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.
Canada Gairdner Foundation
Global Health
2013

King K. Holmes, M.D., Ph.D.
University of Washington
October 24, 2013
Chapters featured:
- syphilis
- gonorrhoea
- “tropical” venereal diseases
- trichomoniasis
- NGU
• Today, there are 35 known sexually transmitted pathogens including HIV 1 and 2.
• The microbial etiology of several common STD syndromes still remains substantially undefined (e.g. NGU, MPC, PID, GUD).
• Microbiome studies will define many more.
1960s: Era of contraceptives, global urbanization, the sexual revolution, the SE Asia war, and WWII baby boomers came of age

- Epidemic spread of STIs begins
- *N. gonorrhoeae*: decreased penicillin susceptibility appears in Asia
- Growing incidence of NGU and genital herpes, recognition as STDs
1970s: Continued rapid spread of STI, and newly recognized STI pathogens and syndromes

- Epidemics of syphilis, GC, and viral STI, particularly in MSM
- Penicillinase-producing *N. gonorrhoeae* appears in Philippines
- Recognition of STI impact on cancers: cervix, liver
- Recognition of STI impact on women
- “Gay Bowel Syndrome” epidemic begins in MSM
Despite this, aspirations for sexual freedom prevailed
Chlamydia trachomatis Proctitis

Thomas C. Quinn, M.D., et al.

Includes three cases of severe LGV proctitis masquerading as Crohn’s disease.

The Polymicrobial Origin of Intestinal Infections in Homosexual Men

Thomas C. Quinn, M.D., et al.
Things were getting much worse; diagnosis and treatment weren’t bringing STIs under control

INTRODUCTION

David G. Ostrow, MD, PhD

The final presentation on Friday was the keynote address by King Holmes, MD, PhD, Professor of Medicine at the University of Washington at Seattle, who summarized major advances as well as still unanswered questions in the specialty of STDs. Dr. Holmes’s discussion suggested that behavioral and sociological factors may well be the most important areas of research and modification in the battle against the growing list of STDs.

- 1980-81—PCP; KS; Gay-Related Immunodeficiency Syndrome ("GRIDS")
- HIV incidence rises globally
- Early syphilis, other STIs begin declining in mid 80s, esp. in MSM, in developed countries
- GUD found associated with HIV in men and women
- WHO guidelines on synd. management of GUD
- Chancroid, and also syphilis and gonorrhea, began declining in LMICs, with syndromic management

1. In Vancouver, the 11th International AIDS Conference ("One World, One Hope") highlights the effectiveness of highly active antiretroviral therapy (HAART), creating a period of optimism.
Oops: Elimination and reintroduction of primary and secondary (P&S) syphilis by year in King County, Washington

Rates of primary and secondary syphilis among MSM, by race or ethnicity, in 27 US states in 2005 to 2008

1996-2013: Sexual behavior trends post-HAART in high income countries

- Serosorting (HIV seroconcordant sexual mixing) and seropositioning in MSM; UAI increases
- More densely connected sexual networks
- Concurrent sex partners
1996–2013: Epidemiology of HIV and STI in No. America and Europe post-HAART

- **Dramatic resurgence of some STI** in MSM in US and in Western Europe, esp. in MSM
  - Syphilis, gonorrhea epidemics, LGV proctitis, hepatitis C in MSM
- GC fluoroquinolone resistance spreads from Asia to US, concentrated in MSM
- GC decreasing cephalosporin susceptibility, concentrated in MSM
- Azithromycin-resistant *T. pallidum* in US, Ireland, MSM
- US: 50,000 new cases of HIV infection annually

Source: Gonococcal Isolate Surveillance Project (GISP)
Percentage of NG Isolates that are QRNG by Sex of Sex Partner, 1999–2010*

Source: Gonococcal Isolate Surveillance Project (GISP)
* 2010 data are preliminary

Note: MSM = Men who have sex with men; MSW = Men who exclusively have sex with women, QRNG = Quinolone-resistant N. gonorrhoeae (MIC to ciprofloxacin ≥ 1µg/ml)
Proportion of NG isolates with Elevated MICs by Sex of Sex Partner

Cefixime (≥ 0.25 μg/ml) n=50,873

- MSW: 0.9% (n=64)
- MSM: 3.9% (n=15)

Ceftriaxone (≥ 0.125 μg/ml) n=62,321

- MSW: 0.9% (n=15)
- MSM: * p trend < 0.05

Source: Gonococcal Isolate Surveillance Project (GISP)

Note: MSM = Men who have sex with men; MSW = Men who exclusively have sex with women

* p trend < 0.05
Percentage of Urethral *N. gonorrhoeae* isolates with elevated MICs to Cefixime, 2011*

* Jan-Aug 2011

Source: Gonococcal Isolate Surveillance Project (GISP)
Antimicrobial Susceptibility Among Urethral *N. gonorrhoeae* Isolates with Elevated Cefixime MICs (≥ 0.25), 2010–2011

- Susceptible: 20%
- QRNG: 3%
- PenR/QRNG: 1%
- PenR/TetR: 1%
- TetR/QRNG: 7%
- Azithromycin: 99% susceptible, 1 had MIC of 2 µg/ml
- Spectinomycin: 100% susceptible

Resistance to Penicillin, Tetracycline & Quinolones: 69%

Source: Gonococcal Isolate Surveillance Project
1996-2013: STI/HIV trends in lower income countries

- STD syndromic management, condom promotion scaled up beginning 1990
- HAART scale up beginning mid-1990s
UNAIDS 2013: New HIV Infections Fall by Third

NEW HIV INFECTIONS, GLOBAL, 2001–2012

AIDS DEATHS, GLOBAL, 2001–2012

PEOPLE LIVING WITH HIV, GLOBAL, 2001–2012

- High estimate
- Estimate
- Low estimate
Durban, KZN, So Africa: *Haemophilus ducreyi*

Durban, KZN, So Africa: *Treponema pallidum*

![Graph showing the percentage positive over years with a decline from 1998 to 2006. The x-axis represents the years 1982 to 2006, and the y-axis represents the percent positive ranging from 0 to 50. The method used is Serology + darkfield or PCR.](image)
Prevalence of Syphilis, GC Among Kenyan ANC Attendees (1992-2001)

Genital ulcer trends
Madras Medical College STD Clinic 1993-2003

Source: Dr Usman, Madras Medical College
2010-11: New Evidence for ART and PrEP for Prevention

- CAPRISA 004: 1% tenofovir vaginal gel prophylaxis — 39% ↓ HIV acquisition
- iPrEx: daily oral Truvada for MSM — 43.8% ↓ HIV acquisition
- HPTN052: Early ART — 96% ↓ HIV transmission
- Partners PrEP: serodiscordant couples 62% (tenofovir), 72% (Truvada) ↓ HIV acquisition; even better with high adherence
- CDC PrEP TDF2: 62% ↓ HIV acquisition
Perfect Storm

Simultaneous call for

Development agenda broader than health

Health assistance agenda broader than HIV

Expand ART coverage

Omission of STD control from HIV programs

Earlier ART

Global Recession

PrEP?
Eight questions for the future

1) What will be the impact of scaled up ART on sexual behavior? (STI incidence will continue to be an indicator for unprotected sex and more connected sex networks)

2) Will STI epidemics accelerate even further in MSM and other populations at high risk?

3) Will the resurgence of STIs again increase transmission of HIV?

4) What will be the impact of increasing unprotected sex on emergence of new STIs (analogous to the emergence of HIV as a new STI in 1980)? On the emergence of new variants of existing STI pathogens, perhaps more virulent variants (past evidence of rapid spread enhancing virulence of other pathogens)?
Eight questions for the future (cont.)

5) What will be the impact of increasing STI incidence on antimicrobial resistance in STI pathogens (including HIV)?

6) Will increasing unprotected sex in the context of scaled-up ART or PrEP accelerate ARV\textsuperscript{R}, similar to the emergence of azithro-resistant \textit{T. pallidum} and multidrug-resistant GC? (How could it not?)

7) Will the combined negative impact of increased unprotected sexual exposure plus reemerging STI epidemics together outweigh the positive impact of increasing ART coverage on HIV transmission?

8) Will local, national, global resources for STI control continue to decline, despite increasingly rapid reemergence of STI, including antimicrobial-resistant STI?
Bonus Question

- What can be done to optimize the beneficial prevention impact of scaling up ART, and reduce the risks of negative impact?
The Science of “Complex” Interventions
Thank You!