Modelling the transmission and prevention of HBV: Can we meet goals for elimination by 2030?

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Aim to ‘eliminate HBV as a public health problem by 2030’
Challenges

- Endemic in many populations
  - 250 million chronically infected
  - >90% not diagnosed
  - 1/3 of world’s population has been exposed
- Co-evolution with *Homo sapiens*
- Complex biology: cccDNA reservoir
- No good animal model
- Complex social challenges: poverty, stigma, beliefs and behaviour
- High disease burden: HCC rates are increasing
- Overlap with HIV, e.g. in South Africa
What’s in the toolbox?

Antiviral drugs
3TC/TDF/ETV

- Relies on diagnosis
- Are drugs available?
- Suppressive not curative

PMTCT
TDF/HBIg/Vaccine

- Relies on diagnosis
- Are drugs available?

Infant vaccination
3 doses from birth

- Relies on coverage
- Impact of HIV?


Image credit: http://www.icwglobal.org/
• Expanded Programme on Immunisation (EPI): 3 doses in infancy (0-14 weeks)
• Rolled out in South Africa from 1995
• Global coverage of 1st dose within 24h of birth: 39% (WHO)
Kimberley, South Africa

- Antenatal HBsAg prevalence: 11%
- HBeAg prevalence: 25%
AIMS:

• To investigate the prevalence of HBV in children in South Africa

• To investigate the proportion of children age 9-60 months who have serologic evidence of vaccine-mediated HBV immunity (HBsAb);

• To use our own HBsAg and HBsAb prevalence data (alongside existing data for HBV transmission, infection and immunity) to model the timeframe for HBV elimination.
Prevalence of HBV infection in children

- 0.8% of children HBV infected; similar irrespective of HIV status
- HBV not necessarily virologically suppressed even on ART
  including 3TC or TDF

Proportion of children with vaccine response

Whole cohort (HBsAb ≥10)

<table>
<thead>
<tr>
<th></th>
<th>Proportion of cohort (%)</th>
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<tbody>
<tr>
<td>HIV+</td>
<td>23.2%</td>
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<tr>
<td>HIV-</td>
<td>76.8%</td>
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</tbody>
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P < 0.0001

Average HBsAb titre (mIU/ml)

- HIV-: Decreasing over time
- HIV+: Stable over time
Developing a model

(i) Steady state

(ii) Dynamics in a population

Susceptible (S)
Recovered (R)
Infected (I) acute/chronic
What we are currently doing is immunising 75% of young children. In 50 years, this will reduce population prevalence of HBV by <1%.
PMTCT can also reduce prevalence, but the effects are slower.

- What we are currently doing is immunising 75% of young children
- In 50 years, this will reduce population prevalence of HBV by <1%
COMBINED INTERVENTIONS

Neonatal vaccination plus:
(i) Catch-up vaccination
(ii) PMTCT
(iii) Catch-up vaccination AND PMTCT
Conclusions

• Vaccination works! Existing strategies are very effective at reducing seroprevalence in children....

BUT

• First vaccine dose at age 6 weeks is too late;
• HIV interferes with vaccine-mediated immunity;
• Overall: nearly 1/4 children with no HBsAb response;
• We cannot assume ART is effective at suppressing HBV...

AND

• At population level, immunisation and PMTCT will move us towards elimination only over decades/centuries;
• Other strategies are needed to achieve elimination – we need a cure.
Next steps: OxSA-Hep

- Recruitment of a large chronic HBV cohort (n=1000);
- Full-length HBV sequence and host genome (focus on HLA class I);
- Identify associations between viral polymorphisms, host genotype and clinical/serological markers of outcome.
Next steps: OxSA-Hep

1000 adults with chronic HBV infection

HOST GENOME

VIRAL GENOME

Clinical outcomes

Identify host and viral correlates of control or clearance

John Radcliffe Hospital
Oxford, UK

Pelonomi Hospital
Bloemfontein, South Africa

Tygerberg Hospital
Cape Town, South Africa
Can we ‘eliminate HBV as a public health problem by 2030’?

NO

- Endemic virus
- Complex biology
- Poor resources and data
- Huge social challenges
- Current tools are inadequate(ly deployed)
Can we ‘eliminate HBV as a public health problem by 2030’?

**BUT WE CAN**

- Deploy existing tools better
  - Birth dose vaccine
  - Screening
  - Treatment and PMTCT
- Gather and share high quality data
- Advocate for resources, education
- Exploit the technological revolution
Acknowledgements

• Prof Paul Kleereman, Prof Ellie Barnes, Prof Philip Goulder, University of Oxford

• Dr Anna McNaughton, Jolynne Mokaya, Dr Louise Downs, Dr Sheila Lumley, Dr Emily Adland, Dr David Bonsall, University of Oxford

• Dr Sunetra Gupta, Dr Jose Lourenco Dept of Zoology, University of Oxford

• Dr Katie Jeffery, Dr Monique Andersson, Oxford University Hospitals

• Prof Thumbi Ndung’u and team, Durban, SA

• Dr Pieter Jooste and team, Kimberley, SA

• Dr Nickie Goedhals and team, Bloemfontein, SA
Thank you

https://www.expmmedndm.ox.ac.uk/hepatitis-b-virus

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