Toward global prevention of sexually transmitted infections: the need for STI vaccines

Sami Gottlieb - WHO
STIs and global public health

- STIs have profound impact on sexual, reproductive, and maternal-child health
- STI control is a core component of WHO’s Global Strategy on Reproductive Health
- Essential to achieving MDGs 4 (child health), 5 (maternal health), 6 (HIV prevention)
- STI control remains challenging in most settings
HPV and HBV vaccines: major advances

- Safe, highly efficacious vaccines against HPV and HBV have been major advances in STI prevention

- Limitations of other interventions provide important reasons for working toward new STI vaccines
Outline

- Global epidemiology of STIs and STI-associated complications
- Challenges to existing interventions for STI control
- The need for new STI vaccines for future prevention efforts
Global epidemiology of STIs
WHO estimates 499 million new cases of curable STIs in 2008

Curable STIs: chlamydia, gonorrhea, syphilis, trichomoniasis

Curable STIs: a global snapshot

- Individual curable STIs, 2008

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<table>
<thead>
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<tbody>
<tr>
<td>Chlamydia</td>
<td>106 million</td>
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<tr>
<td>Gonorrhea</td>
<td>106 million</td>
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<tr>
<td>Syphilis</td>
<td>11 million</td>
</tr>
<tr>
<td>Trichomoniasis</td>
<td>276 million</td>
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- Overall, numbers not decreasing compared with 2005 estimate of 448 million

Viral STIs: large proportion of prevalent STIs

- HSV-2 infection affects an estimated 536 million people globally
- An estimated 291 million women have HPV infection at any point in time
  - Numbers of men likely similar
- Approximately 360 million people suffer chronic HBV infections
  - Most acquired perinatally
STI-associated complications
### Genital symptoms

- Most STIs asymptomatic or unrecognized
- When symptoms occur, can have important impact on quality of life

<table>
<thead>
<tr>
<th>STI</th>
<th>Symptoms</th>
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<tbody>
<tr>
<td>Chlamydia, gonorrhea, trichomoniasis</td>
<td>Vaginal discharge syndromes, urethritis</td>
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<tr>
<td>HSV, syphilis</td>
<td>Genital ulceration</td>
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<tr>
<td>HPV</td>
<td>Genital warts</td>
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Pregnancy complications

- Untreated syphilis in pregnancy leads to more than half a million adverse outcomes each year.

Pregnancy complications

- Remaining STIs can lead to variety of adverse maternal-child outcomes

<table>
<thead>
<tr>
<th>Curable STIs</th>
<th>Preterm labor</th>
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<tbody>
<tr>
<td>Chlamydia, gonorrhea</td>
<td>Ophthalmia neonatorum</td>
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<tr>
<td>Chlamydia</td>
<td>Neonatal pneumonia</td>
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<tr>
<td>HSV</td>
<td>Neonatal herpes</td>
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Cancer

- HPV and HBV are oncogenic
- HPV infection: 530,000 cervical cancer cases and 275,000 cervical cancer deaths each year
- Highest cervical cancer rates in resource-poor settings

Upper genital tract disease

- Chlamydia, gonorrhea can ascend to upper genital tract and cause pelvic inflammatory disease (PID)

- Long-term sequelae
  - Tubal factor infertility
  - Ectopic pregnancy
  - Chronic pelvic pain

Scanning electron microscopy photos courtesy of Dorothy L. Patton, University of Washington, Seattle, WA, USA
Upper genital tract disease

Untreated chlamydial infections → 10-15% → Clinical PID → 10-15% → Tubal factor infertility
Upper genital tract disease

Untreated chlamydial infections → 10-15% → Clinical PID → 10-15% → Tubal factor infertility

? Risk → Asymptomatic inflammation → ? Risk
Upper genital tract disease

- Untreated chlamydial infections → Clinical PID (10-15%) → Tubal factor infertility (10-15%)
- Asymptomatic inflammation

- Almost 100 million chlamydia & gonorrhea infections among women globally each year
Increased HIV risk

- HSV-2 infection: 3-fold increased risk of acquiring HIV
  - Co-infection: more likely to transmit HIV

- Curable STIs may also be associated with increased HIV acquisition, by up to 2- to 3-fold
  - Urethritis and cervicitis increase HIV shedding
Psychosocial consequences

- Difficult to quantify profound psychosocial impact
- STI diagnosis: stigma, shame, decreased self-worth
- Anxiety about sexual relationships, future reproductive health
- Disruption of partnerships, even intimate partner violence
Challenges to existing interventions for STI control
Public health approach to STI control

- Primary prevention
- STI case management
Public health approach to STI control

Primary prevention

- Behavioral, e.g.
  - Counseling
  - Condoms

- Biomedical, e.g.
  - Vaccines
  - Circumcision

STI case management
Public health approach to STI control

Primary prevention
- Behavioral, e.g.
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STI case management
- Diagnosis
  - Symptomatic
  - Screening
- Treatment
- Partner management
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**Primary prevention**
- Behavioral, e.g.: Counseling, Condoms
- Biomedical, e.g.: Vaccines, Circumcision

**STI case management**
- Diagnosis: Symptomatic, Screening
- Treatment
- Partner management

**Implementation**
- Availability & access
- Scale-up
Public health approach to STI control

Primary prevention

- Behavioral, e.g.- Counseling
- - Condoms

- Biomedical, e.g.- Vaccines
- - Circumcision

Challenges

- Behavioral, sexual
  network factors

STI case management

- Diagnosis
  - Symptomatic
  - Screening

- Treatment

- Partner management

Implementation

- Access & availability
- Scale-up
Challenges: behavioral and network factors

- Limits to progress made with condom promotion as main primary prevention measure
- Cultural factors affect acceptability of condoms, comfort level with discussing sex
- Sustainability of behavior change
- Individual behavior may be less important than network risk
Public health approach to STI control

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  - Biomedical, e.g.
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Primary prevention
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Challenges
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STI case management
- Diagnosis
  - Symptomatic
  - Screening
- Treatment
  - Antimicrobial resistance
- Partner management
  - Repeat infections

Challenges
- Most infections asymptomatic

Implementation
- Access & availability
- Scale-up
Challenges: asymptomatic infection

- Vast majority of STIs cause few or no symptoms
  - But can still lead to harmful sequelae

- Symptomatic case management just “tip of the iceberg”

- Syndromic management inaccurate for syndromes like vaginal discharge
Challenges: antimicrobial resistance

- Drug-resistant gonorrhea is major threat to STI control globally
  - Resistance to cephalosporins, only first-line drugs, increasingly reported

- Nitroimidazoles only class active against trichomoniasis
  - Low-level resistance being reported
Challenges: repeat infections

- Curable STIs do not result in strong, lasting protective immunity

- Repeat infection rates for chlamydia, gonorrhea, trichomoniasis: 10-20% after treatment

- Repeat infection more common when little attention to partner management
  - Challenging in most settings
Public health approach to STI control

Primary prevention
- Behavioral, e.g.
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  - Condoms
- Biomedical, e.g.
  - Vaccines
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Challenges
- Behavioral, sexual network factors

STI case management
- Diagnosis
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- Partner management
- Most infections asymptomatic
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Implementation
- Access & availability
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# Public health approach to STI control

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<td></td>
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<td>Implementation</td>
<td>Access &amp; availability</td>
<td>Scale-up</td>
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<td>Policy, cost, lack of tests, no platform to reach infected</td>
<td>Political will, resources, sustainability</td>
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</table>
Challenges: policy and political will

- STIs are stigmatizing; lack of champions
- Many STI interventions either not fully effective or difficult to quantify impact
  - Harder to garner support
Challenges: implementation factors

- Lack of availability and access to affordable, easy-to-use diagnostic tests in much of world
  - New rapid tests for syphilis
  - Rapid tests for others may be on horizon

- Availability does not ensure effective implementation
  - Platform to access target population
  - Commitment, resources for scale-up
  - Sustainability
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**STI case management**
- Diagnosis
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- Partner management
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**Challenges**
- Most infections asymptomatic

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- Access & availability
  - Policy, cost, lack of tests, no platform to reach infected
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  - Political will, resources, sustainability
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Challenges
- Behavioral, sexual network factors
- Need for new technologies

STI case management
- Diagnosis
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- Treatment
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- Partner management
  - Repeat infections

Challenges
- Most infections asymptomatic
- Policy, cost, lack of tests, no platform to reach infected
- Political will, resources, sustainability

Implementation
- Access & availability
- Scale-up
The need for new STI vaccines for future prevention efforts
HSV-2 infection

- >500 million HSV-2 infections globally
  - Incurable, lifelong
  - Marked synergy with HIV

- Current HSV-2 prevention strategies may not have feasible, sustainable population impact

- HSV vaccine could have impact on HIV spread, neonatal herpes, genital symptoms
Chlamydia

- Global burden of chlamydia-related PID, infertility likely very high
  - Lower-income countries: most chlamydia missed

- Screening programs difficult to bring to scale
  - Do not appear to have reduced chlamydia prevalence

- Repeat infections: arrested immunity?

- Complexities of current chlamydia control efforts highlight need for work toward chlamydia vaccine
Gonorrhea

- Prevention threatened by antimicrobial resistance to only first-line drugs for 106 million cases/year

- Trials of new treatment regimens ongoing
  - *N. gonorrhoeae* has developed resistance to 4 different classes of antibiotics since first treatable

- Progress toward gonorrhea vaccine also needed
Syphilis

- Over half a million adverse pregnancy outcomes/year
- New point-of-care diagnostic tests, cheap on-site treatment, antenatal care access
  - WHO: global strategy for elimination of mother-to-child transmission of syphilis
- If implementation remains challenging, no decrease in community transmission
  - Syphilis vaccine will be an important pursuit
Trichomoniasis

- More cases of trichomoniasis than other curable STIs combined
  - Vaginal symptoms, preterm delivery, HIV enhancement
- Lack of diagnostic tests hampers control globally
- Reports of low-level nitroimidazole resistance worrisome; only one drug class
- New diagnostic tests and drug regimens needed, with continued work toward developing vaccine
Summary

- More than half a billion STIs occur annually
- Large burden of sexual, reproductive, maternal-child health consequences
- Current STI control challenged by several behavioral, biological, and implementation factors
- Coordination and advancement of STI vaccines is a major priority for sustainable global STI control
Acknowledgments

Nicola Low
Lori Newman
Gail Bolan
Mary Kamb
Nathalie Broutet
2010 Global Burden of Disease study

- Curable STIs accounted for 11 million DALYs lost

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<th>STI</th>
<th>DALYs in 1000s</th>
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<tr>
<td>Chlamydia</td>
<td>714</td>
</tr>
<tr>
<td>Gonorrhea</td>
<td>282</td>
</tr>
<tr>
<td>Syphilis</td>
<td>9,600</td>
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<tr>
<td>Trichomoniasis</td>
<td>167</td>
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- Cervical cancer: another 6.4 million DALYs
- Did not calculate DALY estimates for HSV-2

Financial costs

- In US, $3 billion in direct costs to diagnose and treat 19.7 million cases of STIs and complications
  - Excluding HIV and pregnancy-related outcomes

- Costs associated with adverse STI outcomes less well documented in resource-poor settings
Implementation of STI vaccines

- HPV vaccine not yet implemented in countries with highest cervical cancer rates

- Lessons learned will inform future STI vaccine delivery