Disclaimer

This document was produced by its author/and or organization and has been published on the PHO website for your use as outlined in our Website Terms of Use. PHO did not produce this document and is not responsible for the information provided within this document.
Chlamydia Control Requires a Vaccine

Dr. Robert C. Brunham
Professor of Medicine, The University of British Columbia
Provincial Executive Director, BC Centre for Disease Control
• No disclosure

• A program science – “getting research out of practice” – and basic science perspective

• Overview
  • *Chlamydia* and global public health
  • Evaluation of BC *Chlamydia* control program
  • Emerging insights into a *Chlamydia* vaccine
STIs and Global Public Health

- STIs have a profound impact on sexual, reproductive and maternal-child infant health
- STI control is a core component of WHO’s Global Strategy on Reproductive Health
- STI control is essential to achieving MDGs
  - 4 (child health), 5 (maternal health), 6 (HIV prevention)
- STI control remains a challenge
Curable STIs: a Global View 2008

- 106 million Chlamydia
- 106 million Gonorrhea
- 11 million Syphilis
- 276 million Trichomoniasis

Not decreasing from 2005 (448m → 499m)
Upper Genital Tract Disease

• *Chlamydia* and gonorrhea ascend to cause PID
• Post PID sequelae: infertility, ectopic pregnancy, chronic pain

Images from Dorothy L. Patton, University of Washington
Childlessness Among African Women Aged 45-49

- A good indicator of overall infertility in the population

- Seroepidemiological and clinical studies demonstrate that tubal damage due to *Chlamydia* and gonococci is major cause

Public Health Approaches to STI Control

- **Primary prevention**
  - Population
  - Medical Services
    - Syndromic (developing)
    - Case finding (developed)
  - Rehabilitation Services
    - in vitro fertilization
    - ectopic pregnancy
    - methotrexate
    - surgery

- **Secondary prevention**
  - Individual
  - Behavioral and Biological Approaches
    - Safe sex message
    - Vaccines
Epidemiological Principle of Treatment of Curable STIs

• Based on shortening duration infection
  – Prevent disease pathogenesis
  – Prevent transmission

• Trade off between preventing disease pathology and transmission versus development of immunity
Treatment of Genital *Chlamydia* after Spontaneous Resolution Correlates with Protection from Reinfection

<table>
<thead>
<tr>
<th>Number Studied</th>
<th>Number (%) Reinfection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous Clearance</td>
<td>44</td>
</tr>
<tr>
<td>Persistent Infection</td>
<td>156</td>
</tr>
</tbody>
</table>

*P = 0.016

Geisler et al., *JID* 207:1850, 2013
Treatment Suppresses Cellular Immune Responses to *Chlamydia*

Brunham et al., *I&I* 34:98, 1981
Top 10 Notifiable Diseases in British Columbia - 2011

- **Chlamydia (genital)**: 12,000 cases (Sexually transmitted and bloodborne pathogens)
- **Hepatitis C**: 2,000 cases
- **Campylobacteriosis**: 4,000 cases
- **Gonorrhea**: 6,000 cases
- **Hepatitis B (chronic)**: 8,000 cases
- **Salmonellosis**: 10,000 cases
- **Giardiasis**: 12,000 cases
- **Yersiniosis**: 4,000 cases
- **Amebiasis**: 2,000 cases
- **Pneumococcal Disease (invasive)**: 1,000 cases
Chlamydia Rates in BC and Canada, 1991 - 2003

Brunham et al., JID 192:1886, 2005
Rising Reinfection Rates

Number of 2nd Infections vs. Reinfection Rate per 100,000 population

- Rising Reinfection Rates
- Number of 2nd Infections
- Reinfection Rate

BC Centre for Disease Control
Cox Proportional Hazards Model

Number of first infections each year superimposed on the individual year effects.

Solid line is the linear effect.
Immunologic Paradigm of Chlamydia
20 Years of *Chlamydia* Control in BC

Rekart et al., *JID* 207:30, 2013
Chlamydia trachomatis Control Requires a Vaccine

Dodet, Vaccine, 2013
Chlamydia Vaccine Design

Two promising preclinical approaches that accelerate clearance in mice and partially protect primates

• Subunit recombinant outer membrane proteins
• Live attenuated (plasmid-deficient) vaccine
Chlamydia T cell Vaccine Antigen

- 27 proteins were identified that contained 78 MHC II binding peptides
- Selected 4 polymorphic membrane proteins and the major outer membrane protein for vaccine studies

Yu et al., *Infect Immun* 80:1510, 2012
Multiple component *Chlamydia* Outer Membrane Protein Vaccine

**C57**

**Balb/c**

**C3H**
Live-Attenuated *Chlamydia* vaccine

- Plasmid regulates expression of *Chlamydia* pathogenicity
- Plasmid deleted strain avirulent

Kari et al., *JEM* 208:2217, 2011
Conclusions

- *Chlamydia* is a global health problem
- Seek and Treat programs are expensive, have variable accessibility and perturb herd immunity
- Early stage vaccine solutions are in the offing but require a coordinated coalition to advance into public health evaluation