• 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


1996

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


King County: Reintroduction of Early syphilis*, 1997-2011

Early syphilis cases

- In 2011, 4.1% of all HIV+ MSM were diagnosed with early syphilis
- Syphilis rate in HIV+ MSM was >17x higher than in HIV- MSM

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


Legend:
- MSM syphilis**
- Heterosexual syphilis
- 2005 total cases = 193
- 2006 total cases = 185
- 2007 total cases = 194
- 2008 total cases = 191
- 2009 total cases = 160
- 2010 total cases = 289
- 2011 total cases = 355

**Excludes some male cases with unknown MSM status
Incidence of reported gonorrhea among MSM, women, and heterosexual men 15 years and older
King County, WA, 1993-2012

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*

Proportion of NG isolates with Elevated MICs by Sex of Sex Partner

Percentage of Urethral * N. gonorrhoeae isolates with elevated MICs to Cefixime, 2011*

Antimicrobial Susceptibility Among Urethral * N. gonorrhoeae isolates with Elevated Cefixime MICs (≥ 0.25), 2010–2011

* 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)

Source: Gonococcal Isolate Surveillance Project (GISP)

* Jan-Aug 2011

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

- STD syndromic management, condom promotion scaled up beginning 1990
- HAART scale up beginning mid- 1990s

### Durban, KZN, So Africa: *Haemophilus ducreyi*

![Graph showing decrease in H. ducreyi positive rate](image)


### Durban, KZN, So Africa: *Treponema pallidum*

![Graph showing decrease in T. pallidum positive rate](image)

UNAIDS 2013: New HIV Infections Fall by Third

- NEW HIV INFECTIONS, GLOBAL, 1995-2012
- AIDS DEATHS, GLOBAL, 2001-2012
- PEOPLE LIVING WITH HIV, GLOBAL, 2005-2012

[UNAIDS](http://www.unaids.org/en/)
Prevalence of Syphilis, GC Among Kenyan ANC Attendees (1992-2001)

Genital ulcer trends
Madras Medical College STD Clinic 1993-2003

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

Simultaneous call for
- Development agenda broader than health
- Health assistance agenda broader than HIV

Expand ART coverage

Perfect Storm

- 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)?

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-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?
STI outcomes for 2006, GP
(N=6556 18-29 y.o. women in 20 cities)

Intervention vs. control cities: 24% reduction in combined prevalence of any of 4 curable STIs (CT, NG, TV, Σ) after 3 years (p=0.02), comparing intervention cities vs. control cities

STI outcomes in FSW
(N=4130 in 20 cities for 2006)

Intervention vs. control cities: 35% reduction in combined prevalence of any of 4 curable STIs (CT, NG, TV, Σ) after 3 years (p=0.02), comparing intervention cities with control cities

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http://www.proyectopreven.org
**Vancouver Collaborators!**


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**The Prevention and Treatment Cascades**

  - Now about 1.8 million results on Google for HIV Treatment Cascade.
- Prevention and Treatment Cascades now widely adapted and used:
  - GAVI, Roll Back Malaria, Stop Tuberculosis Partnership, IMCI, Reproductive Health Care, Water and Sanitation

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**Conclusions**

- At First, I Thought
  - Just need more and better diagnostics and treatments
- Later
  - Safer sex: change sexual behaviors
- Still Later
  - Vaccines
- Now
  - Above, plus program science for focused, efficient, cost-effective, integrated, combination interventions, with ongoing needs-assessments; enabling policies and structural changes; and innovative integration of clinical and public health systems to expand access, coverage, and quality of interventions.

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**“STD care management”, Fig. 48-2, from Sexually Transmitted Diseases, 3rd Edition, McGraw-Hill, 1999**

<table>
<thead>
<tr>
<th>Ecology of Infection</th>
<th>Behavior Leads to Exposure</th>
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<tr>
<td>Exposure</td>
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<td>Symptoms</td>
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<tr>
<td>Symptoms</td>
<td>Symptoms Recognized</td>
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- Care Seeking for Symptoms | Access Appropriate Care
- Access to Appropriate Care | STD Diagnosis Considered
- Correct Diagnosis | Effective Treatment Prescribed
- Effective Treatment Prescribed | Comply with Treatment, Cured
- Patient Cured | Exposed Partner(s) Treated
Thank You!