AGGIORNAMENTI IN TEMA DI STIs

INFECTION 2018

16 marzo

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AGENDA

- Why should we pay attention to STIs?
- Epidemiology
  - HIV
  - Syphilis
  - Gonorrhoeae
  - Chlamydia
- Treatment and follow-up
  - N. gonorrhoeae
  - C. trachomatis
  - M. genitalium
AGENDA

- **Why should we pay attention to STIs?**
  - Epidemiology
    - HIV
    - Syphilis
    - Gonorrhoeae
    - Chlamydia
  - Treatment and follow-up
    - *N. gonorrhoeae*
    - *C. trachomatis*
    - *M. genitalium*
INCIDENCE OF STIs

357 million new cases of curable STIs in 2012: chlamydia, gonorrhea, syphilis, trichomoniasis

http://dx.doi.org/10.1371/journal.pone.0143304
Estimated new cases (and 95% UI) of four curable STIs amongst adults (15-49 years) by WHO region, (WHO 2012)*

Boom malattie legate a sesso, +400% casi di sifilide dal 2000
EFFECTIVELY ADDRESSING STIs CAN HAVE THE FOLLOWING OUTCOMES

- Combating antimicrobial resistance
- Eliminating adverse neonatal outcomes
- Reducing HIV transmission
- Preventing cancer
- Decreasing burden of infertility
- Supporting health of young people

STIs remain significant global health issues
TARGETS TOWARDS THE END OF STIs EPIDEMICS IN 2030

- 90% reduction of *T. pallidum* incidence
- 90% reduction in *N. gonorrhoeae* incidence
- ≤ 50 cases of congenital syphilis per 100 000 live births in 80% of countries
- 90% HPV vaccine coverage at national level at least 80% in every district
Symptomatic vs Asymptomatic infections

Syndromic approach vs Screening

General population vs Key/Vulnerable populations

Individual level of care vs Public health approach
Symptomatic vs Asymptomatic infections

Syndromic approach vs Screening

General population vs Key/Vulnerable populations

Individual level of care vs Public health approach
STIs TRANSMISSION DYNAMICS AT POPULATION LEVEL
Each country needs to define the specific populations that are most affected by sexually transmitted infections epidemics. The response should be based on the epidemiological and social context. Specific populations that focus on sexually transmitted infections will include populations most likely to have a high number of sex partners, such as sex workers and their clients.

Other populations for consideration include men who have sex with men, transgendered people and people with an existing sexually transmitted infection, including people living with HIV. Many of these groups overlap with groups recognized as key populations for HIV. Other groups considered to be particularly vulnerable to sexually transmitted infections include young people and adolescents, women, mobile populations, children and young people living on the street, prisoners, drug users and people affected by conflict and civil unrest.
NUMBERS...
NEW HIV DIAGNOSES, BY TRANSMISSION MODE AND COUNTRY, EU/EAA, 2016

Source: ECDC, WHO Regional Office for Europe. HIV/AIDS surveillance in Europe 2007 - 2016 data

HIV PREVALENCE IN MSM

MSM

RATE OF REPORTED CONFIRMED SYPHILIS CASES PER 100,000 POPULATION, EU/EEA, 2015

Source: Country reports from Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, the United Kingdom.

GONORREA

MSM
CHLAMYDIA EPIDEMIOLOGY IN 23 EU/EEA COUNTRIES, 2014

• The number of reported cases of chlamydia in Europe has gradually increased since 2004.

• Chlamydia is the most commonly reported STI in Europe despite many countries not having nationally comprehensive reporting systems.

• Most people who have chlamydia have no symptoms
...NO SYMPTOMS...
CHLAMYDIA

Source: Country reports from Denmark, Estonia, Finland, Iceland, Ireland, Latvia, Lithuania, Malta, Norway, Poland, Romania, Slovakia, Slovenia, Sweden, and the United Kingdom.

CHLAMYDIA CASES PER 100 000 POPULATION, BY AGE GROUP AND GENDER, EU/EEA, 2015

Source: Country reports from Bulgaria, Cyprus, Denmark, Estonia, Finland, Greece, Iceland, Ireland, Latvia, Lithuania, Luxembourg, Malta, Norway, Portugal, Romania, Slovakia, Slovenia, Sweden and the United Kingdom.

CHLAMYDIA EPIDEMIOLOGY IN 23 EU/EEA COUNTRIES, 2014

• The number of reported cases of chlamydia in Europe has gradually increased since 2004.

• Chlamydia is the most commonly reported STI in Europe despite many countries not having nationally comprehensive reporting systems.

• Most people who have chlamydia have no symptoms

• It can cause serious, permanent damage to a woman's reproductive system, making it difficult or impossible to get pregnant later on.
DISTRIBUTION OF CHLAMYDIA INFECTIONS BY TRANSMISSION CATEGORY AND GENDER, EU/EEA, 2015

- Heterosexual males, 30424, 51%
- Heterosexual females, 21082, 36%
- MSM, 4495, 8%
- Mother-to-child, 40, <1%
- Unknown, 2997, 5%
Transmission category was reported 37% of all reported cases. All but six were reported among MSM.;

In 2015 almost 2000 cases of LGV were reported in 23 EU/EEA countries (87% France, the Netherlands and the United Kingdom);

Information on HIV status was available for 39% of all reported LGV cases. Among these cases, 69% were HIV positive.
TREATMENT AND FOLLOW-UP
TREPONEMA PALLIDUM
SYPHILIS MANAGEMENT IN
HIV INFECTED
AND
UNINFECTED SUBJECTS
FIRST ASSESSMENT

Clinical evaluation:

- chancre, fever, mucocutaneous rash, hepatitis, patchy alopecia or other abnormalities?
  - YES: Symptomatic patient with primary or secondary syphilis --> Pattern A
  - NO: Asymptomatic patient with latent syphilis --> Pattern B
SYPHILIS PATTERNS

A. SYMPTOMATIC PATIENT with PRIMARY & SECONDARY SYPHILIS:

Benzatilpenicillin 2,4 MUI im once
Doxycycline 100 mg/12h for 14 days
Due to the emergence of macrolide-resistant *T. pallidum*, azithromycin should be used with caution and only when treatment with penicillin or doxycycline is not feasible. Azithromycin should not be used in the treatment of pregnant women and MSM.
DRUG-RESISTANT *T. PALLIDUM*

- Emergence of penicillin resistance appears unlikely since it would presumably require multi-step mutational changes in a bacterium that lacks horizontal gene transfer mechanism.

- Nowadays, the macrolide resistance is the only clinically significant resistance.

- Failure of erythromycin therapy was first reported in 1964 and 1976.

- Later *in vitro* studies demonstrated that macrolide-resistant phenotype (often due to point mutation of the peptidyl transferase in the domain V of 23S rRNA – A2058G) is highly stable, despite multiple passage in absence of antibiotic pressure.

- Macrolide-resistant *T. pallidum* with the A2058G mutation is now present in several areas of the USA, Canada, Europe, China and Australia.

- The persistence of low levels of azithromycin in tissue for weeks after treatment for unrelated infections is likely to allow for selection of resistant mutants of *T. pallidum* that arise *de novo*.
SYPHILIS FOLLOW-UP

- HIV-negative patient
  3 – 6 – 9 – 12 (if necessary) months after treatment

- HIV-positive patient
  3 – 6 – 9 – 12 – 24 months after treatment
SYMPHILIS FOLLOW-UP

Clinical evaluation
- Assess risk of reinfection
- Look for symptoms and signs of syphilis

Serologic monitoring
- HIV-negative patient: usually NT titre decreases 4-fold within 3-4 months and 8-fold within 6-9 months
- HIV-positive patient: NT titre could decrease slowly, thus if the NT titre does not increase and the patient is asymptomatic, we can wait till 12 month. At this time, NT titre should have declined at least 4-fold

NB
4-fold = 2 dilution (es: 32 -> 8)
8-fold = 4 dilution (es: 128 -> 8)
A double-edged sword: does highly active antiretroviral therapy contribute to syphilis incidence by impairing immunity to *Treponema pallidum*?

Michael L Rekart, Wilfred Ndifon, Robert C Brunham, Jonathan Dushoff, Sang Woo Park, Sanjana Rawat, Caroline E Cameron

Protection against the extracellular pathogen *T. pallidum*, the causative agent of syphilis, is dependent upon T cell expansion and the generation of an early Th1-stimulating, interferon γ (IFN-γ)-producing host proinflammatory response that potentiates the primary clearance mechanism of *T. pallidum*, macrophage-mediated opsonophagocytosis. The latter process is dependent on unperturbed mitochondrial function to ensure peak metabolic activity within macrophages, opsonic antibody production and IFN-γ-mediated macrophage activation. Opsonic antibody quality is reduced in individuals infected with HIV-1 and certain HAART agents significantly suppress mitochondrial function, the proinflammatory response and macrophage activation, leading to reduced treponemal clearance via opsonophagocytosis. INSTIs have been shown to suppress the proinflammatory response in cohort studies and opsonophagocytosis is reduced in vitro following treatment of macrophages with NRTIs, consistent with mitochondrial damage.
A double-edged sword: does highly active antiretroviral therapy contribute to syphilis incidence by impairing immunity to *Treponema pallidum*?

Michael L Rekart, Wilfred Ndifon, Robert C Brunham, Jonathan Dushoff, Sang Woo Park, Sanjana Rawat, Caroline E Cameron

*Sex Transm Infect* 2017;93:374–378. doi:10.1136/sextrans-2016-052870

Further, the well-documented depletion of CD4\(^+\) memory T cells in individuals infected with HIV-1\(^{30}\) would enhance their susceptibility to syphilis reinfection. NRTIs, especially TDF, have been shown to inhibit telomerase activity leading to accelerated shortening of telomerase length in peripheral blood mononuclear cells (PBMCs),\(^{31}\) which may lead to the accumulation of replicative senescent cells\(^{32}\) with limited ability to protect against pathogens such as *T. pallidum*. Reciprocally, upregulation of monocyte expression of CCR5 receptors by treponemal lipoproteins enhances the susceptibility of monocytes to HIV-1 infection,\(^{33}\) further weakening the innate and adaptive immune responses to *T. pallidum*. 
Collectively, these observations provide viable explanations for (1) an enhanced susceptibility of individuals infected with HIV-1, especially those on HAART, to syphilis infection and reinfection and (2) higher syphilis incidence among individuals treated with HAART compared with chlamydia and gonorrhoea, infections caused by pathogens that are less reliant on opsonophagocytosis for clearance.
MANAGEMENT OF SEXUAL PARTNERS OF PATIENT WITH SYPHILIS

1. Patient with primary or secondary syphilis:
   a. If the sexual contact has been occurred **within last 90 days:**
      
      Perform clinical and serologic assessment but treat regardless their results with Benzatilpenicillin 2,4 MUI im once or Doxycycline 100 mg/12h for 14 days
   
   b. If the sexual contact has been occurred **more than 90 days** before:
      
      Perform clinical and serologic assessment and treat based on their result
E LE ALTRE STIS BATTERICHE?
UNITA' OPERATIVA COMPLESSA DI MICROBIOLOGIA E VIROLOGIA dU - Direttore: Prof. Giuseppe Cornaglia
Borgo Trento - P.le A.Stefani, 1 - 37126 Verona tel.045-8122461 fax 045-8122783
Borgo Roma - P.le L.A.Scurio, 10 - 37134 Verona tel.045-8124720 fax 045-8124158
UNITA' OPERATIVA CON SISTEMA DI QUALITA' CERTIFICATO

Sig.ra: Data di nascita: 08/03/1996
Reparto: AMBULATORIALI B.ROMA (000998)

RICHIESTA N.: 201712220504 (22/12) PRELIEVO DEL (LU121700005681637)

-- PATOLOGIA MOLECOLARE --

**Ricerca patogeni genito-urinari su urina**

- C. trachomatis (met. RT-PCR) Non Rilevabile
- N. gonorrhoeae (met. RT-PCR) Non Rilevabile
- Trichomonas vaginalis (met. RT-PCR) Non Rilevabile
- Mycoplasma genitalium (met. RT-PCR) Non Rilevabile
- Mycoplasma hominis (met. RT-PCR) Non Rilevabile
- Ureaplasma urealyticum (met. RT-PCR) Non Rilevabile
- Ureaplasma parvum (met. RT-PCR) Non Rilevabile
NEISSERIA GONORRHOEAE
Gonorrhoea strains across Europe becoming more susceptible to main treatment options

ECDC 2017 Gonococcal antimicrobial susceptibility surveillance in Europe, 2015.
ECDC 2017 Gonococcal antimicrobial susceptibility surveillance in Europe, 2015.
NG ANTIMICROBIAL RESISTANCE

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<th>Euro-GASP</th>
<th>Italy</th>
<th>Trend</th>
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<td>Cefixime</td>
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<td>Ceftriaxone</td>
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ECDC 2017 Gonococcal antimicrobial susceptibility surveillance in Europe, 2015.
# NG Antimicrobial Resistance

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<td>Ciprofloxacin</td>
<td>53</td>
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ECDC 2017 Gonococcal antimicrobial susceptibility surveillance in Europe, 2015.
Cefixime

Azithromycin

Ciprofloxacin

ECDC 2017 Gonococcal antimicrobial susceptibility surveillance in Europe, 2015.
Multidrug-resistant Neisseria gonorrhoeae infection with ceftriaxone resistance and intermediate resistance to azithromycin, Denmark, 2017

David Terkelsen1, Jacob Tostrup2, Camilla Hvidahl Johnsen3, Ole Lund4, Helle Kielbier Larsen5, Peder Warming5, Magnus Unemo6, Henrik West7

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These authors contributed equally to the work.

These authors share last authorship.

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https://doi.org/10.1111/j.1471-6975.2017.00659.x
GENITAL AND ANO-RECTAL INFECTION

_Dual therapy_
- ceftriaxone 250 mg im as a single dose + azithromycin 1 g os as a single dose
- cefixime 400 mg os as a single dose + azithromycin 1 g os as a single dose

_Single therapy_ (based on recent local resistance data on antimicrobial susceptibility)
- ceftriaxone 250 mg im as a single dose
- cefixime 400 mg os as a single dose
- spectinomycin 2 g im as a single dose

ORO-PHARYNGEAL INFECTION

**Dual therapy**
- ceftriaxone 250 mg im as a single dose + azithromycin 1 g os as a single dose
- cefixime 400 mg os as a single dose + azithromycin 1 g os as a single dose

**Single therapy** (usually not recommended!)
- ceftriaxone 250 mg im as a single dose

WHO GUIDELINES FOR THE TREATMENT OF NEISSERIA GONORRHOEAE. AUG 2016

However, during 2006–2011, the minimum concentrations of cefixime needed to inhibit in vitro growth of the *N. gonorrhoeae* strains circulating in the United States and many other countries increased, suggesting that the effectiveness of cefixime might be waning.


In addition, treatment failures with cefixime or other oral cephalosporins have been reported in Asia, Europe, South Africa, and Canada.

Ceftriaxone treatment failures for pharyngeal infections have been reported in Australia, Japan, and Europe.

As a result, CDC no longer recommends the routine use of cefixime as a first-line regimen for treatment of gonorrhea in the United States.

A 400-mg oral dose of cefixime should only be considered as an alternative cephalosporin regimen because it does not provide as high, nor as sustained, bactericidal blood levels as a 250-mg dose of ceftriaxone; further, it demonstrates limited efficacy for treatment of pharyngeal gonorrhea (92.3% cure; 95% confidence interval [CI] = 74.9%–99.1%); in older clinical studies, cefixime cured 97.5% of uncomplicated urogenital and anorectal gonococcal infections (95% CI = 95.4%–99.8%).

Furthermore, as cefixime becomes less effective, continued used of cefixime might hasten the development of resistance to ceftriaxone, a safe, well-tolerated, injectable cephalosporin and the last antimicrobial known to be highly effective in a single dose for treatment of gonorrhea at all anatomic sites of infection.

Other oral cephalosporins (e.g., cefpodoxime and cefuroxime) are not recommended because of inferior efficacy and less favorable pharmacodynamics.
Cefixime 400 mg oral as a single dose

Only advisable if an intramuscular injection is contraindicated or refused by the patient.

Observations in Asia have raised serious concerns over the adequacy of the 400 mg cefixime dose for the treatment of genital tract gonorrhoea. Repeated treatment failures have been reported with cefixime and other oral extended spectrum cephalosporins;

RETREATMENT

A. Suspicion of REINFECTION: re-treat with a WHO-recommended regimen, reinforce sexual abstinence or condom use and provide partner treatment.

B. If TREATMENT FAILURE occurred and resistance data are available, re-treat according to susceptibility.

If antimicrobial susceptibility test is not available:

- If the first treatment was a regimen not recommended by WHO, re-treat with a WHO-recommended regimen,
- If it was a WHO-recommended single therapy, re-treat with WHO-recommended dual therapy,
- If it was a WHO-recommended dual therapy, re-treat with one of the WHO dual therapies with doubled doses.

UNCOMPLICATED GENITAL INFECTION

Single therapy

- azithromycin 1 g os as a single dose
- doxycycline 100 mg os twice a day for 7 days

or one of these alternatives:
- tetracycline 500 mg os four times a day for 7 days
- erythromycin 500 mg os twice a day for 7 days
- ofloxacin 200–400 mg os twice a day for 7 days.

GENITAL INFECTION IN PREGNANT WOMEN

Single therapy

1. azithromycin 1 g os as a single dose
2. amoxicillin 500 mg os three times a day for 7 days
3. erythromycin 500 mg os twice a day for 7 days.

WHO guidelines for the treatment of Chlamydia trachomatis.
ANO-RECTAL INFECTION

This recommendation applies to people with known anorectal infection and to people with suspected anorectal infections with genital co-infection.

Single therapy

- doxycycline 100 mg os twice a day for 21 days
- azithromycin 1 g os weekly for 3 weeks.

LYMPHOGRAINULOMA VENEREUM (LGV)

C. trachomatis immunotype L1 – L2 – L3

Single therapy

- doxycycline 100 mg os twice a day for 21 days
- azithromycin 1 g os weekly for 3 weeks.

WHO guidelines for the treatment of Chlamydia trachomatis.
BUT...

- In the European and Australian Guidelines the recommended treatment for an ano-rectal infection due to CT is only doxycycline!!!

*Single therapy*

- doxycycline 100 mg os twice a day for 7 days
- azithromycin 1 g os as a single dose.

REPEAT CT INFECTION

Community cohorts of women in UK -> 25.5%

Women attending GP clinics in UK -> 29.9%

Women attending GP clinics in Australia -> 22.3%

Men with urethral CT infection -> 18.3%

Men with rectal CT infection -> 21.7%
AZITHROMYCIN vs DOXYCYCLINE
RE-INFECTION EXCLUDED

In men with NGU -> Treatment failure: 23% vs 5,2%
Handsfield HH. Sex Transm Dis 2011, 38:1028-9

In men with rectal CT -> Azithro failure 6%

In women -> Azithro failure 8%
Horner PJ. Sex Transm Infect 2006,82:340-3
# ASYMPTOMATIC RECTAL CT INFECTIONS IN MSM

<table>
<thead>
<tr>
<th>Study</th>
<th>Aim</th>
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<tr>
<td>King FY, et al. JAC 2015,70:1290-7</td>
<td>Treatment efficacy</td>
<td>82.9%</td>
<td>99.6%</td>
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<tr>
<td>Kong FY, et al. Epidemiol Infect 2016,144:2587-96</td>
<td>Treatment efficacy</td>
<td>83.6%</td>
<td>-</td>
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<tr>
<td>Hathorn E, et al. Sex Transm Infect 2016,92:115</td>
<td>Failure/recurrence</td>
<td>5.2%</td>
<td>0.9%</td>
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<tr>
<td>Australian Azithro vs Doxy, double-blind RCT</td>
<td>Aug 2016 -&gt; 2019</td>
<td></td>
<td>Ongoing</td>
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</table>

Batteigere BE. Sex Transm Dis 2017 44,7:403-5
ADHERENCE:
ONE DAY VS 7-DAY COURSE

In real life settings, doxycycline complete adherence proved to be low (16-25%)

However, despite this data, the microbiological cure rate based on NAAT, was high (94%)

THEORIES AND POSSIBLE EXPLANATIONS

A. Quinolones, macrolides and tetracyclines are **bacteriostatic** and not bactericidal when exposed to the bacterium for <48 h


B. Whereas Doxy is highly lipid soluble, Azithro is **delivered** to site of infection via phagocyte cells. Unlike the urogenital site, the immune-response in the gastrointestinal tract is down-regulated -> CT can replicate and growth, phagocytes which can deliver Azithro are reduced.


C. Heterotypic antimicrobial resistance is exhibited by CT in **high burden** infections. Patients with urethritis have a high load of CT, but higher load are present in the genital tract of younger women and in the rectum.


D. Homotypic resistance (genetically inherited) -> no published cases **in vivo**! Azithro resistance could be selected **in vitro**, but it seems to be associated with reduced fitness (slower replication rate)

Horner PJ. Sex Transm Infect 2012,88(3):154-6
Treatment challenges for urogenital and anorectal Chlamydia trachomatis

Fabian Yuh Shiong Kong*† and Jane Simone Hocking†
Organism load may be important for treatment efficacy. Heterotypic resistance is demonstrated in vitro at high levels of chlamydial organism load, but is not evident at lower levels of organism load leading to the hypothesis that treatment efficacy may reduce as organism load increases. A recent systematic review found that organism load is higher at the anorectal site than at cervical or urethral sites raising the possibility that anorectal infections may be more susceptible to treatment failure because of heterotypic resistance [32]. A recent Australian study investigating the association of organism load with repeat anorectal chlamydia infection among men, found that for every log_{10} increase in organism load, the odds of a repeat anorectal infection within 3 months of treatment with azithromycin increased by 70 % (OR 1.7; 95 % CI: 1.2–2.5) providing support for the hypothesis that high loads contribute to treatment failure [33].
A recent *in vitro* study examining the impact of β-lactam antibiotics on chlamydia persistence [39] found that all penicillins tested induced the formation of ABs with a 95% reduction in chlamydia's infectivity. Upon removal of the antibiotics, the chlamydia became infectious again, but β-lactam-induced persistent chlamydia was less susceptible to azithromycin *in vitro* [35]. Therefore, the question begs whether the marked increase in the use of beta-lactam antibiotics in recent years, [42] including its use in treating increases numbers of syphilis infections among gay men, [43] is contributing to antibiotic-induced persistence and whether increasing the duration of treatment can overcome this persistence [34] as has been demonstrated in animals [35].
POSSIBLE SOLUTIONS

- Prescribe Doxycycline

- Prolonged courses of bacteriostatic antibiotics could be clamydicidal:

  Since the half-life of Azithromycin is 68 h, increasing its dose to 3 g total would be likely to maintain tissue levels for over 12 days

  1000 mg QD on day 1

  500 mg QD from day 2 to 5

- For those individuals with apparent Azithromycin treatment failure with no risk of re-infections, antimicrobial resistance should be assessed and genotyped if positive

- With NAATs, false positive results may occur up to 3 weeks after treatment due to non-viable CT DNA. Persistence of infection (EB) may take up to 5 weeks to emerge - > test of cure should be deferred for at least 5 weeks.
IS THE CT RECTAL INFECTION FREQUENT?

- Asymptomatic rectal CT infections are common among MSM and frequently exist apart from urethral infections: up to 88% of those with rectal CT are negative at the urethra.

- Anal sex is increasing among heterosexual couples (15-17% - 2-3 fold increase since 1990).

- There is evidence that women may acquire rectal CT infection in the absence of anal sex -> rectal testing for women with repeat cervical CT infection < 3 months and for high risk women who reported anal sex.

Kong FYS, Hocking JS. BMJ Infect Dis 2015,15:293
GENITAL INFECTION

Single therapy

- metronidazole 2 g os as a single dose
- tinidazole 2 g os as a single dose
- metronidazole 500 mg os twice a day for 7 days

The treatment for individuals with persistent or recurrent trichomoniasis, where reinfection or nonadherence are unlikely it is suggested that longer courses or additional doses of the same medications used in standard therapy should be successful:

- tinidazole 1 g twice daily for 2 weeks + tinidazole vaginal tablets 500 mg twice daily for 1 week
MYCOPLASMA GENITALIUM
MG is nowadays an established sexually transmitted pathogen that causes NGU and recent evidence indicates that it increases the risk for cervicitis, PID, preterm delivery and spontaneous abortion.

According to community-based studies in UK, USA, Australia and Scandinavia the prevalence of MG infections is 1-3% in men and women.

Studies among MSM attending clinics report rectal MG infection prevalence 1-5%, predominantly asymptomatic. However, a recent study of MSM with proctisis in Australia found 8% of HIV-negative and 20% of HIV-positive MSM had rectal MG infection.

Whereas MG presumptive treatment of sexual contact of MG-infected people is not recommended in the US and European STI treatment guidelines, it is in the Australian one.
Mycoplasma genitalium Infection in Adults Reporting Sexual Contact with Infected Partners, Australia, 2008–2016

377 patients:
139 women,
126 heterosexual men,
112 MSM

- WOMEN -> Cervical/vaginal swabs/first catch urine -> 48.2% positive result
- STRAIGHT MEN -> first catch urine -> 31.0%
- MSM -> First catch urine only (42.8%) -> 6.3%
  Rectal swab only (14.3%) -> 43.8%
  Urine and rectal swab (42.9%) -> 41.7% (17/20 infection were at the rectal site!)

Overall 8/96 urethral sites were positive (8.3%) compared with 24/59 rectal sites (40.7%)
In the multivariate analysis MSM contacts had an 8-fold increase in probability in MG infection if they were tested at the rectum instead at the urethra (aOR 8.39)

Overall 8/96 urethral sites were positive (8.3%) compared with 24/59 rectal sites (40.7%)
MG INFECTION MANAGEMENT

Single therapy
- Azithromycin 1 g os as a single dose

In case of failure
- Moxifloxacin 400 mg os daily for 10 days
- Pristinamycin 1 g os/6 hours for 10 days (based on in vitro data – personal communication by J. Jensen)

USA and European Guidelines for the management of STIs.
MG ANTIMICROBIAL RESISTANCE

Macrolide Resistance and Azithromycin Failure in a Mycoplasma genitalium–Infected Cohort and Response of Azithromycin Failures to Alternative Antibiotic Regimens

Pre-treatment MRM (23S rRNA gene) was present in 36% of urine samples.

This significantly increases the odds of azithromycin failure: 87% (in the multivariate analysis aOR 56.0)

Moreover, treatment failure was significantly related to organism load (for each log10 increase aOR 1.8)

Overall, azithromycin failure rate was 39% (60/160) and moxifloxacin failure rate was 12% (7/60).
MACROLIDE RESISTANCE

- Rapid selection of resistant mutants
- Single nuceotide change confers high-level MR
- Macrolides are bacteriostatic -> in high organism load a larger number of bacteria could survive the initial peak concentration of azithromycin with replication of surviving cells when concentrations drop below the MIC.

Scandinavian Guidelines suggests the use of the extended azithromycin regimen:

- 1 g os QD day 1
- 250 mg os QD day 2 to 5
QUINOLONE RESISTANCE

Mutations in the parC gene

- 2° Generation (Cipro, Oxi) are not efficient to eradicate MG infection both in vitro and in vivo (cure rate 59%),

- 3° Generation (Levo) appeared more promising, but it failed in observational studies, (overall cure rate 54%),

- 4° Generation (Moxifloxacin) is bactericidal and in early studies appeared to have a cure rate approaching 100%

A declining cure rate has now been observed

Asia-Pacific Region: 30% MG isolates
Japan: 33% (20% in 2011 – 47% in 2013)
Australia: 15%
Europe: low rate
UK: 5%
Denmark: <5%
QUINOLONE RESISTANCE

Mutations in the *parC* gene

- 2° Generation (Cipro, Oxi) are not efficient to eradicate MG infection both *in vitro* and *in vivo* (cure rate 59%),

- 3° Generation (Levo) appeared more promising, but it failed in observational studies, (overall cure rate 54%),

- 4° Generation (Moxifloxacin) is bactericidal and in early studies appeared to have a cure rate approaching 100%

- Next Generation (gatifloxacin, sitafloxacin) has been used in 5 studies with an overall cure rates of 95%
OTHER ANTIMICROBIALS

Licensed but less used -> PRISTINAMYCIN

- Oral streptogramin with bactericidal activity on Gram+bacteria, including MRSA.
- It has a high activity against both macrolide susceptible and resistant MG stains, even in those with macrolide and moxifloxacin resistance
- The maximal recommended dose in 1 g 4 times/day for 10 days -> last known eradication chance
- Several cases have been successfully treated both in Scandinavia and Australia

Under development

- Solithromycin (new fluoroketolide)
- Lefamulin (pluromutulin class)
- AZD0914 (spiropyrimidinetrione)
- LBM415 (peptide deformylase inhibitors)

Jensen JS, Bradshaw C. BMJ Infect Dis 2015, 15:43
OLD BARRIERS, NEW PERSPECTIVES
# The Global Strategy for Prevention and Control of STIs

## Priority Interventions

- Scale up STI-diagnosis and treatment at primary care sites
- Elimination of Congenital Syphilis
- Strengthen STI-surveillance, SGS HIV including STIs
- Targeted interventions for key/vulnerable populations, and PLWHA
- Age-appropriate comprehensive sexual health education and services
- Scale-up of effective vaccines
- Promote partner management
- Increase access to HIV-counselling and -testing for STI-patients

## Create Enabling Environment

- Increase political commitment for STI-prevention and control
- Advocate for resource mobilization and reallocation of resources
- Promote policies, laws and initiatives in STI-control – non-stigmatizing and gender sensitive services
- Harness strengths and capacities of partners and institutions to scale up and sustain interventions
Lo studio europeo conferma: gay, lesbiche e trans discriminati in ospedale

Al nuovo studio internazionale ha partecipato anche l’Azienda Ospedaliera Universitaria Integrata di Verona.

I professionisti socio-sanitari e gli utenti dei servizi sanitari sono d’accordo: le persone LGBT frequentemente si trovano di fronte a barriere culturali, discriminazioni e disuguaglianze quando accedono ai servizi sanitari. In ospedale insomma si viene ancora discriminati.
La PrEP è disponibile in farmacia: costa un po’ e serve la prescrizione di uno specialista

Ecco come provare ad acquistarla.

Le persone sieronegative che desiderano utilizzare la PrEP per prevenire l’infezione da HIV, possono acquistare il farmaco in una farmacia territoriale, dietro presentazione di ricetta medica fatta da un medico infettivologo e pagandolo di persona.

Le persone senza HIV che hanno necessità di utilizzare la PrEP per prevenire l’infezione da HIV, possono acquistare il farmaco in una farmacia territoriale, dietro presentazione di ricetta medica fatta da un medico infettivologo e pagandolo di persona. Il prezzo di Truvada originale è di oltre 700 euro a confezione ma da ottobre 2017 sono disponibili versioni generiche al prezzo di circa 115 euro. La prima ad essere commercializzata è quella della DOC, una casa farmaceutica di Milano; il codice del farmaco – che è possibile fornire al farmacista per facilitarlo nella ricerca – è 044113013.
DON'T.
EVER.
QUIT.

BUT IN THE END,
IT DOESN'T MATTER
WHEN YOU QUIT.

If you quit after five years
of effort, the net result is the
same as if you gave up two
gave up on your dreams.
Do the hard work.