textsuperscript{a}, Pierre Gomez\textsuperscript{a}, Yusuke Shimakawa\textsuperscript{d},

• Only 1% are vaccinated at birth
  – Home birth 1.3%
  – Facility birth 0.6%
Low coverage even in facility-birth

• Hospital
  – No hep B vaccine (as there is no EPI team)

• Health Centers
  – There are vaccines, but no communication between maternity staff & EPI staff (two vertical programs)

• Reluctance of EPI staff to open multi-dose vial (10 doses/vial)
  – Although opened vial can be used for 28 days under the cold chain

Miyahara R, et al., Vaccine, 2016
WHO, 2014
NéoVac

Neonatal Vaccination Against Hepatitis B in Africa

• To develop and evaluate a community-based intervention to improve the coverage of:
  – A timely birth dose of Hep B vaccine
  – Neonatal care practices that can improve child survival

• Senegal / Burkina Faso / Madagascar
OTHER PREVENTIVE MEASURES
HBeAg+ mothers, Asia

No prophylaxis: 70-90%
Timely birth dose vaccine alone: 20%
Timely birth dose vaccine + HBIG: 5-10%
Timely birth dose vaccine + HBIG + antiviral Tx during pregnancy: <2%

HBeAg- mothers, Asia

No prophylaxis: 5-30%
Timely birth dose vaccine: <0.5%

Lee C et al., Cochrane Database Syst Rev, 2006
Machaira M et al., J Antimicrob Chemother, 2015
Keane E, Funk AL, Shimakawa Y. Aliment Pharmacol Ther, 2016
HBeAg+ mothers, Asia

20%

5-10%

<2%

HBeAg+ mothers, Africa

20%

5-10%

<2%

HBeAg- mothers, Asia

5-30%

<0.5%

HBeAg- mothers, Africa

<0.5%

No prophylaxis

Timely birth dose vaccine alone

Timely birth dose vaccine + HBIG

Timely birth dose vaccine + HBIG + antiviral Tx during pregnancy

Lee C et al., Cochrane Database Syst Rev, 2006
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HBeAg+ mothers, Asia: 70-90%
HBeAg+ mothers, Africa: 20%
HBeAg- mothers, Asia: 5-10%
HBeAg- mothers, Africa: <2%

Timely birth dose vaccine alone:
- HBeAg+ mothers, Asia: 32%
- HBeAg+ mothers, Africa: 5-30%
- HBeAg- mothers, Asia: <0.5%
- HBeAg- mothers, Africa: 0%

Timely birth dose vaccine + HBIG:
- HBeAg+ mothers, Asia: <2%
- HBeAg+ mothers, Africa: <0.5%
- HBeAg- mothers, Asia: 0%
- HBeAg- mothers, Africa: 0%

Timely birth dose vaccine + HBIG + antiviral Tx during pregnancy:
- HBeAg+ mothers, Asia: 70-90%
- HBeAg+ mothers, Africa: 20%
- HBeAg- mothers, Asia: 5-10%
- HBeAg- mothers, Africa: <2%

References:
Lee C et al., Cochrane Database Syst Rev, 2006
Machaira M et al., J Antimicrob Chemother, 2015
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Need for additional preventive measures

- Hepatitis B immunoglobulin (HBIG)
  - Not practical in Africa
  - Cost / limited supply / safety

- Antiviral treatment during pregnancy
  - Attractive for Africa
    - % women delivering baby at health facilities: 50%
    - % women attending at least one ANC: 78%
  - Generalizability of Asian studies to African context
    - BD + HBIG + Antiviral Tx
Conclusions

• MTCT is less frequent in Africa than in Asia
• But, MTCT is responsible for 2/3 of HBV-related liver disease in Africa
• Birth dose vaccine is not well implemented
• Additional intervention may be necessary for those born to HBeAg(+) mothers
• Need for African model?
  – Antiviral Tx + birth dose vaccine
  – Antiviral Tx alone (without birth dose vaccine)
Thank you

- MRC Unit, The Gambia
  - Dr. Ramou Njie
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- LSHTM
  - Dr. Christian Bottomley
  - Prof. Hilton Whittle
  - Sir Andrew Hall
- IARC/GHIS
  - Dr. Maimuna Mendy
- Inserm
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  - Dr. Elizabeth Keane
  - Ms. Anna Funk
  - Prof. Arnaud Fontanet
- Institut Pasteur de Dakar
  - Dr. Muriel Vray
- IRD, Dakar
  - Dr. Cheikh Sokhna
  - Dr. Aldiouma Diallo
  - Dr El-Hadji Ba
- LAMIVAC (AMP & Centre Muraz)
  - Dr. Edouard Betsem
  - Dr. Espérence Ouedraogo
  - Prof. Nicholas Meda
- Institut Pasteur de Madagascar
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  - Dr. Rila Ratovoson
  - Dr. Dolorès Pourette
- European Union
- Total Foundation