CASE-BASED UPDATE ON SEXUALLY TRANSMITTED INFECTIONS

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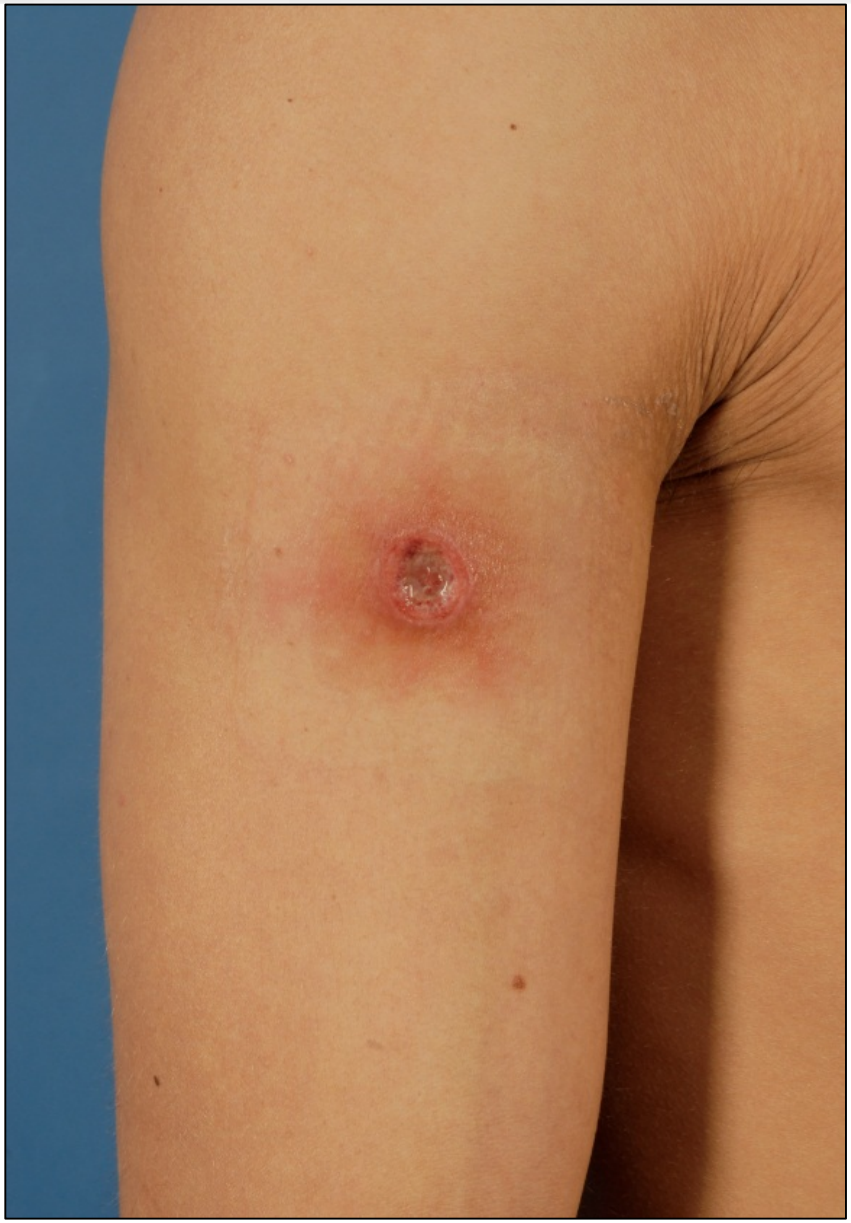
Disclosures

- I have received consulting fees, honorarium and/or travel grants from Gilead, Janssen-Cilag, MSD and ViiV Healthcare
- I have no other potential conflict of interest to declare

CASE 1

Anamnesis

- 32 year-old male patient
- HIV-1 infection since 2002
  - MSM
  - History of cervical diffuse large B-cell lymphoma
  - $CD4^+$ T cells: 448/µl
  - HIV-1 RNA: 85114 copies/ml
  - ART: switch to maraviroc, darunavir and ritonavir due to high-level resistance against both NRTI and NNRTI compounds (K65R, M184I, Y181C, M230L)



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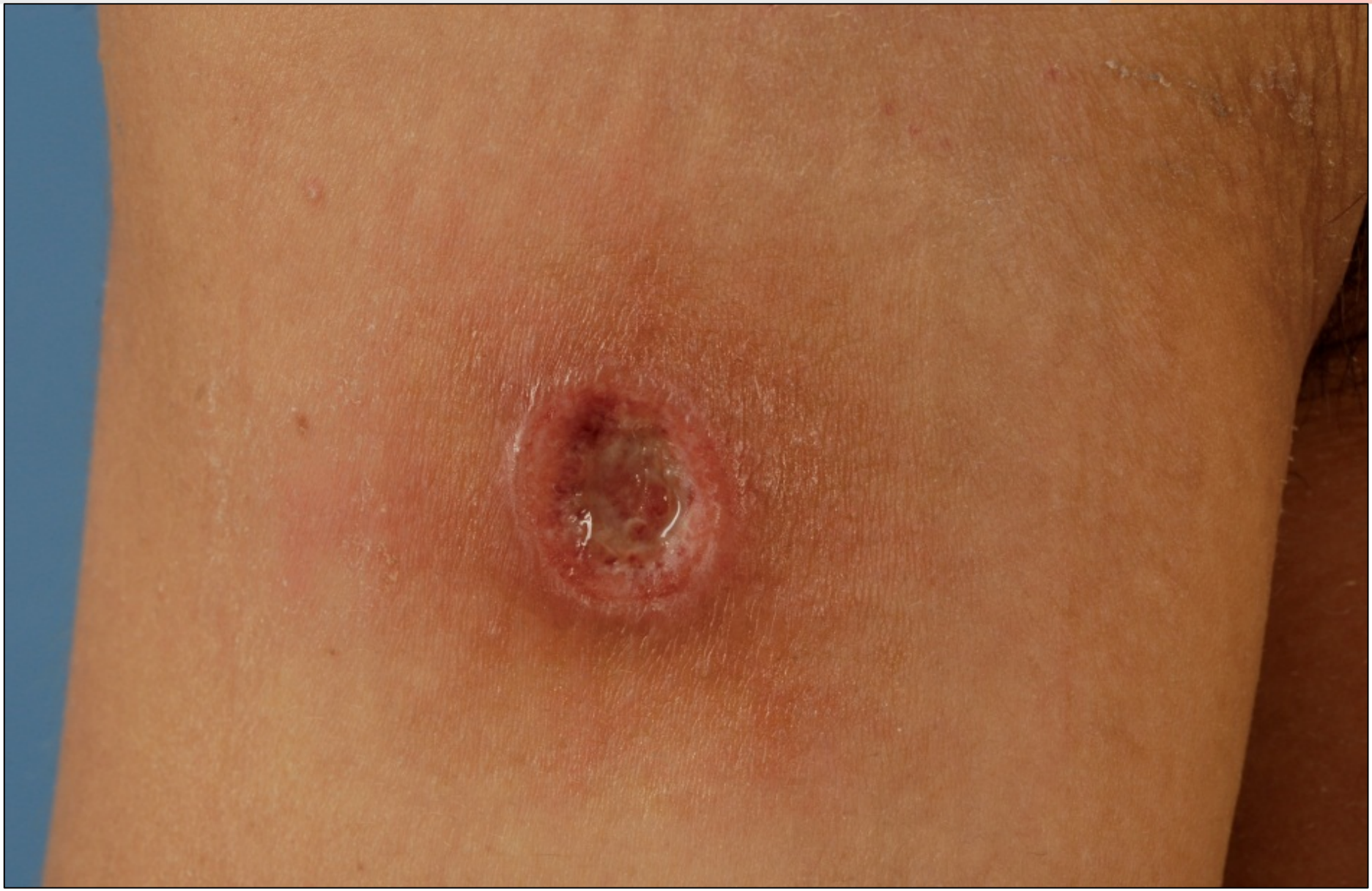


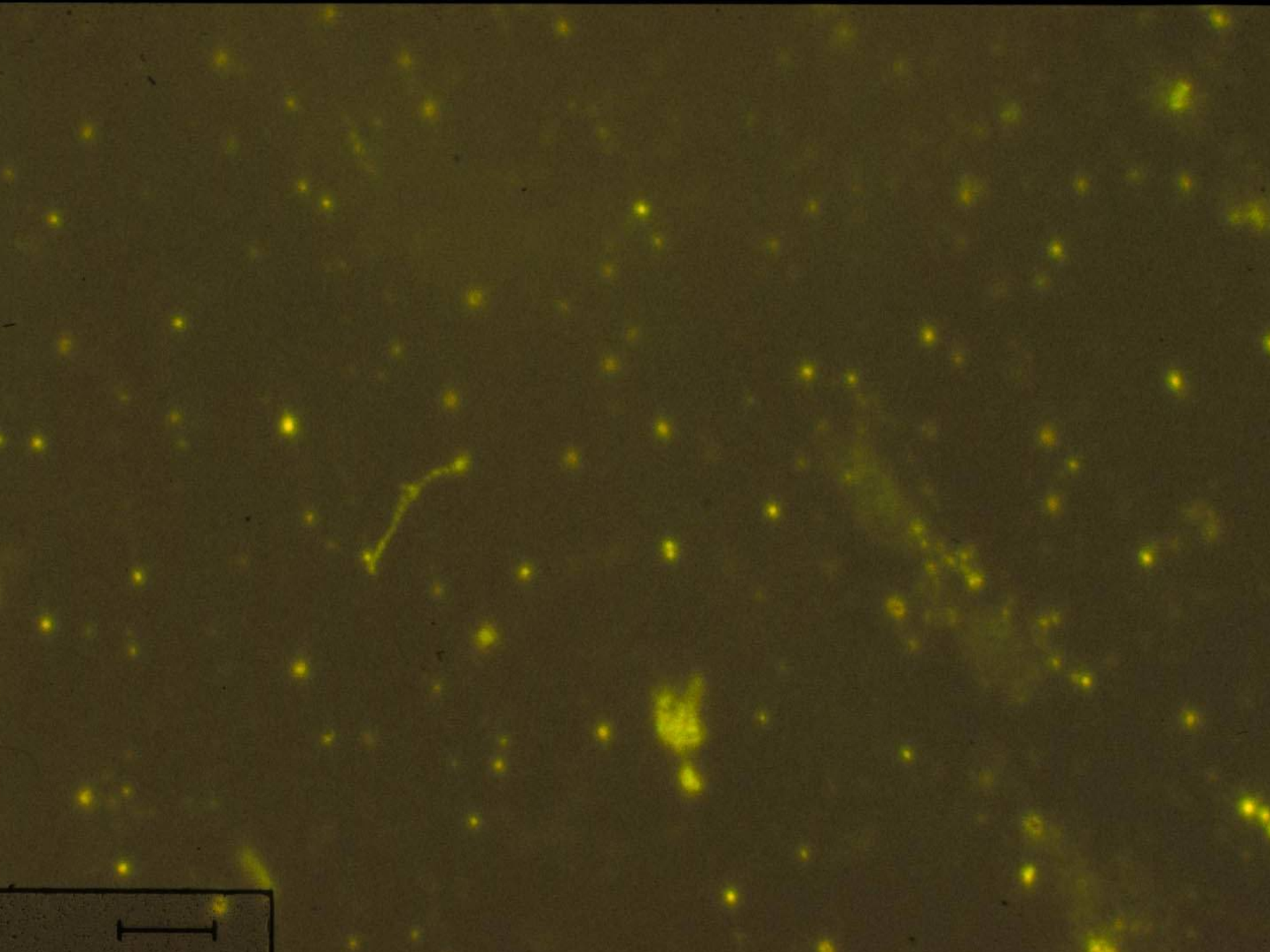
Aichelburg MC, Rieger A. *Int J STD AIDS,* 2012; 23(8):597-8.

Differential diagnoses

- Traumatic ulcer
- Vascular/ischemic ulcer
- Ulcerating tumor
  - Basal cell carcinoma, squamous cell carcinoma, lymphoma
- Pyoderma gangrenosum
- Infectious etiology
  - Ecthyma, cutaneous leishmaniasis, atypical mycobacterial infection (MAC)
  - Erysipeloid, ORF
  - Cutaneous fungal infection: aspergillosis, cryptococcosis
  - STD: syphilis I, ulcus molle, lymphogranuloma venereum

Diagnostics (1)

- Dark-field microscopy performed on exudate derived from the skin ulcer: multiple spirochetes



Diagnostics (2)

- Syphilis serology
  - Treponemal IgM ELISA reactive
  - TPPA reactive with a titre of 1:10240
  - FTA-ABS reactive
  - VDRL reactive with a titre of 1:32

Cardiolipin/non-treponemal tests

- **VDRL** **V**enereal **D**isease **R**esearch **L**aboratory test
- **RPR** **R**apid **P**lasma **R**eagin test

  - Non-treponemal tests correlate with disease activity
  - Higher titre (>1:32) in early stage syphilis
  - Usually become non-reactive after treatment

  - False negative test results
    - **Diagnostic window period**
    - Prozone phenomenon in secondary syphilis (undiluted serum)

  - Biological false positive test results
    - Pregnancy, post-immunization, recent MCI
    - Autoimmune diseases, IVDUs, chronic liver diseases, borreliosis and endemic treponematoses (Framboesia Tropica, pinta)

Treponemal tests

- **TPHA (TPPA)** — **T. P**allidum **H**aem**A**gglutination assay
- **FTA-Abs** — **F**luorescent **T**reponemal **A**ntibody Absorption test
- 19S-IgM-FTA-ABS
- **IgM-SPHA** — **IgM S**olid-**P**hase-**H**aem-**A**dsorption test

Syphilis serology- common constellations

VDRL	TPHA	19S-IgM-FTA-ABS	Interpretation
-	-	-	No syphilis or incubation
+ (≥1:8)	+	+	Active syphilis
+	-	-	Biologically false reactive
-	+/-	+	Early infection
+ (=1:8)	+	-	Late latency or treated syphilis
-	+	-	Treated syphilis or late latency or false reactive

Diagnosis

SYPHILIS I

How would you treat?

A. No therapy necessary

B. Benzathine penicillin G 2.4 million units intramuscularly single dose

C. 24 million units penicillin G intravenously for 14 days

D. Doxycyclin 100mg bid orally for 7 days

Treatment Guidelines

- **Early Syphilis** (primary, secondary, early latent syphilis)
  - **Benzathine penicillin G 2.4 million units IM**, single dose
  - Alternative
    - Doxycycline 100mg orally bid, 14 days
    - Ceftriaxon 1g IV or IM qd, 8-10 days
    - Azithromycin 2g orally single dose

- **Late Syphilis** (late latent, gumma and cardiovascular syphilis)
  - **Benzathine penicillin G 7.2 million units total,** administered as three doses of 2.4 million units IM, each at 1-week intervals
  - Alternative
    - Doxycycline 100mg orally bid, 28 days

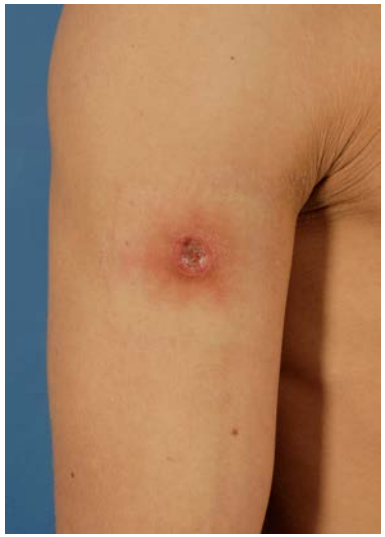
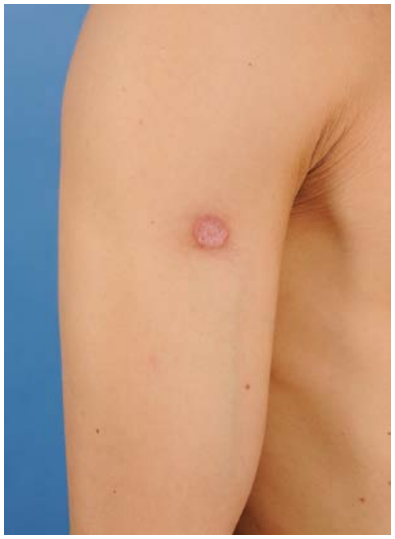
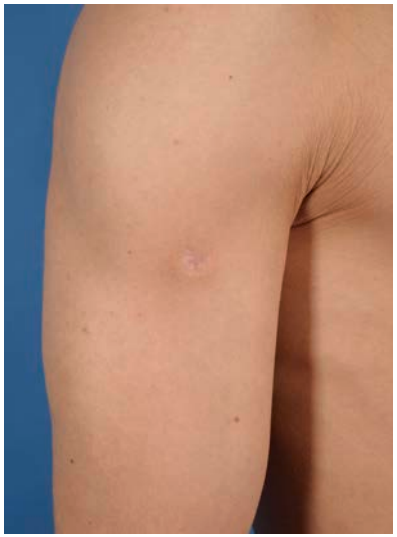
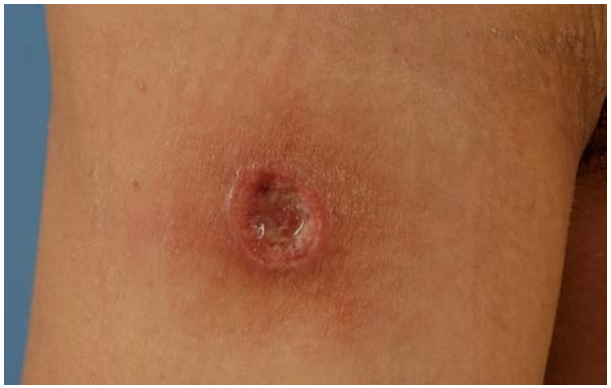
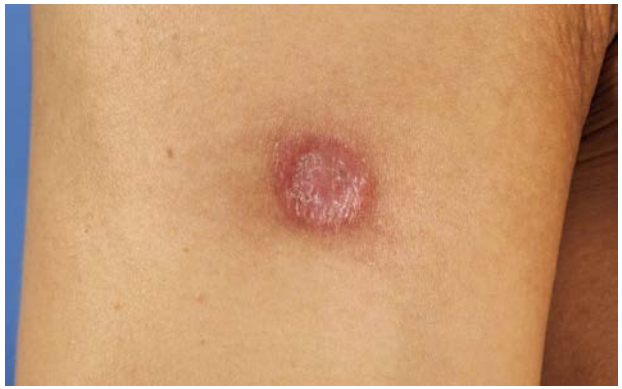
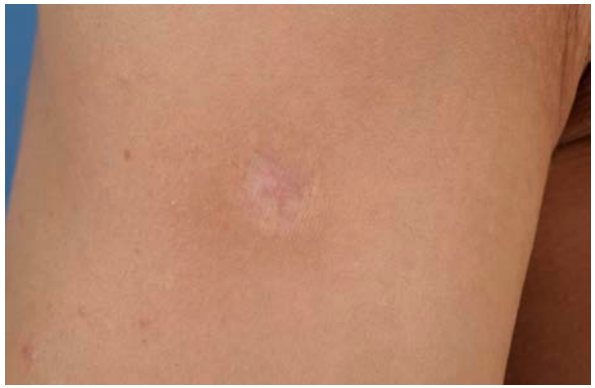
Workowski KA et al. *MMWR Recomm Rep.* 2010; 59: 1-110.

Therapy

Benzathine penicillin G 2.4 million units intramuscularly three times in weekly intervals

Tittes J, Aichelburg MC, Antoniewicz L, Geusau A. *Int J STD AIDS*, 2013; 24: 703–711.

Follow-up

Aichelburg MC, Rieger A. *Int J STD AIDS.* 2012; 23: 597-8.

Extragenital Syphilis I

- Extragenital chancres in 5-12%
- Usually affecting sexually exposed sites of the human body including the rectum, lips, oral cavity, tongue or nipple
- Three cases of syphilitic chancres on the arm, hand and finger have been reported in the medical literature

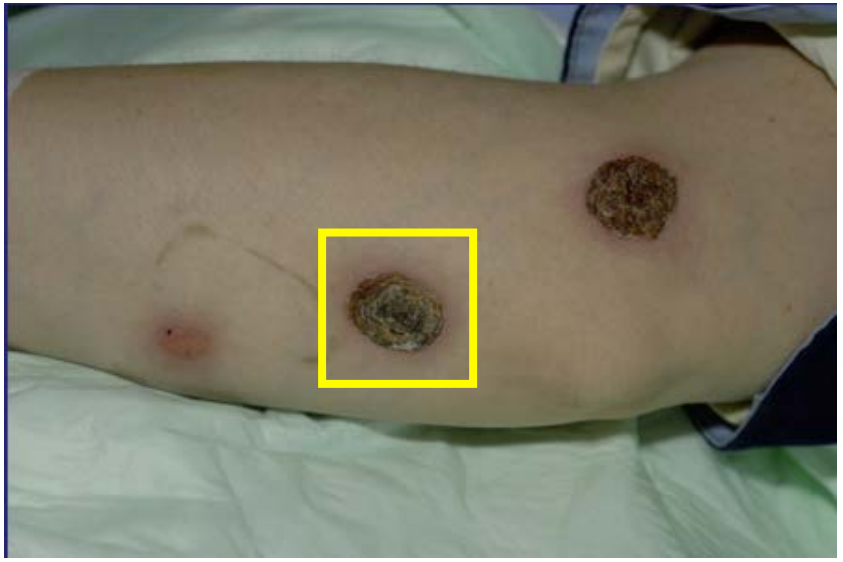
Aichelburg MC, Rieger A. *Int J STD AIDS.* 2012; **23:** 597-8.
Allison SD. *J Am Acad Dermatol.* 1986; **14:** 1094-5.
Bernabeu-Wittel J et al. *Sex Transm Dis.* 2010; **37:** 467.
Donofrio P. *Genitourin Med.*1986; **62:** 59–60.
Ramoni S, Cusini M, Boneschi V, et al. *Sex Transm Dis.* 2010; **37:** 468.

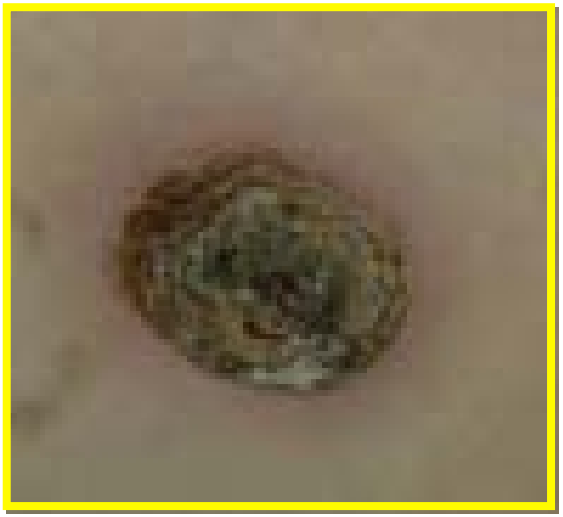
CASE 2

Anamnesis

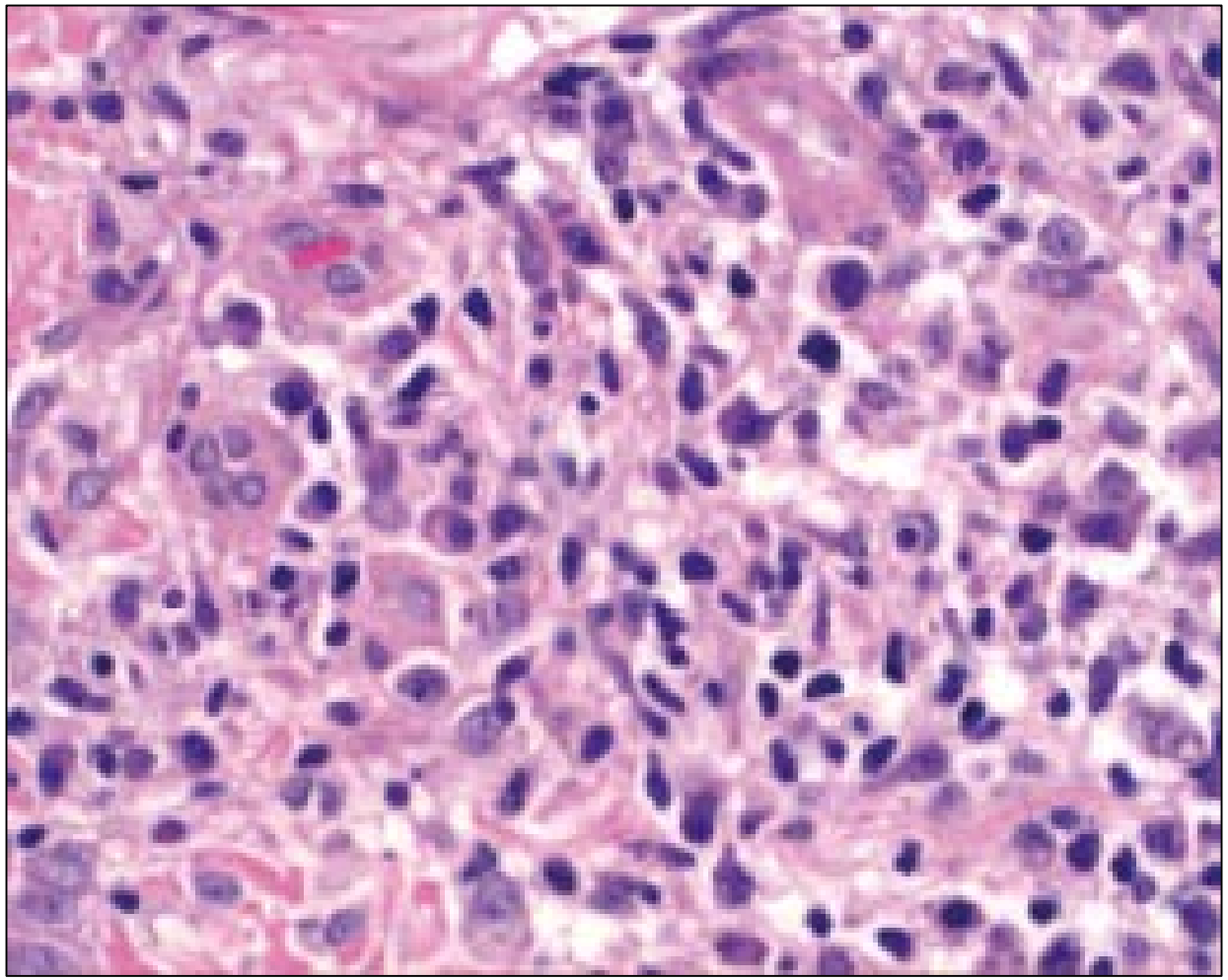
- 47-year old female patient
- HIV-1 infection since 2007
  - IVDU
  - $CD4^+$ T cells: 155/µl
  - HIV-1 RNA: 32414 copies/ml
  - ART naïve
- Schizoaffective disorder for years

- The lesions started 4 weeks ago on patient's lower arms
- Initially small papules and had since spread over the lower extremities, trunk and head
- Finally evolving to ulcers 2-3 cm in DM
- Progressive alopecia
- Fever, weight loss, headache, night sweats, increased lethargy





Histology



Laboratory results

- Blood cell count normal
- C-reactive protein 4.25 mg/dl (normal <1)
- Mycobacterial culture/PCR/AFB, fungal culture, bacterial broad spectrum PCR: negative

- Dark-field microscopy: negative
- Syphilis serology
  - Treponemal IgM ELISA reactive
  - TPPA reactive
  - VDRL reactive with a titre of 1:32

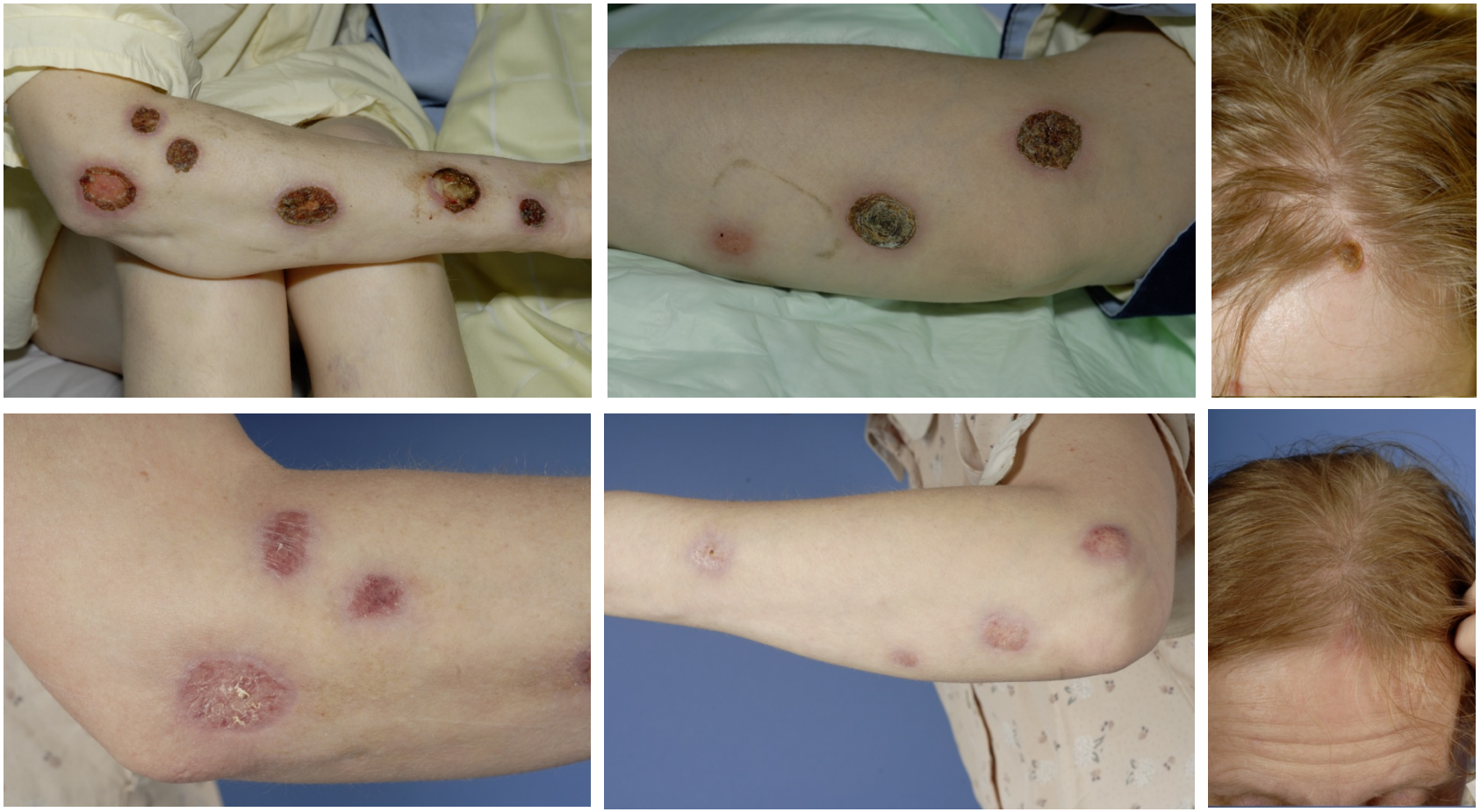
Diagnosis

MALIGNANT SYPHILIS

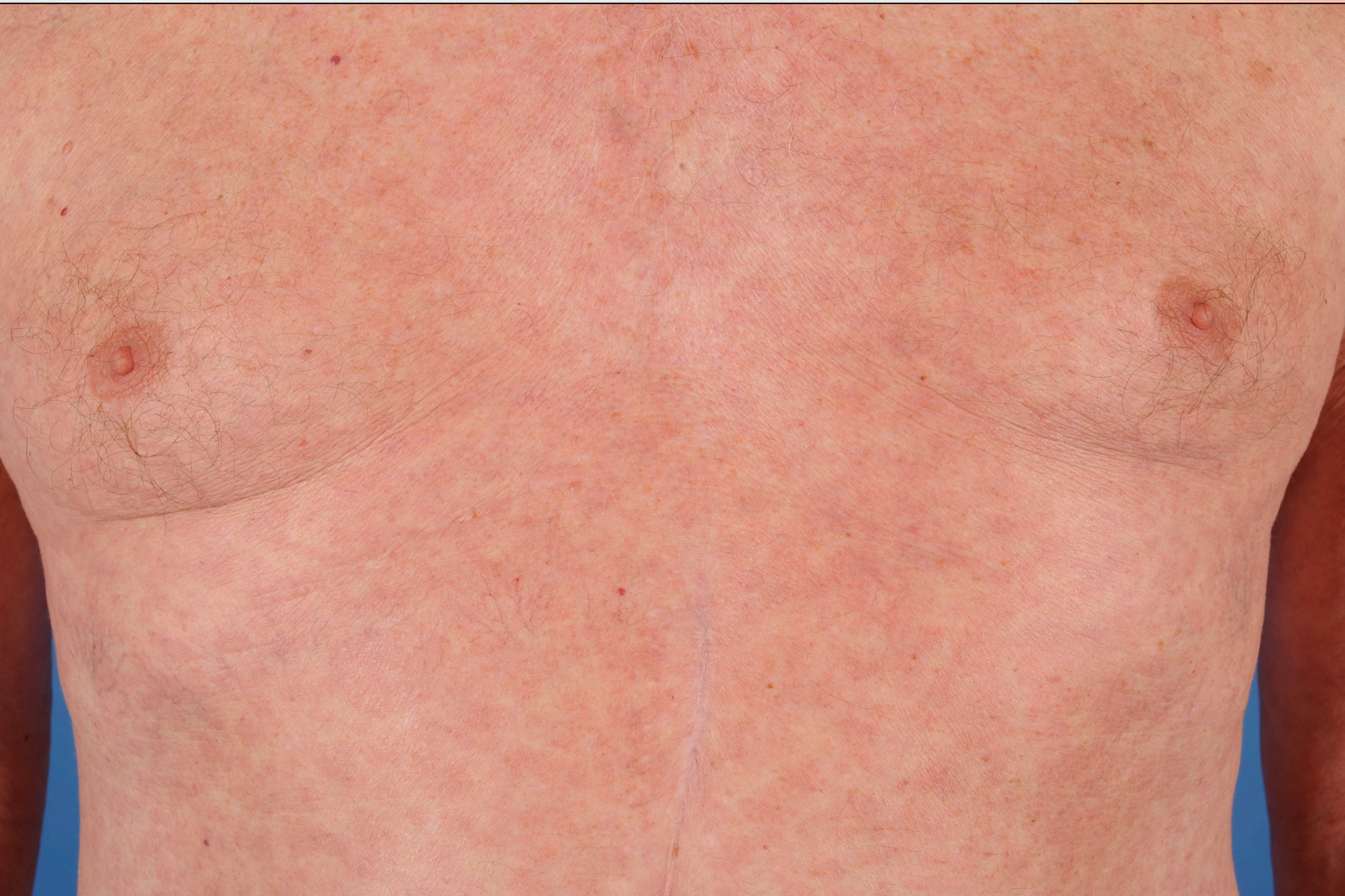
Therapy

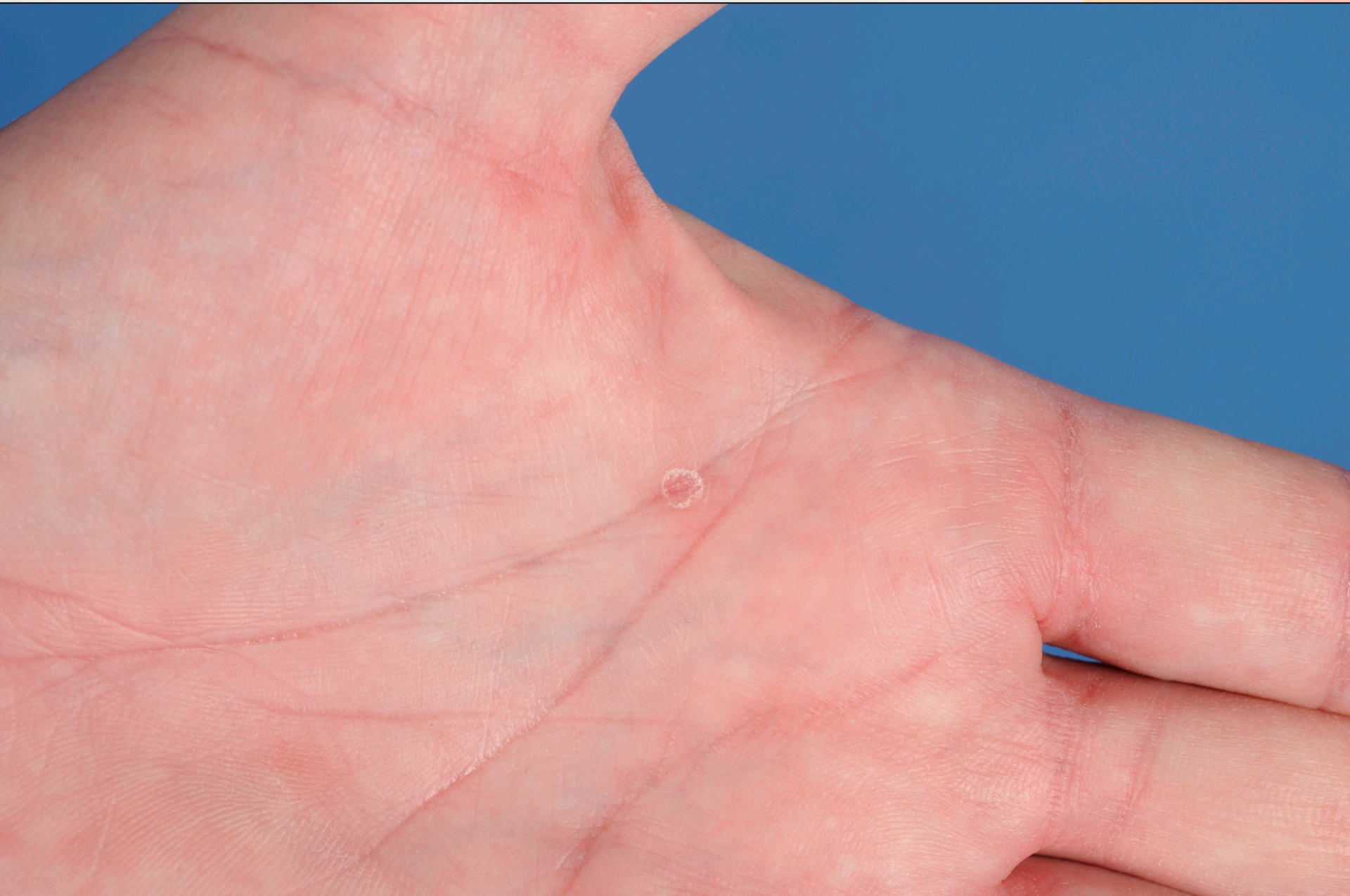
Benzathine penicillin G 2.4 million units intramuscularly three times in weekly intervals

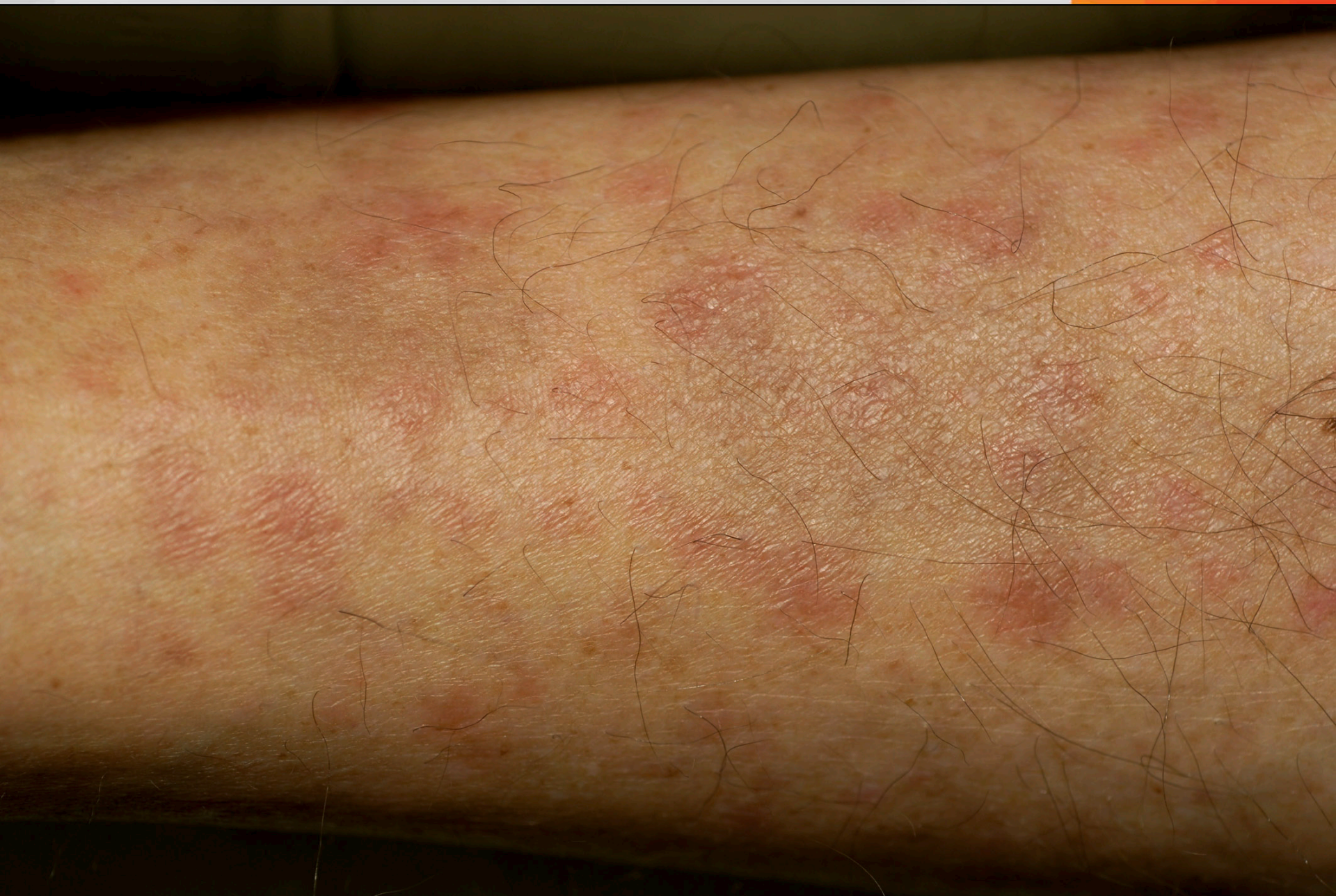
Follow-up

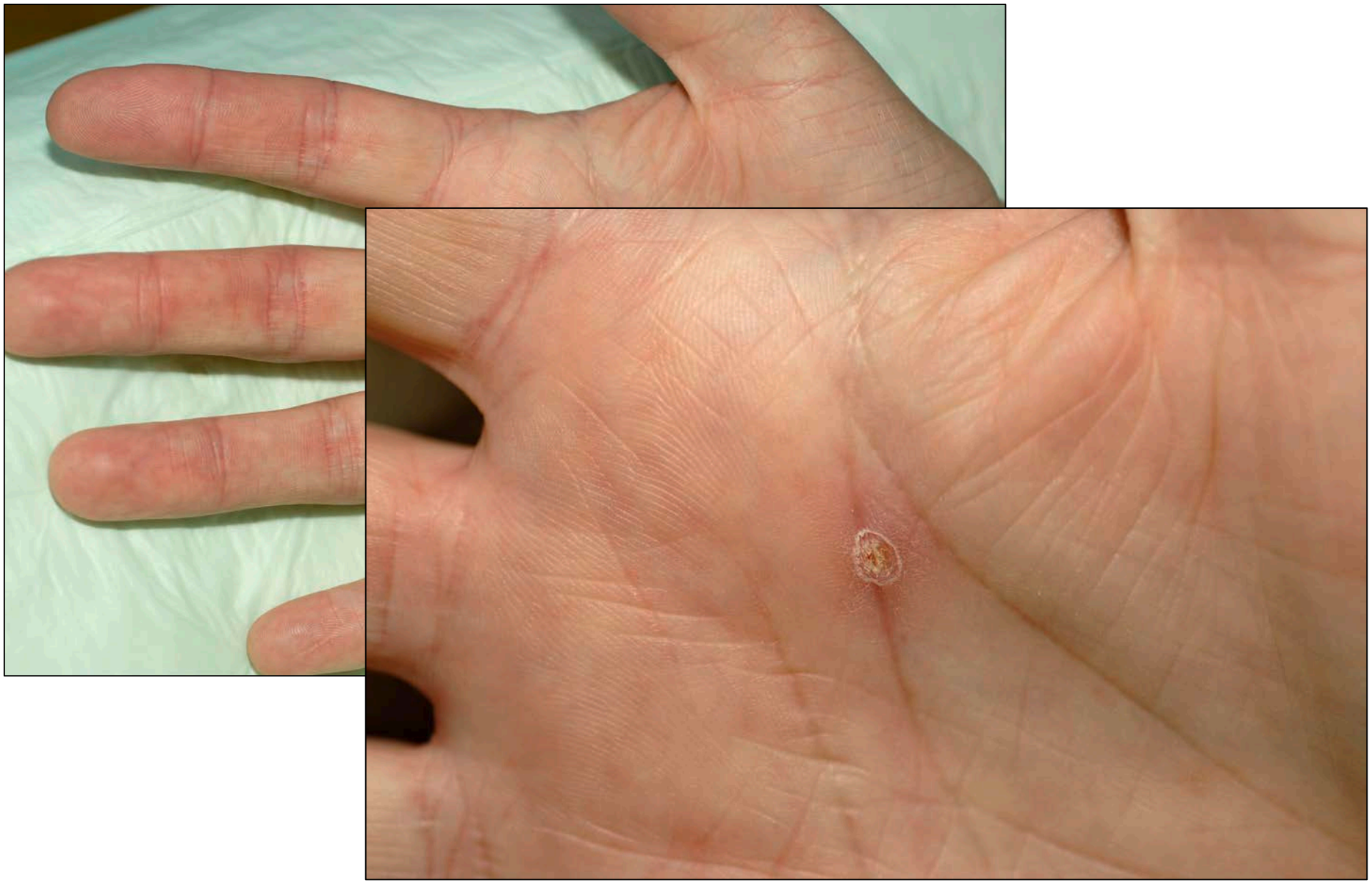


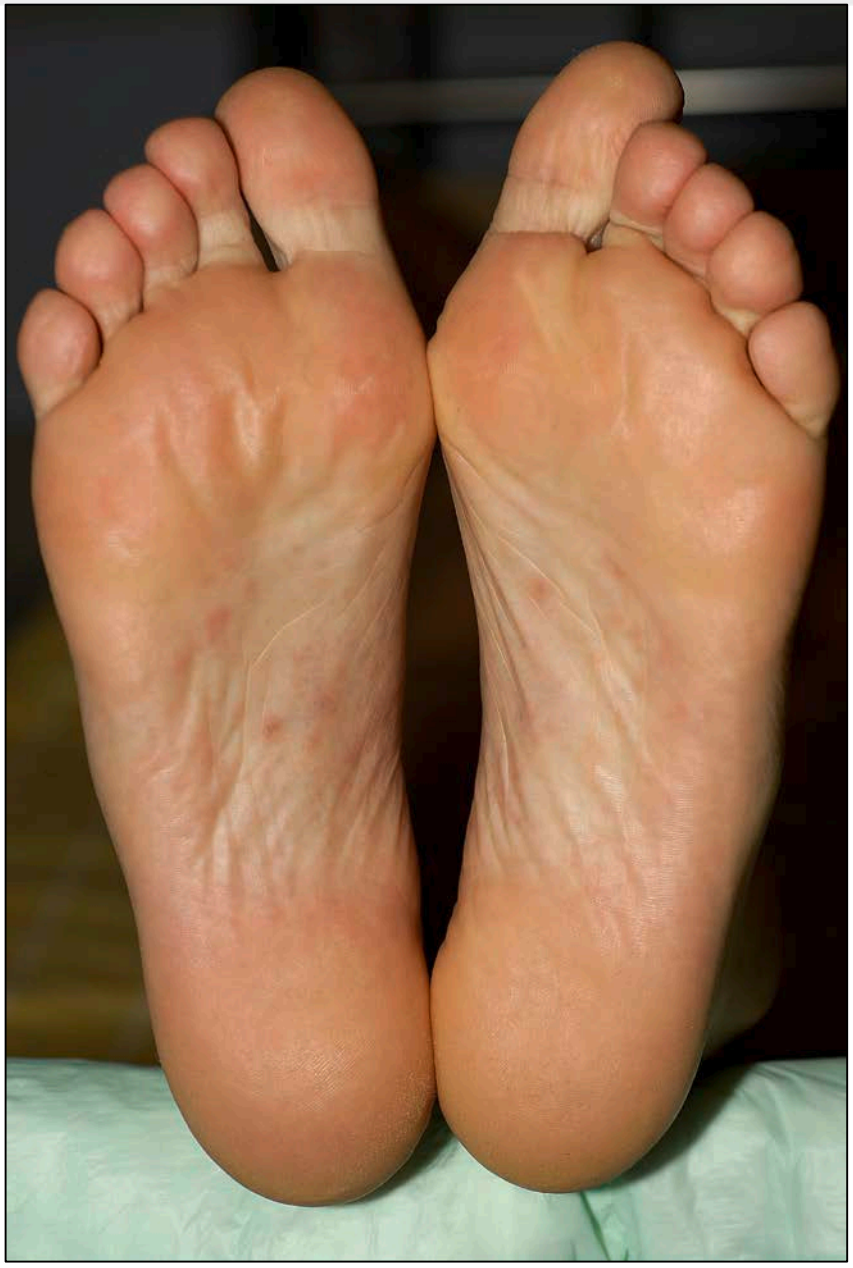
Jalili A *et al. Sex Transm Dis.* 2015; 42(4):223-5.

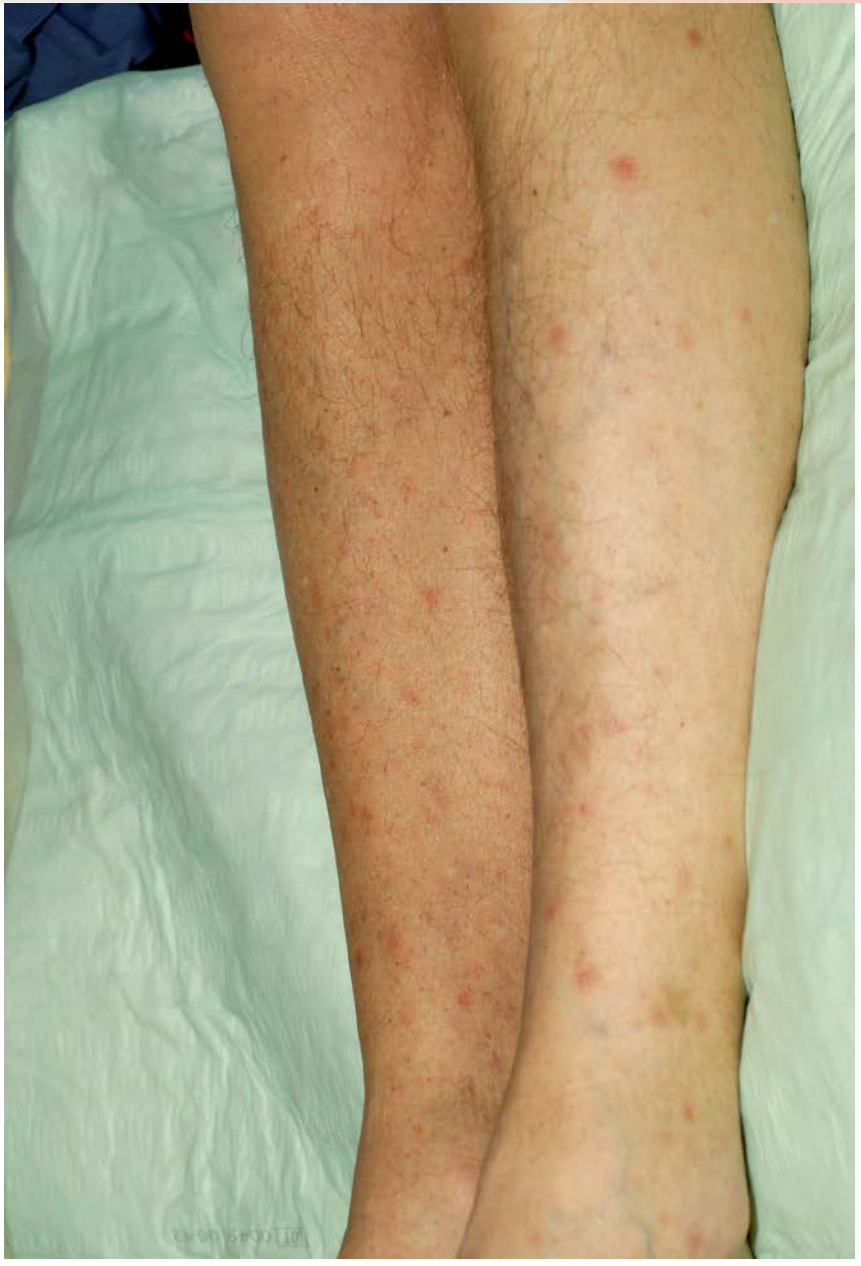






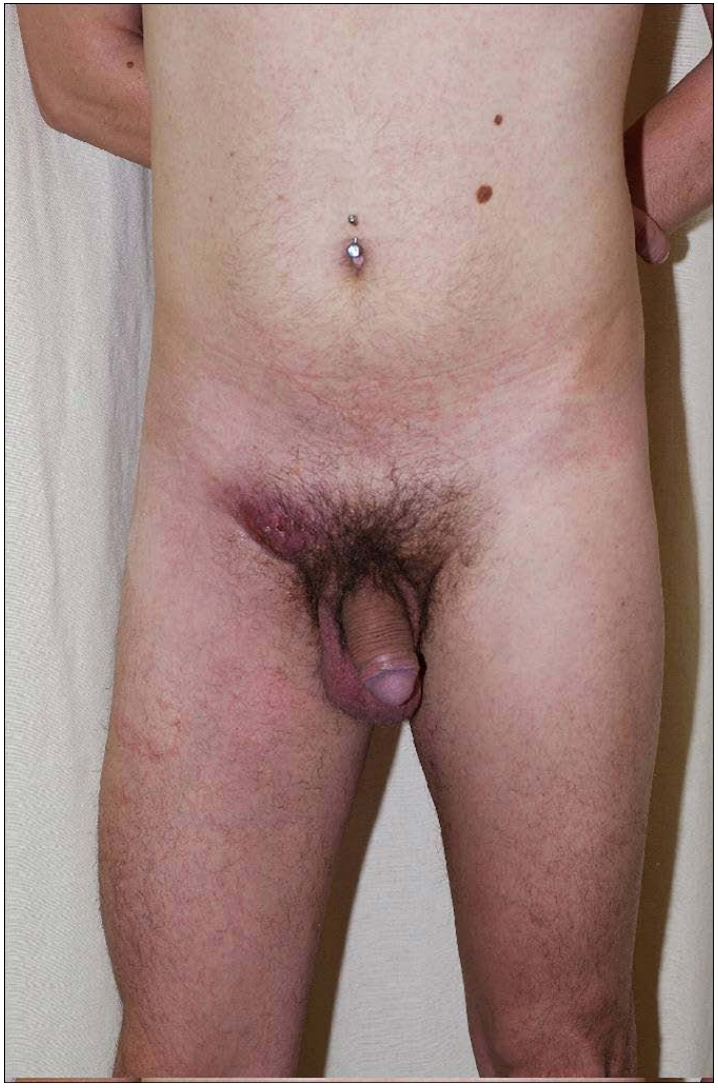


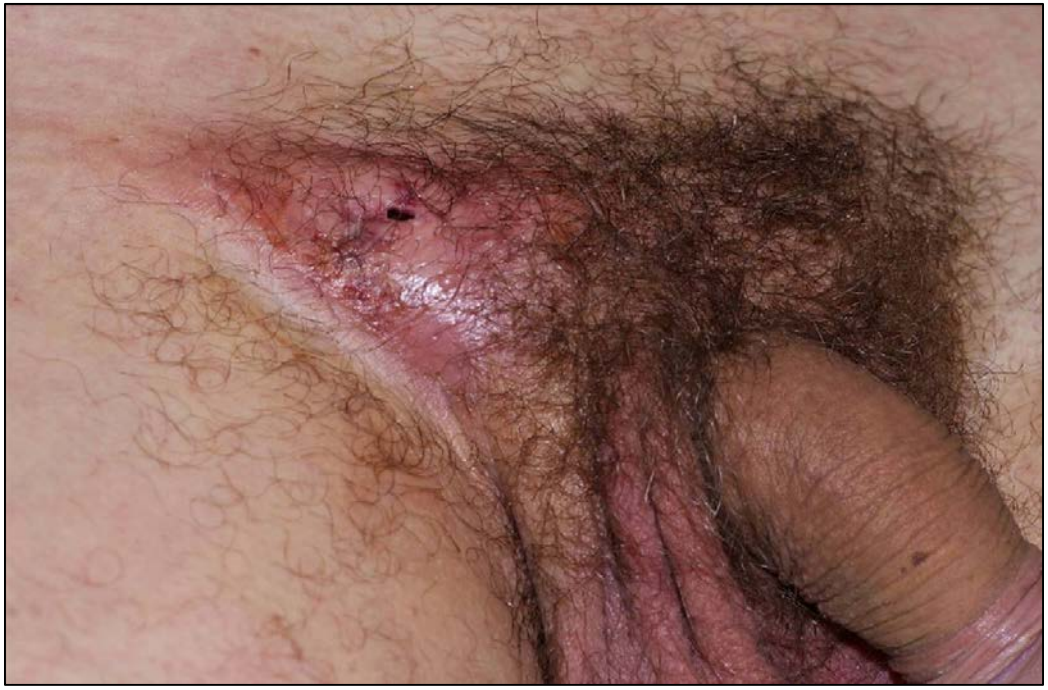




CASE 3

Inguinal lymphadenopathy

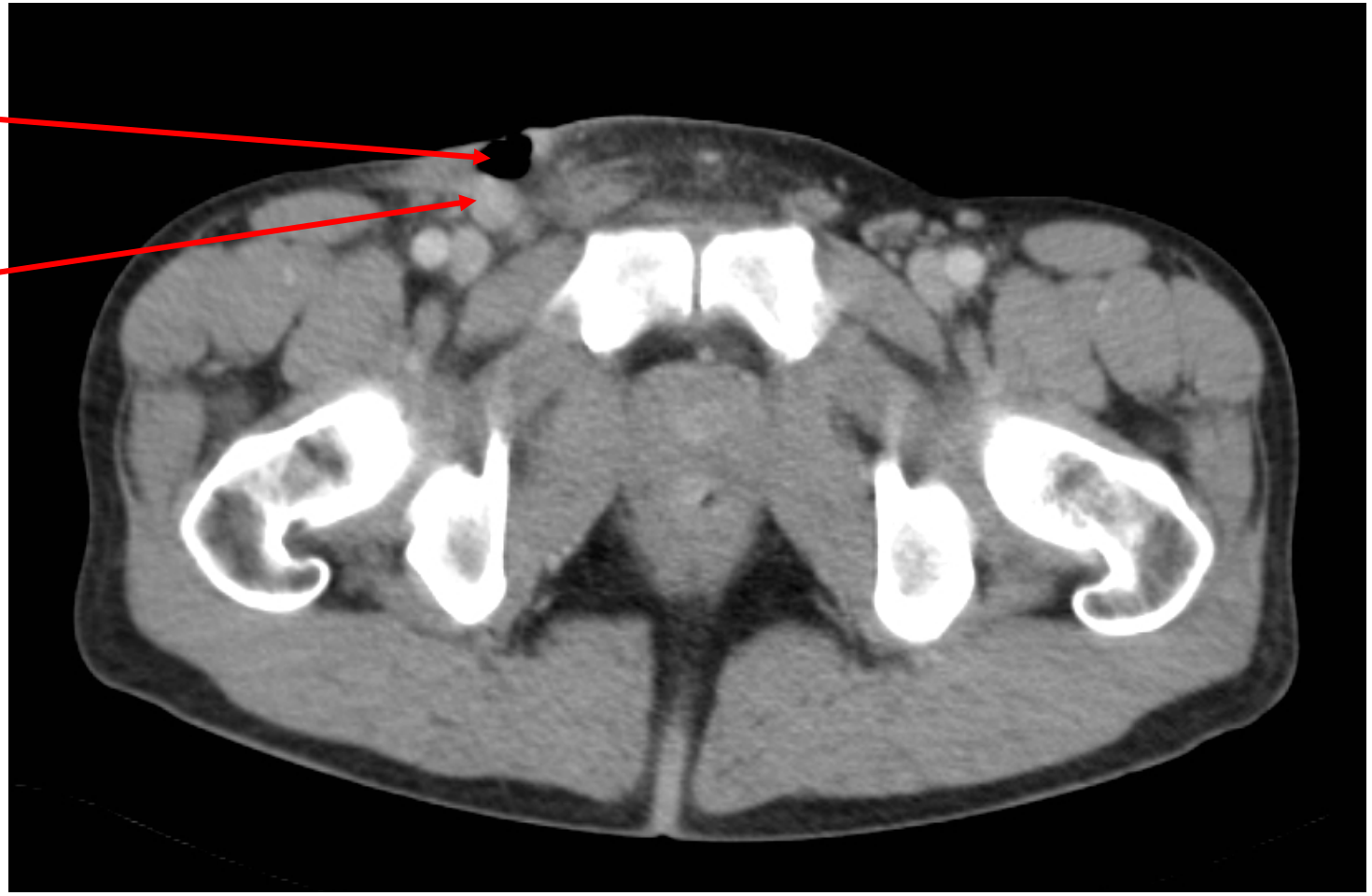




Abscess

Soft tissue swelling

Enlarged lymphnodes



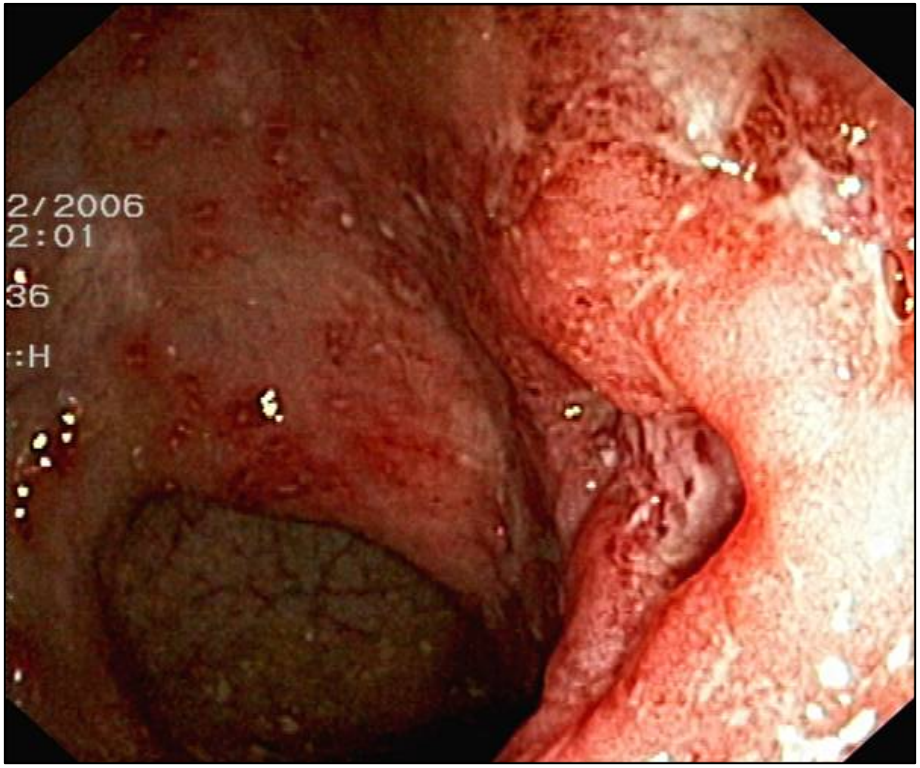
Laboratory results

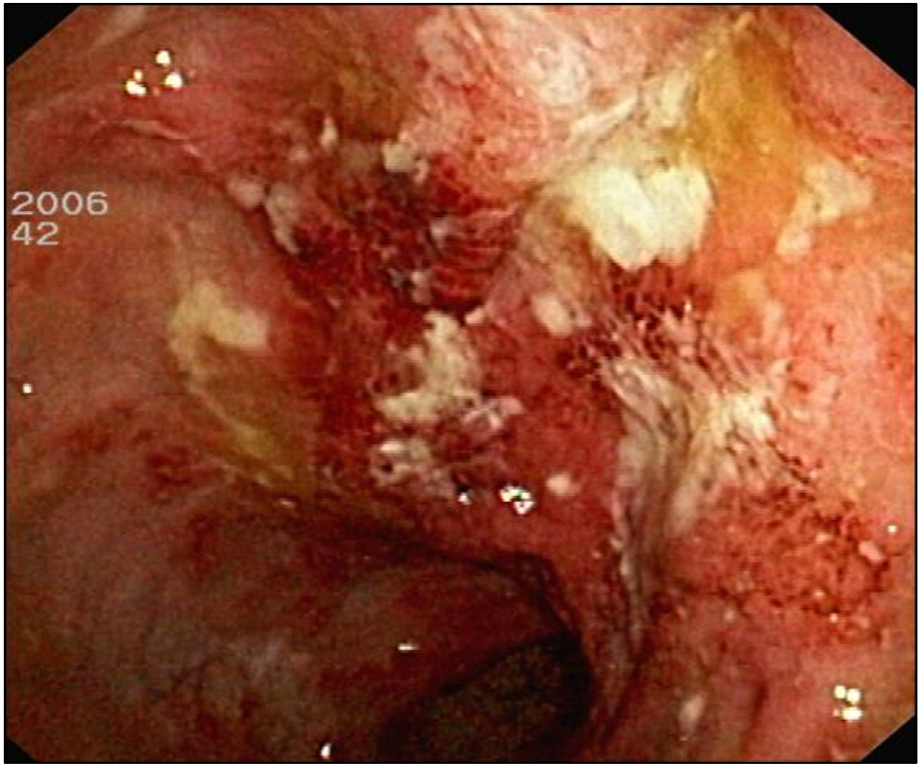
- Blood cell count, C-reactive protein: normal
- Bacterial culture LN aspirate: negative
- Culture/stain (urethral): negative
- Syphilis serology: TPHA and VDRL negative
- *M. tuberculosis* culture: negative

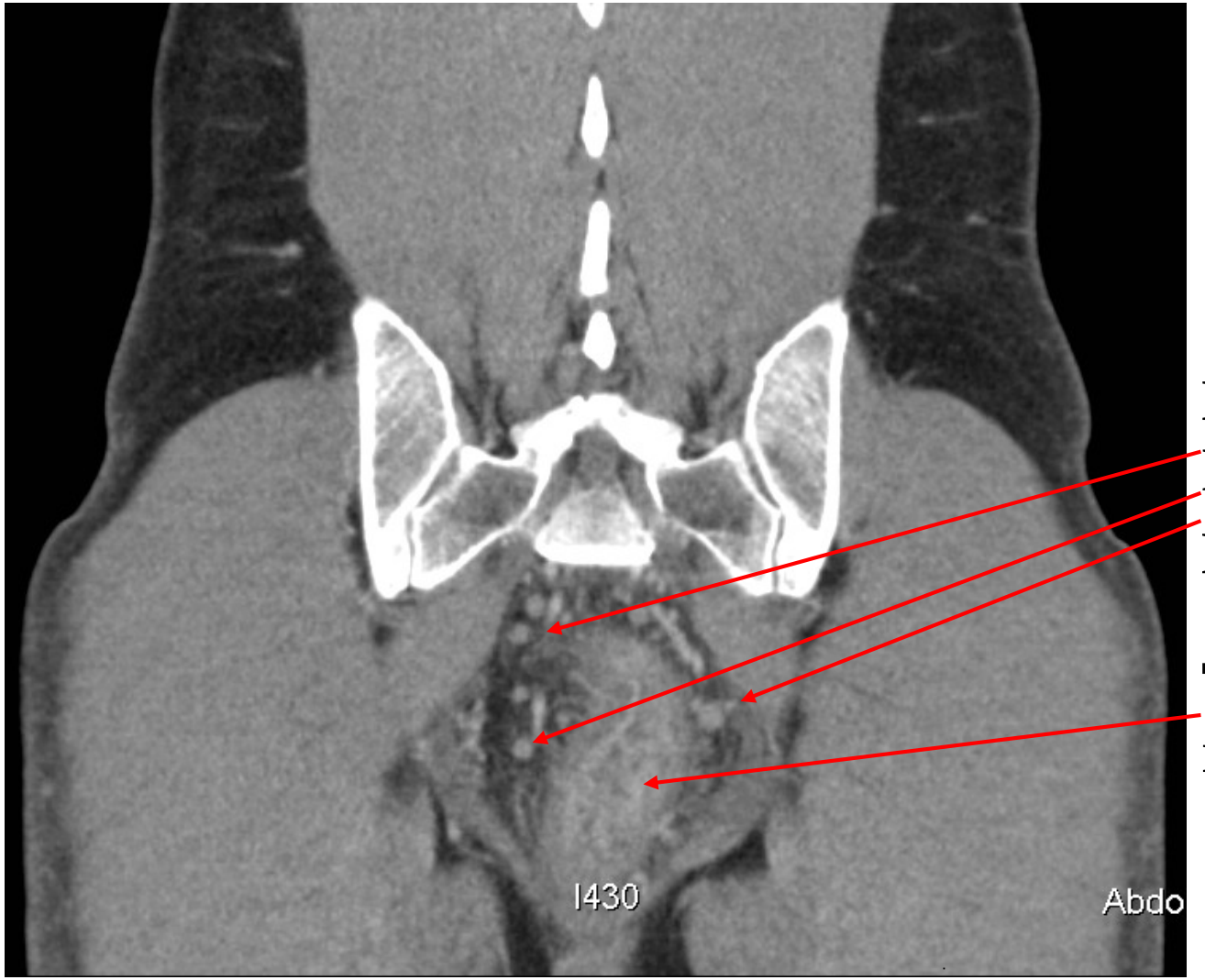
- ***C. trachomatis*** **PCR (inguinal + rectal): positive**

CASE 4

Haemorrhagic proctitis







Enlarged lymphnodes perirectal

Thickening of rectal wall

Laboratory results

- *N. gonorrhoeae* PCR (rectal): negative
- HSV PCR (rectal swab): negative
- CMV PCR (rectal swab): negative
- *M. tuberculosis* culture: negative
- Syphilis serology : TPHA and VDRL negative

- ***C. trachomatis* PCR (rectal): positive**

Diagnosis

LYMPHOGRANULOMA VENEREUM (LGV)

Therapy

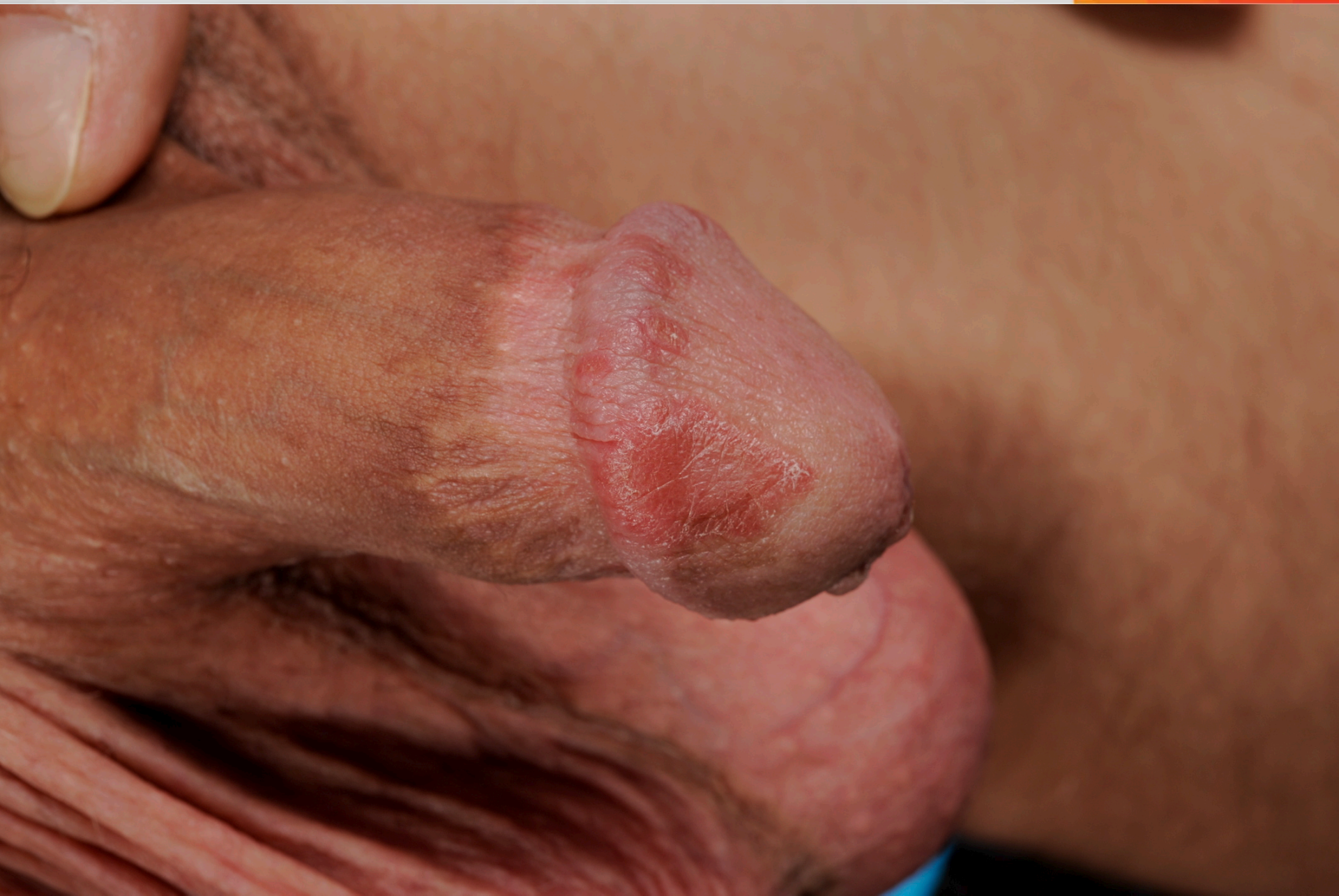
Doxycyclin 100 mg orally bid
for 21 days

Workowski KA et al. *MMWR Recomm Rep.* 2010; 59: 1-110.

CASE 5

Anamnesis

- 32 years-old male patient
- Unprotected sexual intercourse 4 weeks ago
- Urethral discharge for 14 days
- Arthritis for 3 days
- Conjunctivitis for 3 days



Gram stain

- >5 polymorph leucocytes per oil immersion field
- No intracellular diplococci

Diagnosis

NON-GONOCOCCAL URETHRITIS (NGU)

Diagnosis

SEXUALLY ACQUIRED REACTIVE ARTHRITIS (SARA)

(formerly known as Reiter's syndrome)

Therapy

Doxycyclin 100 mg orally bid for 7 days

Diclofenac 100 mg orally bid

Sexually acquired reactive arthritis (SARA)

- Classic triad („can't see, can't pee, can't climb a tree“)
  - Non-gonococcal urethritis
  - Conjunctivitis
  - Asymmetric oligoarthritis
- 90-98% in young males
- Subacute (2-6 months) to chronic (months, years) course
- HLA-B27 positive in 70-90%
- Balanitis parakeratotica circinata

Empiric syndromic treatment of urethritis without a microscope

Agnès Libois

Saint-Pierre University Hospital

Brussels, Belgium

Disclosures

- Consultancy and travel grant from
  - Janssen-Cilag, ViiV Healthcare, MSD and Gilead
- Research grant from
  - ViiV Healthcare and Gilead
- No disclosure with this presentation

Case 1

- A 28 years-old man presented with dysuria since 2 days.
  He had an unprotected sexual relation with a woman 1 week ago
- On genital exam, there is a slight discharge
- A urine test (or a swab) is performed

What are you doing?

A. I have a microscope, I look at the microscope to search a gonorrhea infection and I treat according to the result

B. I don't have a microscope and I treat with doxycycline

C. I don't have a microscope and I treat with azithromycin

D. I don't have a microscope and I treat with ceftriaxone and azithromycin

E. I don't have a microscope and I treat with ceftriaxone and doxycycline

F. I wait for the results of the urine test before treating

Urethritis treatment

1. **Confirm urethritis**: up to 40% patients with complaints do not have urethritis
   - Discharge on examination
   - Microscope: Gram stain of urethral secretions ≥2 (5) WBC per oil immersion field + presence or not of gonorrhoeae infection (intracellular gram negative/diplococci)
   - Sediment from a first-void urine with ≥10 WBC per high power field (≅ 35 WBC/µl)
   - Positive leukocyte esterase test on first-void urine

Moi H *et al.* *Sex Transm Infect*. 2009;85(1):15–8
CDC STD guidelines 2015, European guideline on NGU 2016

Urethritis treatment

2. Treat gonorrheae **or** **NGU**

Ceftriaxone 250-500 mg
+ azithromycin 1 or 2 g

1. Doxycyclin 7 d (to avoid ↑ macrolide resistance in *M.genitalium*)
2. Azithromycin 500 mg then 250 mg od for 4 days

CDC STD guidelines 2015, European guideline on NGU 2016

AND WITHOUT MICROSCOPE? WHICH SYNDROMIC TREATMENT?

Letter to the Editor

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Agnès Libois and Stéphane De Wit

Which empiric syndromic treatment for urethritis?

Dear Editor,

In the new European guideline on the management of non-gonococcal urethritis (NGU), it is recommended to confirm urethritis by urethral smear microscopy before treatment and to test male patients with urethritis for *Mycoplasma genitalium* when possible.[1] The new preferred syndromic regimen for NGU is doxycycline 100 mg twice daily for seven days. Second line includes azithromycin 500 mg single dose, then 250 mg for four days. Azithromycin 1 g is no longer recommended as first-line therapy because of the increased risk of inducing macrolide resistance of *M. genitalium*.

However, in many settings, microscopy is not available to confirm urethritis and to exclude infection with *Neisseria gonorrhoeae* with a point-of-care diagnostic tool (e.g. Gram, methylene blue or gentian violet stain microscopy). As an example, in Belgium, only one centre performs microscopic examination at the sexually transmitted infection consultation in selected cases. A syndromic regimen is given at the first consultation (after specimen collection for laboratory testing) when symptoms are severe, purulent urethral discharge of *M. genitalium* and a decrease of microbiologic cure even after extended courses of azithromycin (five days) and after a single 2 g dose.[2]

If point-of-care diagnostic tools are not available, US and European guidelines recommend to give drug regimens effective against both *N. gonorrhoeae* and *Chlamydia trachomatis*.[3,4] US and European guidelines recommend a dual therapy against gonorrhoea with ceftriaxone and azithromycin (1 g or 2 g according to the US or European guidelines) to avoid development of resistance. The use of azithromycin as the second antimicrobial is preferred to doxycycline because of the substantially higher prevalence of gonococcal resistance to tetracycline than to azithromycin and for convenience and compliance advantages of single-dose therapy.

Ideally, microscopy should be available in more settings, and the clinician should have time to perform a test to exclude *N. gonorrhoeae*. In practice, we are far from this situation in a lot of settings.

What is then the best choice of treatment when syndromic treatment is given and infection with *N. gonorrhoeae* is not excluded? Ceftriaxone and azithromycin 2 g to avoid development of resistance in gonorrhoeae or ceftriaxone and doxycycline to avoid increase macrolide resistance in case of *M. genitalium*?

Answer of authors of the 2016 European NGU guideline: Symptomatic urethritis should be confirmed by microscopy

The role of microscopy is two: To confirm the urethral inflammation; up to 40% of the symptomatic patients do not have a urethritis (1), and to distinguish between gonorrhea and non-gonococcal urethritis (NGU) (2), in order to provide correct treatment for gonococcal or non-gonococcal urethritis without waiting for laboratory results. Providing treatment at the first visit reduces the risk of complications and the risk of further transmission, and saves time for the patient and for the department.

We hope that the strong recommendation in the 2016 European NGU Guideline to confirm urethritis symptoms will encourage those who do not use the microscope to reconsider their practice (3). Gonococcal urethritis often gives severe discharge; however, it is impossible to distinguish non-gonococcal and gonococcal discharge without stained smear microscopy. Microscopy has a very high sensitivity and specificity for confirming or excluding gonococcal urethritis (2), guiding which treatment should be given. If gonorrhea is excluded, doxycycline should be given as recommend in the 2016 European NGU guidelines (3). Doxycycline treatment of NGU will cure >90% of the chlamydia cases (4), and 30-40% of the cases caused by M. genitalium, including macrolide resistant strains, without inducing macrolide resistance. However, a test of cure for M. genitalium should be performed if available. Macrolide resistance is increasing worldwide (5) and a recent study documented up to 50% macrolide resistance (6) in US M. genitalium strains, thus Doxycycline is likely to be almost as effective as Azithromycin (7). Dual infections with N. gonorrhoeae and M. genitalium are rare (6), and the combination of Ceftriaxone and Azithromycin is unlikely to increase macrolide resistance in M. genitalium if this treatment combination is given only when gonorrhea is identified by microscopy, culture or NAAT (3). **If syndromic treatment for a severe urethritis is given without results of microscopy, NAAT or culture, we therefore suggest administering the combination of 500 mg ceftriaxone i.m. and Doxycycline 100 mg twice daily for seven days**.

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A Libois and Horner.

PrEP

Case 2

- A 25-year-old man came to our consultation to discuss PrEP
- He had protected sexual relations except for oral sex. He's working as an escort and has many sexual relations
- He's afraid to have less protected sex if he'll take PrEP but also worried about his numerous unprotected oral sex
- He had syphilis 2 years ago
- He's not using chemsex or very rarely

What do you propose?

A. I encourage him to begin PrEP

B. I discourage him to take PrEP as the risk of HIV acquisition is very low with oral sex

C. I don't give PrEP as this situation is not an indication in PrEP guidelines

D. I encourage him to change his life

E. I give more information on PrEP efficacy, safety and risk of oral sex and I let him decide

PrEP effectiveness

Trials of PrEP efficacy with details on risk reduction

	Trial	Target Group (country)	N	Hiv incidence (per 100 py) PrEP vs control	Risk Reduction	Adherence (bloodlevel)
MSM	IPrex	MSM/TGW (US, S-America, Thailand, S-Africa)	2499	3.8 vs 6.6	44%	51%
	IPrex OLE	MSM/TGW (US)	1603	1.8 vs 2.6	51%	71%
	PROUD	MSM (UK)	544	1.3 vs 8.9	86%	100%
	IPERGAY	MSM (France, Canada)	414	0.94 vs 6.7	86%	86%
	CDC Safety trial	MSM (US)	400	0.0 vs 7.0	100%	n.r.
IDU	Bangkok Tenofovir study	Injecting Drug Users (Thailand)	2413	0.35 vs 0.68	49%	67%
Heterosexual M/W	Partners PrEP	Serodiscordant couples (Kenya, Uganda)	4747	0.5 vs 2.0 (TDF/FTC) 0.65 vs 2.0 (TDF)	75% 67%	81%
	TDF2	Heterosexual M/W (Botswana)	1219	1.2 vs 3.1	62%	80%
	FEM-PREP	Heterosexual F (Kenya, Tanzania, S-Africa)	2120	4.7 vs 5.0	6%	37%
	VOICE	Women (Uganda, S-Afrika, Zimbabwe)	5029	4.7 vs 4.6 (TDF/FTC) 6.3 vs 4.2 (TDF)	-4% -49%	30%
	Phase 2 TDF study	Women (Cameroon, Ghana, Nigeria)	936	0.86 vs 2.48	65%	n.r.

- Open label phase of IPERGAY: efficacy 97%
- Efficacy in IPrex if good adherence (dosage TDF dosage in blood): 92%
- Very few cases of failure when adherence is good

Multidrug-Resistant HIV-1 Infection despite Pre-exposure Prophylaxis

- 1 case of PrEP failure was reported in Toronto in an individual infected with a multi-class resistant virus under adequate TFV-DP levels
  - Resistance to FTC (M184V), TDF (multiple thymidine-associated mutations), NNRTIs (Y181C), and first-generation integrase inhibitors (92Q).

Knox DC *et al. N Engl J Med.* 2017 Feb 2;376(5):501-502

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- 50 y MSM, Amsterdam, daily PrEP, very high risk behaviour
- Good adherence: pill count, daily diary information and TDF-DP at months 6 and 8
- 3 anal STI, chemsex
- HIV+ wild type at 8 months
  - Fever, dysuria
  - ELISA indeterminate, VL<50, WB: + p160 only
  - Sigmoid biopsies and PBMC: no virus
- Stop PrEP
- 3 w later, VL 40000 cp/ml, no mutation

SEROCONVERSION ON PrEP: A PROTOCOL FOR UNTANGLING ADHERENCE *VS* RESISTANCE FAILURE

One seroconversion in a PrEP user in San Francisco

- Inappropriate prescribing and follow-up practices: few HIV tests. But dosage in plasma and hair high

Table 1. Timeline of 34 year old male who has sex with men who acquired HIV infection (positive HIV test on Day 0) while on HIV PrEP.

Day	Timeline
-503	Non-reactive HIV antigen/antibody test
	Denies sexual activity over this period
-441	Starts PrEP with FTC/TDF
	Reports excellent compliance; verified with pharmacy records
-351	Self-discontinues PrEP due to perceived lack of risk
-290	Restarts PrEP
-40	Develops fevers and myalgias; negative rapid influenza A/B
0	HIV antigen/antibody test positive
2	HIV-1 RNA 27,316 copies/mL Genotype with M184V, K65R, and K103N (Table 2) Plasma TFV and FTC levels of 75 ng/mL and 281 ng/mL, respectively, consistent with recent dosing.
13	Started rilpivirine, dolutegravir, and darunavir/cobicistat
27	Segmental analysis of TFV/FTC levels in a hair performed in 1 cm segments from the scalp revealed drug levels commensurate with consistently high PrEP adherence over the last 3 months (Figure)
66	HIV-1 RNA <20 copies/mL; stopped darunavir and cobicistat

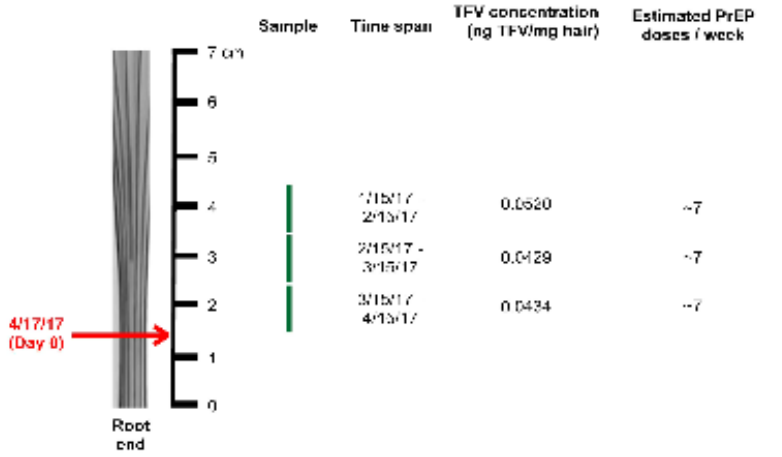


Figure. Segmental hair analysis in patient on FTC/TDF-based PrEP who seroconverted. Dates show first positive HIV test (Day 0), as well as time over which adherence was assessed by hair concentrations in the UCSF Hair Analytical Laboratory (HAL). Data from a dose-concentration study called STRAND (Liu A. PLOS ONE 2014) allows us to estimate number of doses per week from TFV levels in hair.

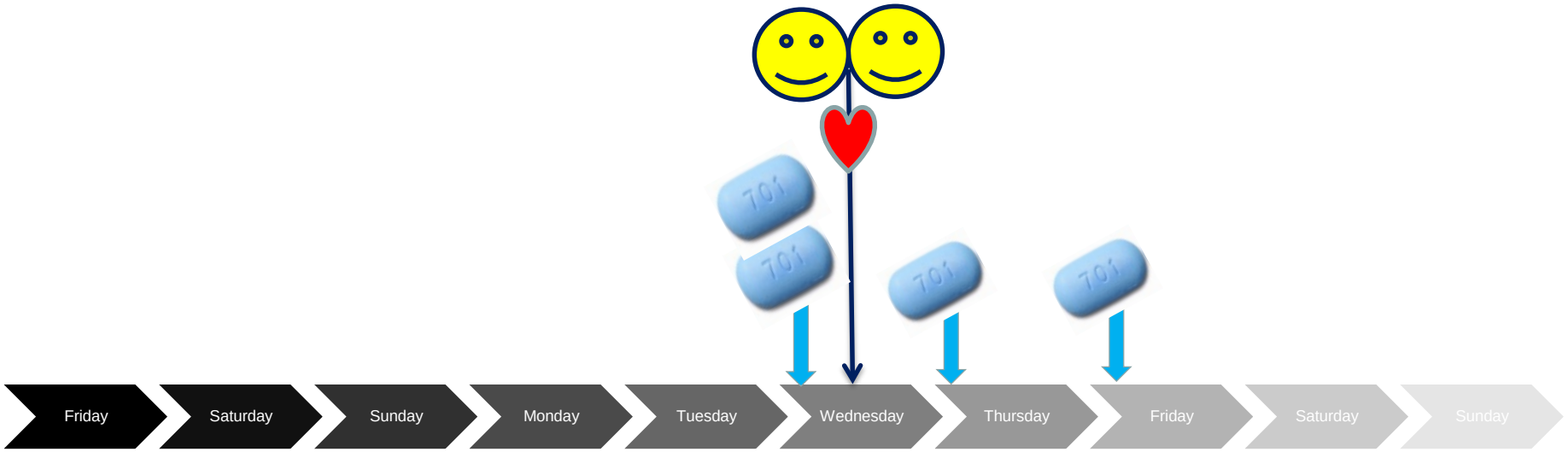
JT Thaden P1041. CROI Boston 2018

2 WAYS TO TAKE PREP: DAILY OR EVENT-DRIVEN

ipergay
ANRS
Intervention Préventive de l'Exposition aux Risques avec et pour les Gays

IPERGAY: Sex-Driven iPrEP

- 2 tablets 2-24 hours before sex
- 1 tablet 24 hours later
- 1 tablet 48 hours after first intake



4 pills of TDF/FTC taken over 3 days to cover one sexual intercourse

Slide from JM Molina

PrEP safety

- Risk of any AE or grade 3/4 AEs is not increased for TDF-based PrEP *vs.* placebo
- 14% self-limited drug-related gastrointestinal events in the OLE of Ipergay
- Bone safety: small net decrease in spine and total hip BMD with TDF/FTC *vs*. PBO at Wk 24 in Iprex substudy, recovered following discontinuation
- Renal function has to be followed
  - No significant change in renal function in Partner PrEP
  - eGFR decrease to < 70 mL/min more frequent at higher levels of TFV exposure among those with BL eGFR < 90 mL/min or who were older than 40 yrs in IprexOLE
  - In OLE of Ipergay: 3 patients had to stop PrEP < ↑ creatinine

Fonner VA, *et al. AIDS.* 2016;30:1973-1983. Mulligan K, *et al. Clin Infect Dis*. 2015;61:572-580. Grant R, *et al. CROI* 2016. Abstract 48LB. Gandhi M, *et al. CROI* 2016. Abstract 866. Molina JM et al. Lancet HIV. 2017 Sep;4(9):e402-e410.

PrEP guidelines

- EACS (2015)
- CDC (2014)
- UK (2016)
- WHO (2015)
- French
- Australian (2015), Canadian…

	WHO?	HOW?
EACS (2017)	Adults at high-risk of acquiring HIV infection when condoms are not used consistently • Recommended: HIV-MSM & transgender not using condoms consistently with casual partners or with HIV+ partners not on ART. • Markers of increased risk: a recent STD, use of post-exposure prophylaxis or chemsex • Consider: HIV-heterosexuals, inconsistent condoms with multiple partners some of whom are likely to be HIV+ not on ART.	Daily or « on demand » Baseline: 4th generation HIV test, HBV, renal, STD 3 monthly: 4th generation HIV test « Regularly »: STD screening Renal: as for TDF treatment

Belgium: reimbursed June 1st, 2017

Criteria allowing re-imbursement in Belgium
❖ **MSM**
• Having had unprotected anal intercourse with at least 2 partners in the last 6 months
• Having had multiple sexually transmitted infections in the last year
• Having taken Post-Exposure Prophylaxis (PEP) in the last year
• Using psycho-active substances during sexual activities
❖ **Other persons at high risk for HIV**
• People who inject drugs and share needles
• Sex workers who are exposed to unprotected sex
• Partners of HIV positive persons without viral suppression
• People exposed to unprotected sex practice with a high risk of HIV infection

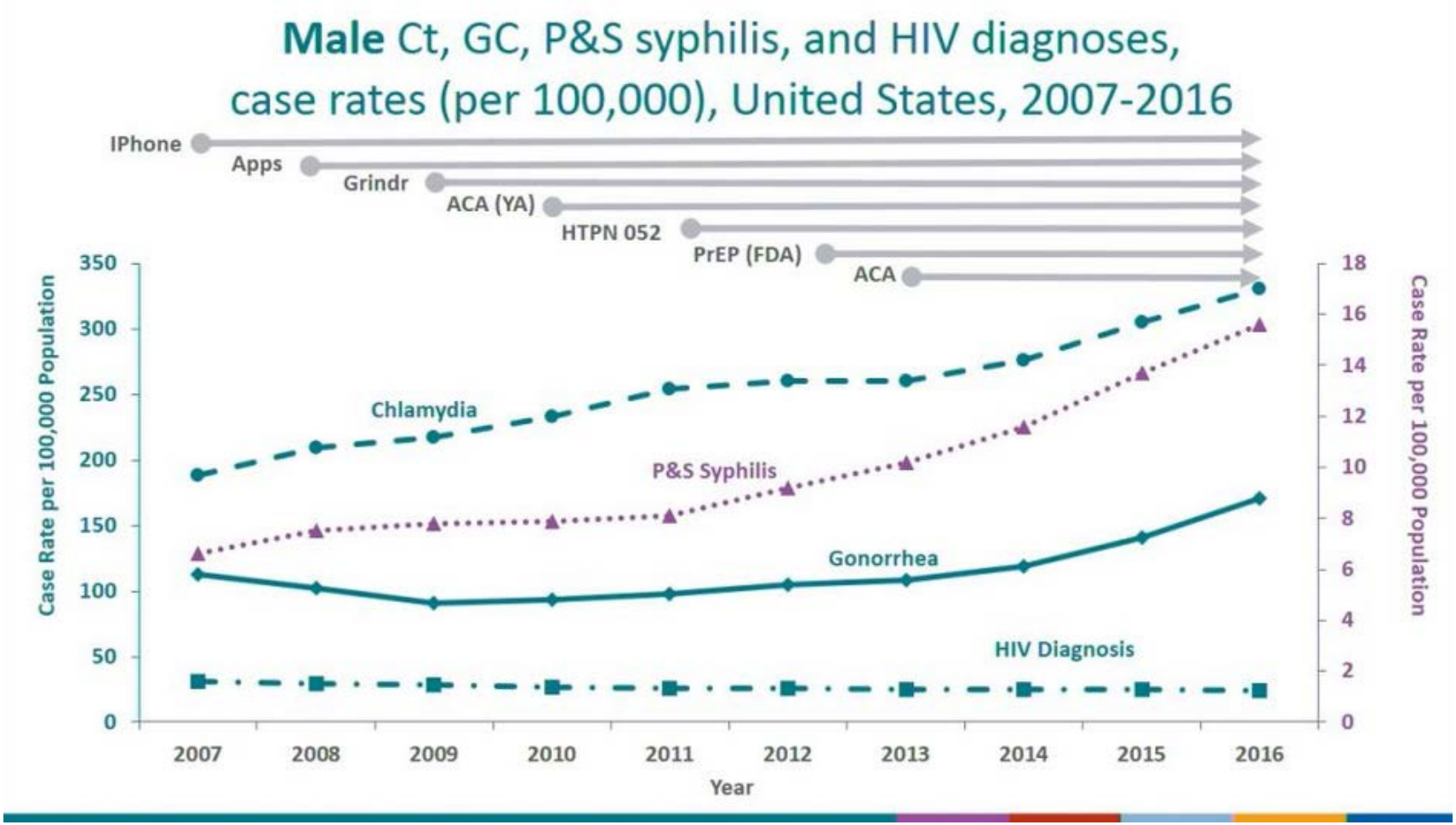
Risk of HIV acquisition with oral sex?

- Risk < 1/10.000
- But ↑ if
  - Primary infection in the partner
  - STI
  - Mouth lesions

Mastro TD *et al. AIDS Res Hum Retroviruses.* 1998 Oct;14 Suppl 3:S223-7
Del Romero J *et al. AIDS.* 2002 Jun 14;16(9):1296-7

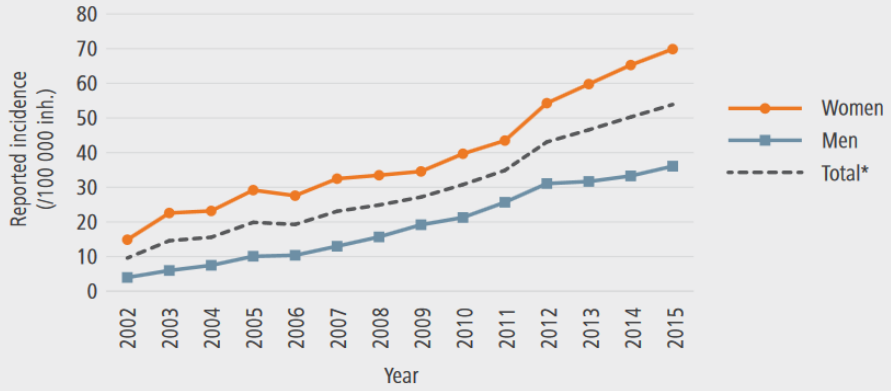
AND WHAT ABOUT THE RISK COMPENSATION? AND THE INCREASE OF STI?

↑ STI before PrEP



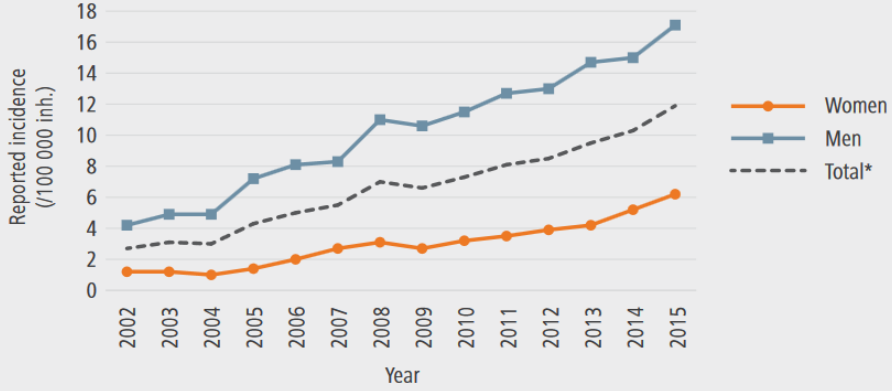
Schillinger J *et al.,* CDC, NYC, CROI 2018

Figure 3 | Tendance de l'incidence rapportée (/100 000 hab.) en fonction du sexe pour l'infection à *Chlamydia*, en Belgique, 2002-2015



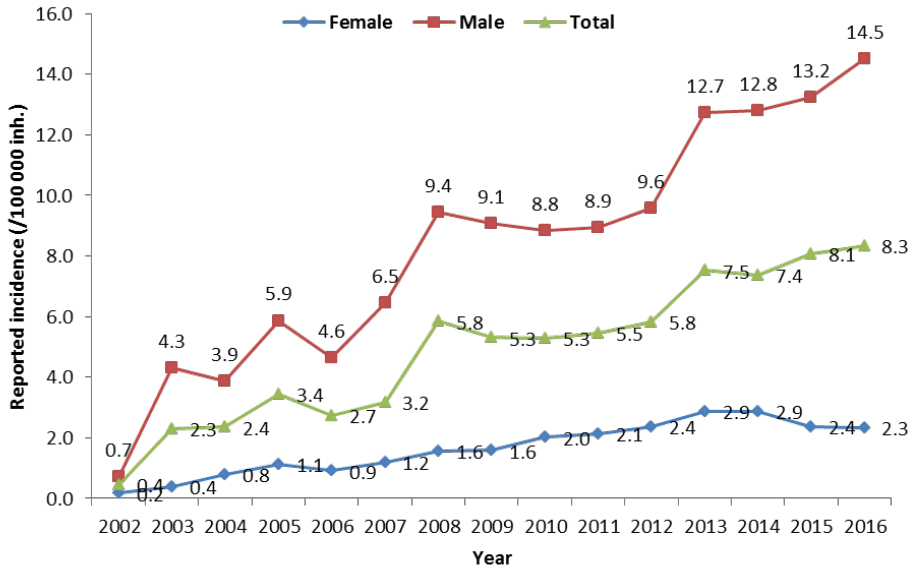
* y compris les cas pour lesquels le sexe n'a pas été enregistré.

Figure 6 | Tendance de l'incidence rapportée (/100 000 hab.) en fonction du sexe pour la gonorrhée, en Belgique, 2002-2015



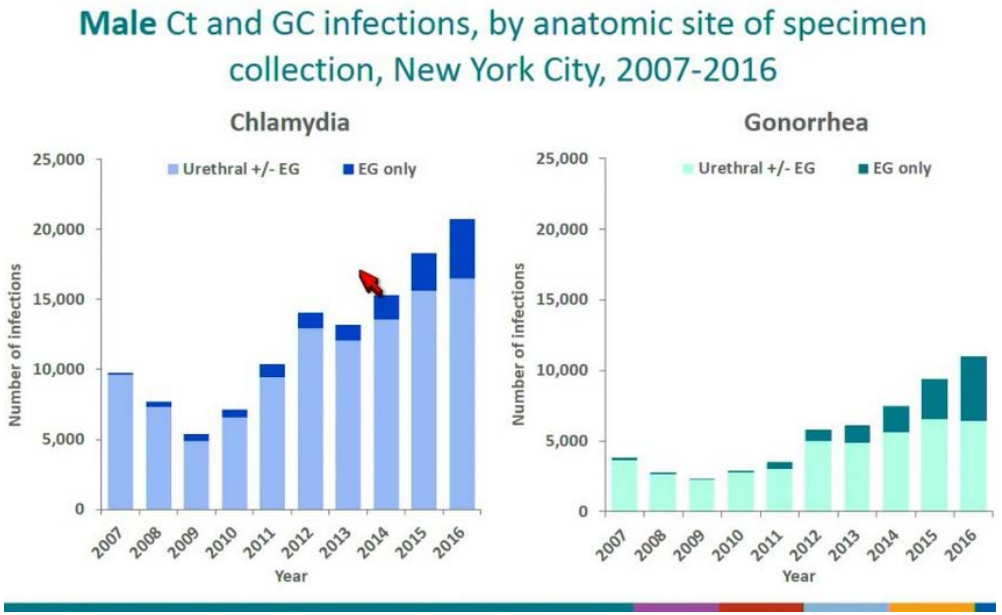
* y compris les cas pour lesquels le sexe n'a pas été enregistré.

Incidence trend (/100 000 inh.) of Syphilis by sex, Belgium, 2002-2016



Increase of STI

1. Increase testing
   - More access to care in US (AcA)
   - ↑↑ extragenital testing
   - Also evidence of true increase



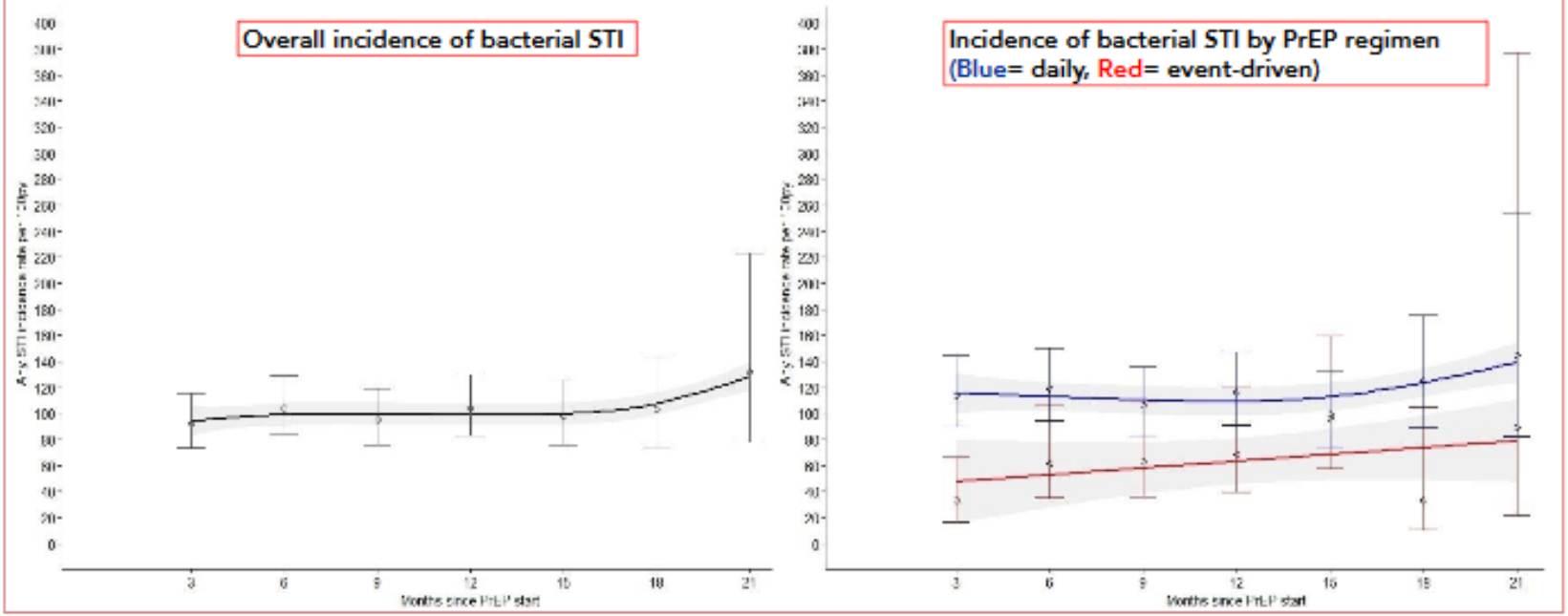
2. Increase transmission

- Evidence of risk compensation among PrEP users?
  - No increase in STI among PrEP users (in open label and cohort studies: iPrEx openlabel extension, Proud in UK, Ipergay, AMPrEP)

Schillinger J *et al.,* CDC, NYC, CROI 2018

Incident HIV, hepatitis C and other STIs in daily and event-driven PrEP users

Figure 1. Modeled incidence rate of any bacterial STI over time since PrEP start among daily or event-driven PrEP users (n=372) participating in the Amsterdam PrEP demonstration project.



No change of STI over time. More STI in dPrEP users.

Hoornenborg S *et al.,* P1026, CROI 2018

Partners, not condom use, drive STI rates among PrEP users in community health center

- SPARK: a PrEP implementation project at a community-based health center in NYC
- 300 MSM and transgender women, analysis on the 261 who were retained at 12 months
- 11% had an STI in the 6 months before starting PrEP
- 12-month follow-up: 44% with an STI

Table 1. Regression Predicting any STI diagnosis in the 12-months after starting PrEP (n = 261)

	aOR	95% CI
Under 25 years old	3.67*	1.11, 12.25
> 5 casual partners at baseline	2.80**	1.43,5.50
STI in 6 months pre-PrEP	2.22*	1.07, 4.59
Increase in number of casual partners from baseline to 12 months	2.16*	1.07,4.38

* $p < .05$, ** $p < .01$

- Condom use ↓ from baseline (60%) to 12-months (45%) but neither overall condom use nor change in condom use were associated with STI diagnosis
- → risk compensation may be less significant than underlying behaviour patterns in post-PrEP STI diagnosis

Golub S *et al.,* P1025, CROI 2018

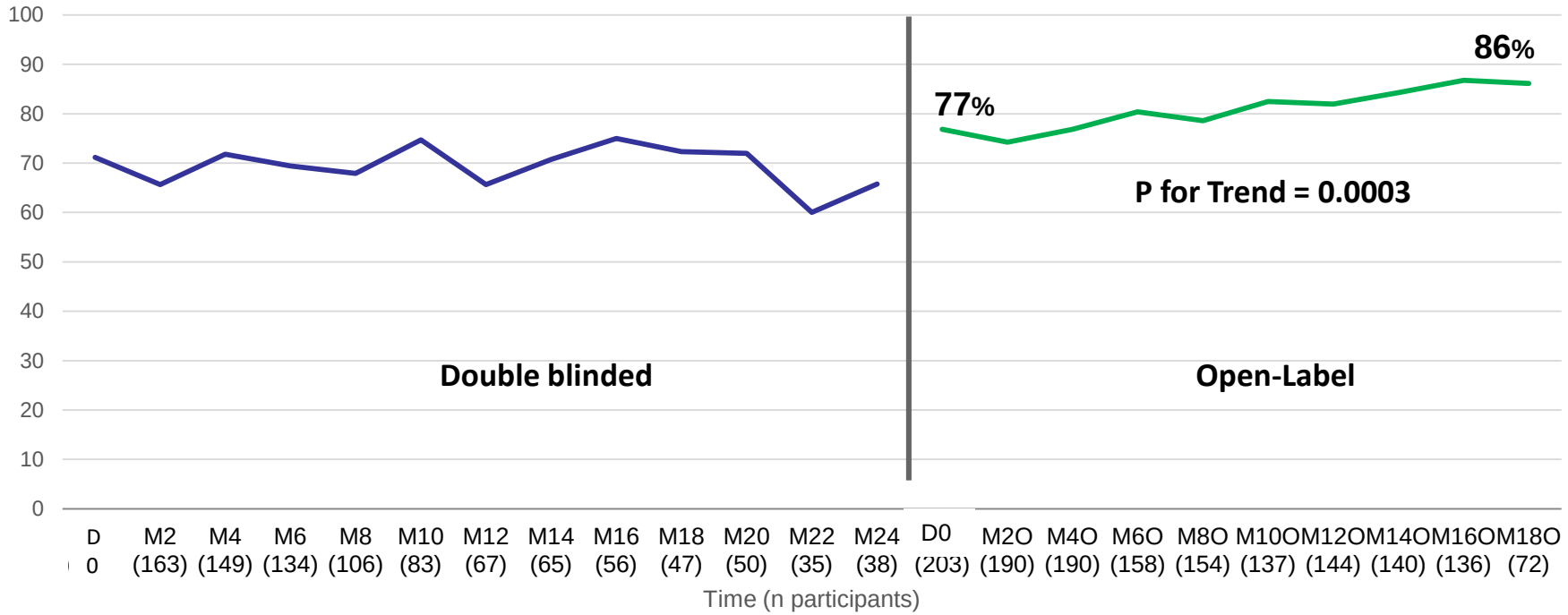
Increase STI

2. Increase transmission:

- Evidence of risk compensation among PrEP users?
  - No increase in STI among PrEP users (in open-label and cohort studies: iPrEx openlabel extension, Proud in UK, Ipergay, AMPrEP)
  - Change in sexual behaviour: many but not all studies showed an ↑ risk behaviour

Sexual Behaviour

Proportion Pts with Condomless Sex for Last Receptive Anal Intercourse



- **No significant change in median Nb of partners or sexual acts during the open-label phase (P= 0.42 and P= 0.12)**
- Incidence of a first bacterial STI during this open-label phase did not change significantly compared with the randomised phase (59.0 *vs*. 49.1 per 100 person-years, p=0.11)

Molina JM *et al., Lancet HIV.* 2017 Sep;4(9):e402-e410

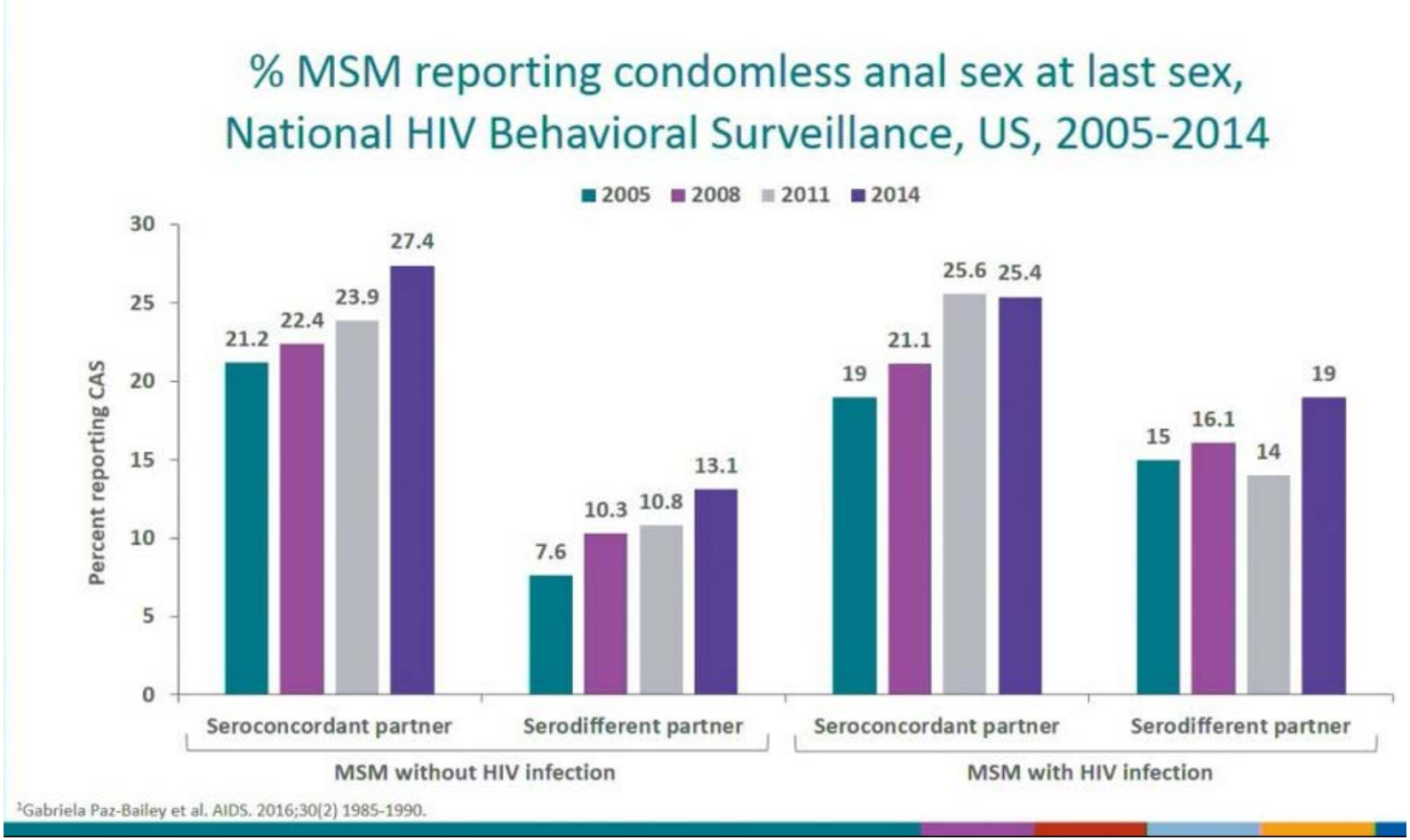
WHAT HAPPENS AT THE COMMUNITY LEVEL?

Risk compensation
Indivudual-level *vs*. community-level

- Individual risk compensation – increases in sexual risk behaviour among people on PrEP due to perception they are at reduced risk for HIV

- Community risk compensation – increases in sexual risk behaviour among members of the community not on PrEP due to perception of reduced risk for HIV acquisition and transmission (« prevention optimism »[1])

Schillinger J *et al.,* CDC, NYC, CROI 2018
1) Holt M *et al., Am J Public Health.* 2017 Oct;107(10):1568-1571



↑Condomless anal sex before PrEP and Tasp

↑ Number sex partners in NYC sexual health clinics

↑ P and S in MSM HIV negative

Schillinger J *et al.,* CDC, NYC, CROI 2018

- **PrEP ↑ STI**

- Systematic review of studies reporting sexual risk outcomes (STI diagnoses, condom use, number of sexual partners) in daily oral PrEP use in MSM and transgender women.
- PrEP use was associated with a significant ↑ in rectal chlamydia (odds ratio [OR]=1.59; 95%CI 1.19-2.13; p=0.002) and ↑ in any STI diagnosis (OR=1.24; 95%CI 0.99-1.54; p=0.059).
- The association of PrEP use with STI diagnoses was stronger in later studies. Most studies showed evidence of an increase in condomless sex among PrEP users.

Traeger MW *et al. Clin Infect Dis* 2018 Mar 2

- **PrEP: ↑ STI screening and treatment**

- PrEP is an STI control intervention
- Mathematical model[1]: PrEP coverage 40%, ↓ CT/NG by 40 %, even with 40 % risk compensation among PrEP users

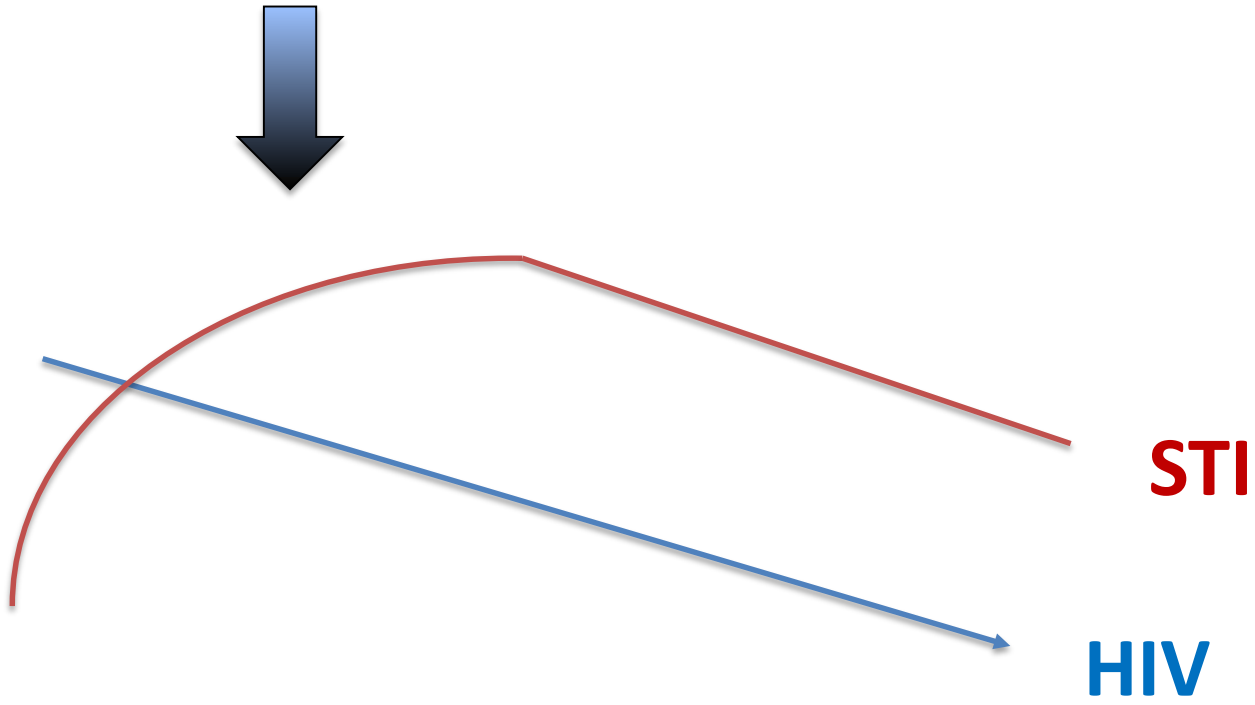
(1) Jenness SM *et al., Clin Infect Dis.* 2017 Sep 1;65(5):712-718

Conclusions

- Behaviours were changing before PrEP and before the results of HTPN 052 (community risk compensation)
- Behaviour changes continue to ↑ in PrEP users and at the community level
- Role of « U=U»

- Number of PrEP users too small to drive the STI increase
- Community-level risk compensation likely to contribute to observed increases in STI diagnoses among MSM
- ↑ Screening and treatment of STI could ↓ STI

TasP, PrEP and screening



CHEMSEX

Dr Dominic Rowley
Consultant Physician Genitourinary Medicine
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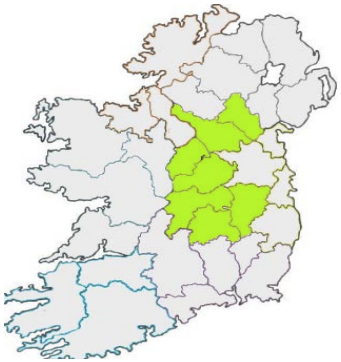
THE GUIDE CLINIC
ST JAMES'S HOSPITAL

Disclosures

- No disclosures

Saturday – Meet Joe



UCD DUBLIN

Sunday? – Joe?

Joe – Meet Monday

Definition

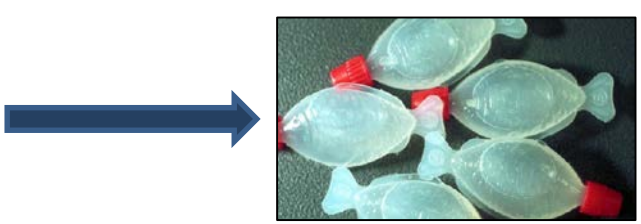
- "Is a word invented on geo-sexual networking apps by gay men (and later adopted by the Gay men's health sector) that defines a syndemic of specific behaviours associated with specific recreational drugs, and is particular to a specific, high risk population"

- Media have included many drugs as part of this syndrome but in reality the drug combination should only include …for accurate definition…

"use of recreational drugs or 'chems' to heighten sexual experience (sexualized drug use) "

Drugs include

- G- gammahydroxybutyrate (GHB)/gamma-butyrolactone (GBL)



- Synthetic cathinones (Mephedrone- Meow Meow, M CAT)–previously known as head shop products/legal highs

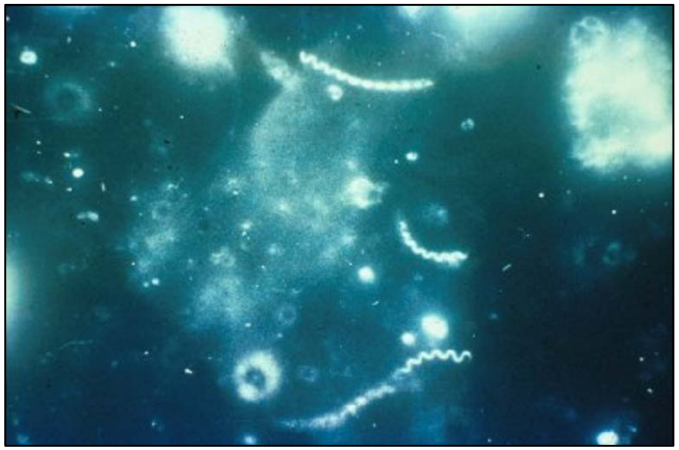
- Crystal methamphetamine (crystal meth / Tina / T / ice)

- Axillary drugs may include
  - Ketamine, Special K
  - Cocaïne
  - Ecstasy
  - Viagra

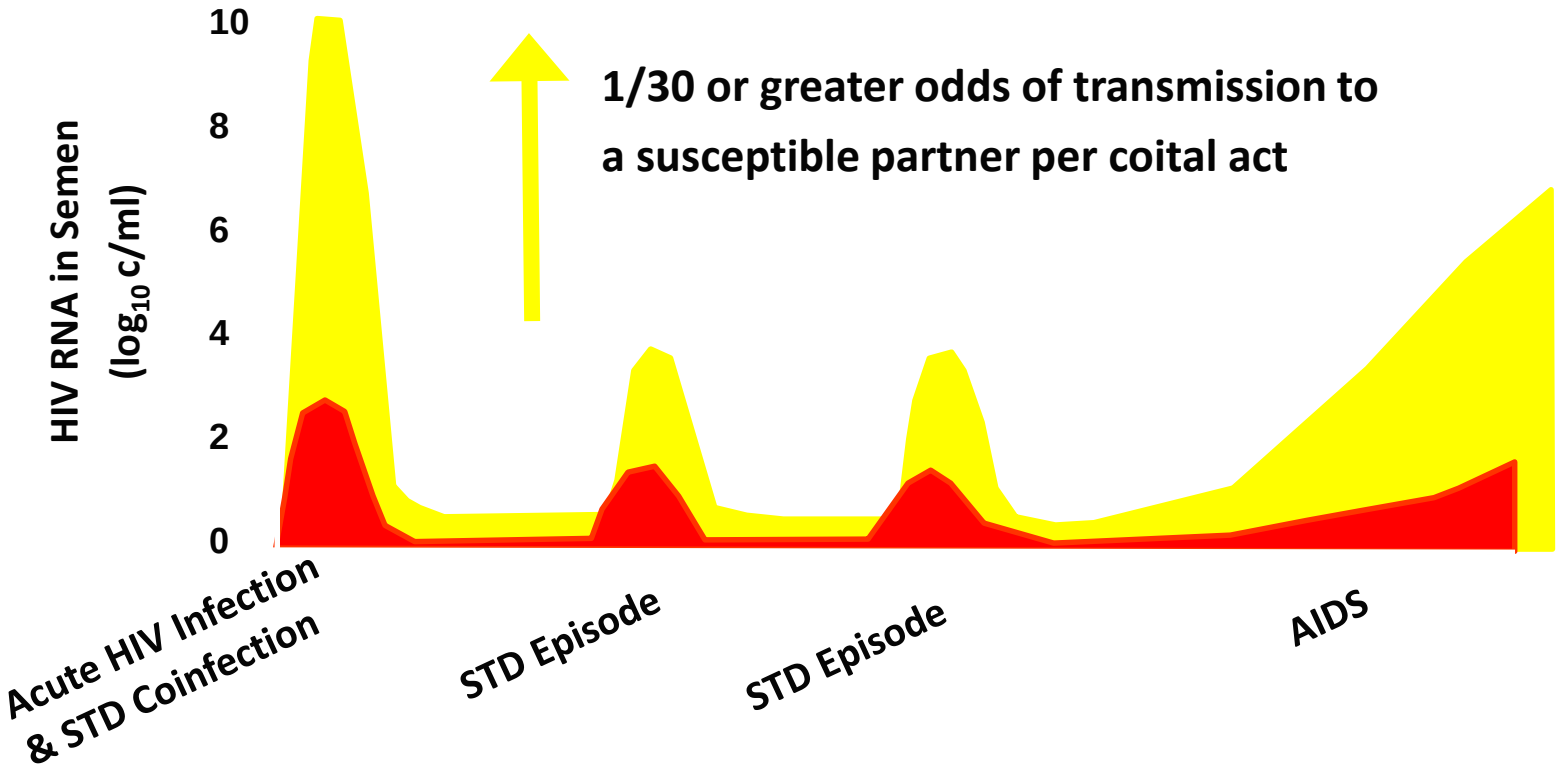
Why is it important?

- Irish and global increase in STI rates + HIV
  - 2016
    - 60% rise gonorrhoea
    - 50% rise in new HIV *vs*. this time last year
    - Syphilis outbreaks Cork + Dublin
    - Sexually acquired HCV GUIDe
- Recreational drug use closely linked to social networking

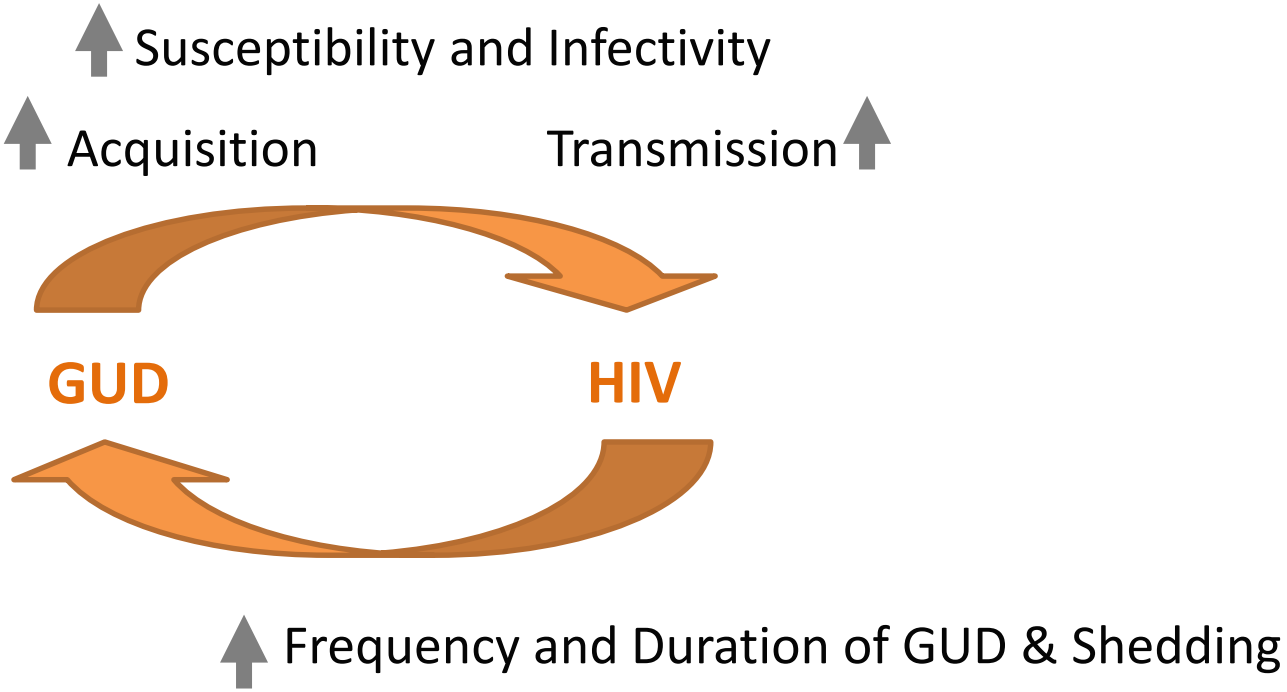
Epidemiological synergy between STI + HIV acquisition



Amplified Transmission of HIV

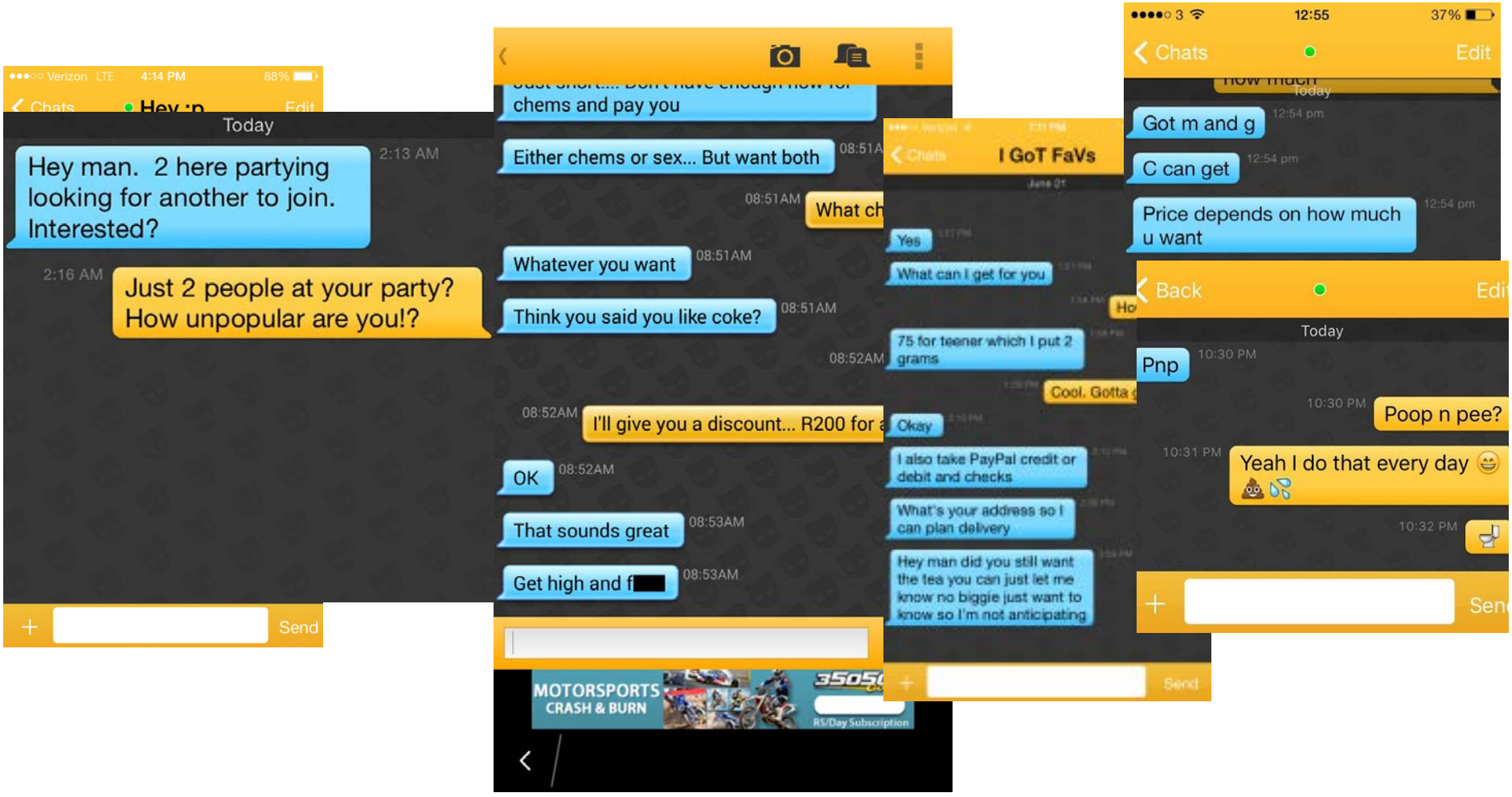


Genital Ulcer Disease and HIV Interactions

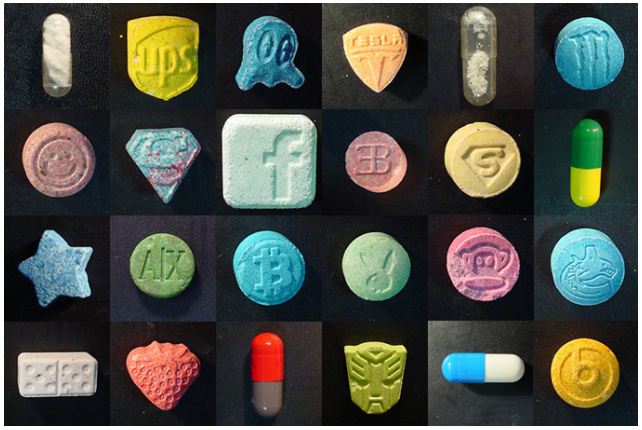


1. Genital ulcer disrupts epithelial / mucosal surface
2. Recruitment of inflammatory cells, CD4 lymphocytes and macrophages to site of mucosal break

Synergy between geo-sexual networking and chems (“PnP” “Wired”)

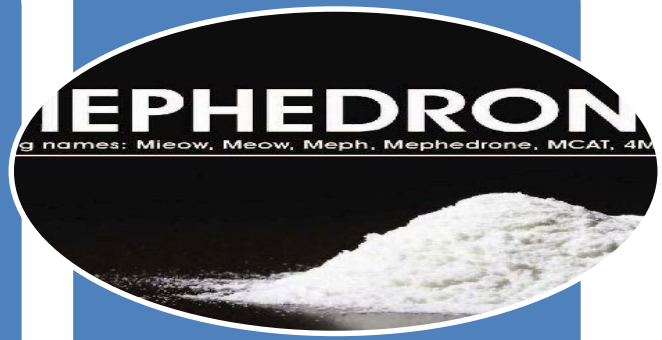


Traditionally



Direct Drug Related Effects

Supreme confidence



Heightened arousal

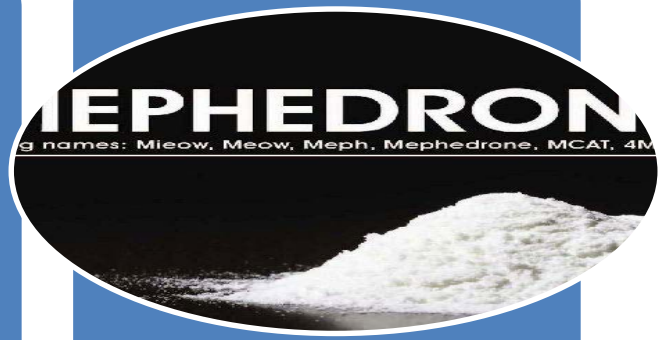
Awake x hours-days

Sexually disinhibited

Direct Drug Related Effects

G “dropping”

Resp depression, arrest



Hyperthermia, tachy, rhabdomalysis, renal failure, death

Paranoia, depression, severe anxiety, psychosis, self harm and extreme aggression

Epidemiology

- First described Berlin, Amsterdam, London, then Sydney, initially anacetodally in GUIDe and GMHS in Dublin

now

- Emergent problem, emergent data

Chemsex and the city: sexualised substance use in gay bisexual and other men who have sex with men

- 59% (n = 73/124) reported chemsex, 13% (n = 15/116) injected
- Drugs: mephedrone (n = 48), GHB/GBL (n = 38), crystal meth (n = 28) and cocaine (n = 8)
- 1/3 disclosed > one chemsex session/month
- Chemsex significantly associated: transactional sex, group sex, fisting, sharing sex toys, HIV and hepatitis sero-discordancy ($p < 0.05$), more reported sexual partners (median 3 *vs*. 2 in past 3 months; $p < 0.0001$) and HIV positivity (35% *vs*. 7% $p < 0.0001$)
- STIs were diagnosed more frequently; *gonorrhoeae* (39% *vs*. 6% $p < 0.0001$), *Chlamydia* (11% *vs*. 4% $p = 0.05$), hepatitis C (5% *vs*. 0.3% $p = 0.03$)
- PEPSE was more frequently prescribed (14% *vs*. 2% $p = 0.001$)
- 42% of patients perceived chemsex to have had an adverse consequences on their physical/mental health or career

Lee T *et al. Sex Transm Infect*. 2015 Jun;91(4):233

Sex, drugs and smart phone applications: findings from semi-structured interviews with men who have sex with men diagnosed with *Shigella flexneri 3a* in England and Wales

- Outbreak 2012 UK *Shigella flexneri 3a*
- 53 men, 34 sexually active
- Median 22 sex partners in past year
- 63% HIV+ve and sero-sorted
- 62% had used chemsex drugs: crystal meth, mephedrone, and γ-butyrolactone/γ-hydroxybutrate
- Many had had *gonorrhoeae* (68%) and *Chlamydia* (52%)
- HIV-positive serostatus was associated with both insertive anal intercourse, fisting and use of web applications that promote and facilitate unprotected sex (adjusted OR=19.8, p=0.02)

Gilbart VL *et al. Sex Transm Infect*. 2015 Dec;91(8):598-602

The new MTV generation: Using methamphetamine, Truvada®, and Viagra® (MTV) to enhance sex and stay safe

- Gay and bisexual men (GBM) often use illicit drugs to enhance sexual pleasure, commonly referred to as 'chemsex' or 'party n play'
  - The use of methamphetamine and Viagra®, and other erectile dysfunction medications, both together and separately are strongly predictive of subsequent HIV infection
- 1831 GBM

- Concurrent MTV use was reported by 6.0% of participants; 3.1% used methamphetamine and Viagra® ('MV only') and 11.2% used emtricitabin (Truvada®) as PrEP ('T only').
- In multivariate: compared to use of 'MV only' or 'T', MTV was independently associated with CLAI with casual partners (aOR = 6.78) and 'fuckbuddies' (aOR = 3.47), being older (aOR = 3.95), engaging in group sex (aOR = 3.31) and having more sexual partners (aOR = 2.30)
- Interventions that promote the use of PrEP during chemsex could mitigate HIV risk

Hammoud MA *et al. Int J Drug Policy.* 2018 Mar 8. pii: S0955-3959(18)30060-4


TECHNICAL REPORT
EMIS 2010:
The European Men-Who-Have-Sex-With-Men Internet Survey
Findings from 38 countries
www.ecdc.europa.eu
CEEIS Cat
Centre d'Estudis Epidemiològics sobre les Infeccions de Transmissió Sexual i Sida de Catalunya
giz
Deutsche Gesellschaft für Internationale Zusammenarbeit (GIZ) GmbH
Maastricht University
Leading in Learning!
REGIONE DEL VENETO
ROBERT KOCH INSTITUT
Sigma RESEARCH
Knowledge for Action

MISI 2015=The Men who have Sex with Men
Internet Survey Ireland 2015

- > 3000 interviewed
- Respondents 18 and 80 (median age 30)
- 86% were born in Ireland, 14% were born outside of Ireland
- 79% identified as gay, 13% bisexual, 2% as straight

- **Recreational Drug**
  - 36% in the last year
  - Most commonly drugs were cannabis (28%), ecstasy (17%), cocaine (13%)
  - <25, students, HIV+ve, those living in Dublin
- **Chemsex Drugs**
  - 7% in past year, including ketamine, mephedrone, crystal meth and G
  - Men who higher education, Dublin, HIV+ve, late twenties
  - 2% IVDU

Population at large

- 27% of Irish adults had ever used drugs in their lifetime

National Advisory Committee on Drugs. National Drug Prevalence Survey in 2010/11

To assess the prevalence of recreational drug use for or during sex among attendees at the GMHS (1)

GMHS
GAY MEN'S HEALTH SERVICE

THE GMHS is Ireland's only MSM-specific sexual health clinic.

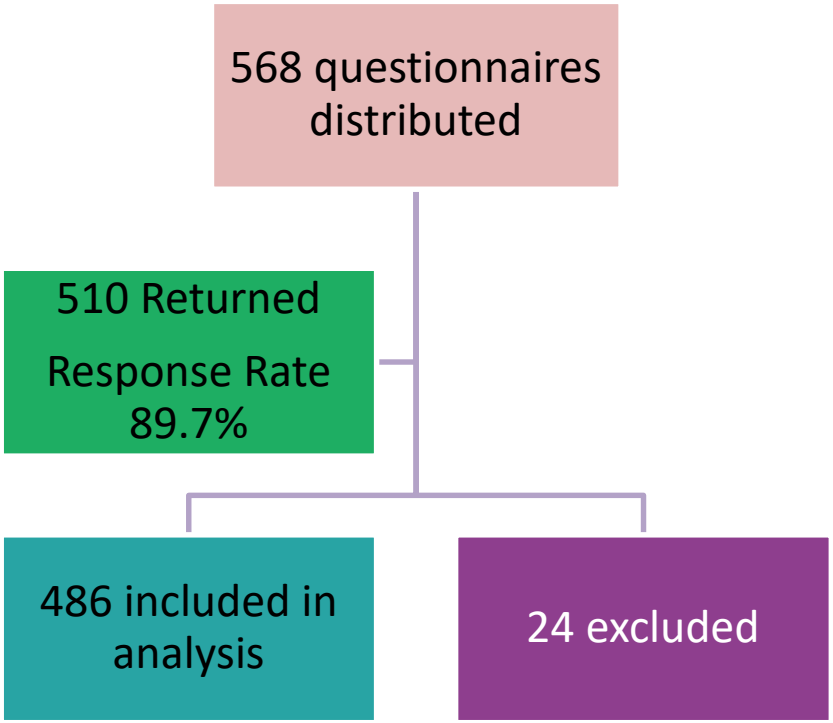
Over 6,000 men attended for screening and management in 2014

1. Dr Ronan Glynn SpR Public Health Medicine

Results

Questionnaire
x
6 weeks

English and Portuguese



Results

- **Demographics**
  - Median age 29 years (range 18-77)
  - 65% had a university degree or higher education
- **Sexuality**
  - 90% identified as gay/homosexual
  - 68% were single

Results

Chemsex practices

30.5% had used drugs for/during sex within previous 12 months

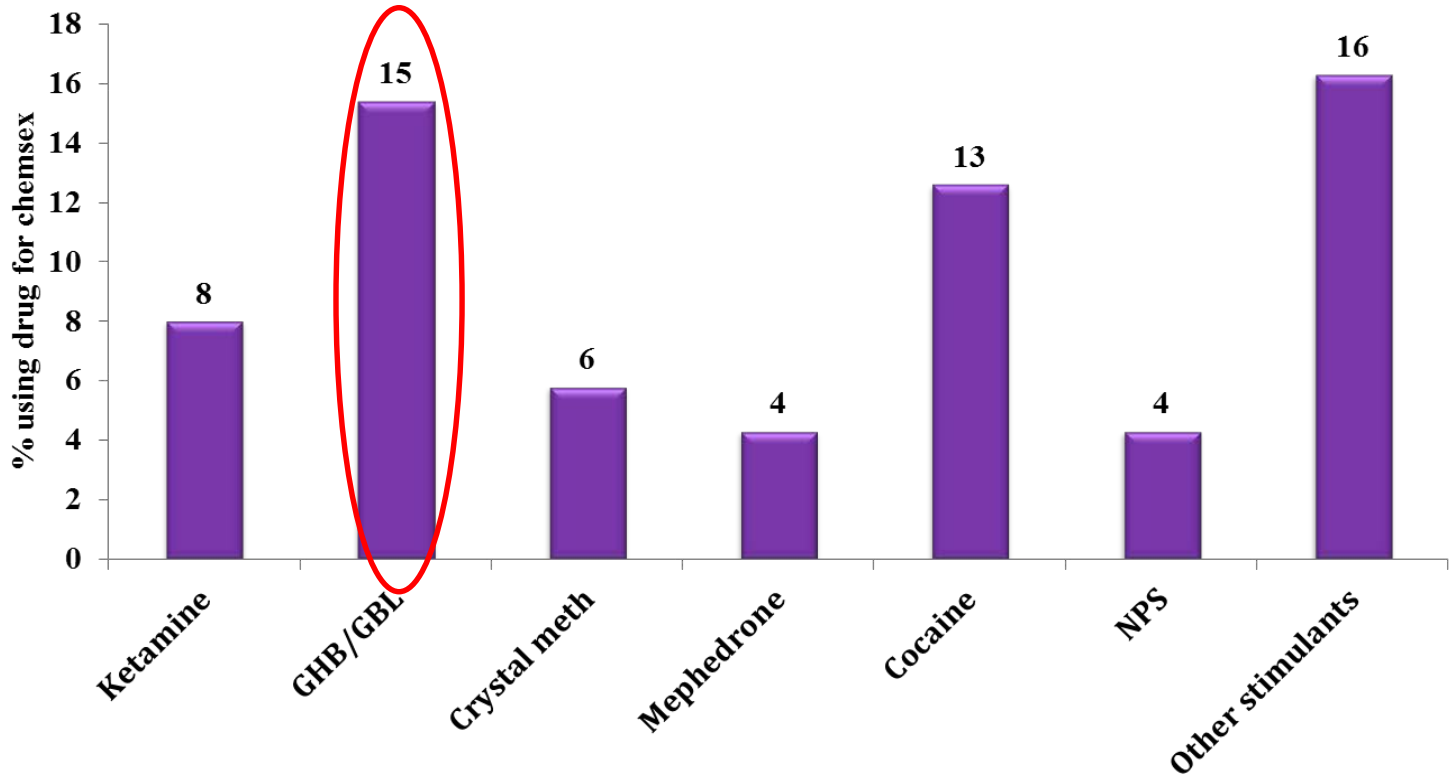
3.5% had used drugs not considered to be 'chemsex drugs'

27% had engaged in "chemsex"

1:4

Results

56% of respondents met their partners for chemsex though phone apps or online



Direct Drug-Related Harms

- **Polydrug use**
  - Half of those engaging in chemsex had used ≥2 drugs the last time they had chemsex
- **Injecting drug use**
  - 9% of those engaging in chemsex had ever injected drugs for chemsex
- **Loss of consciousness**
  - 23% of respondents/their partners had ever lost consciousness as a result of chemsex

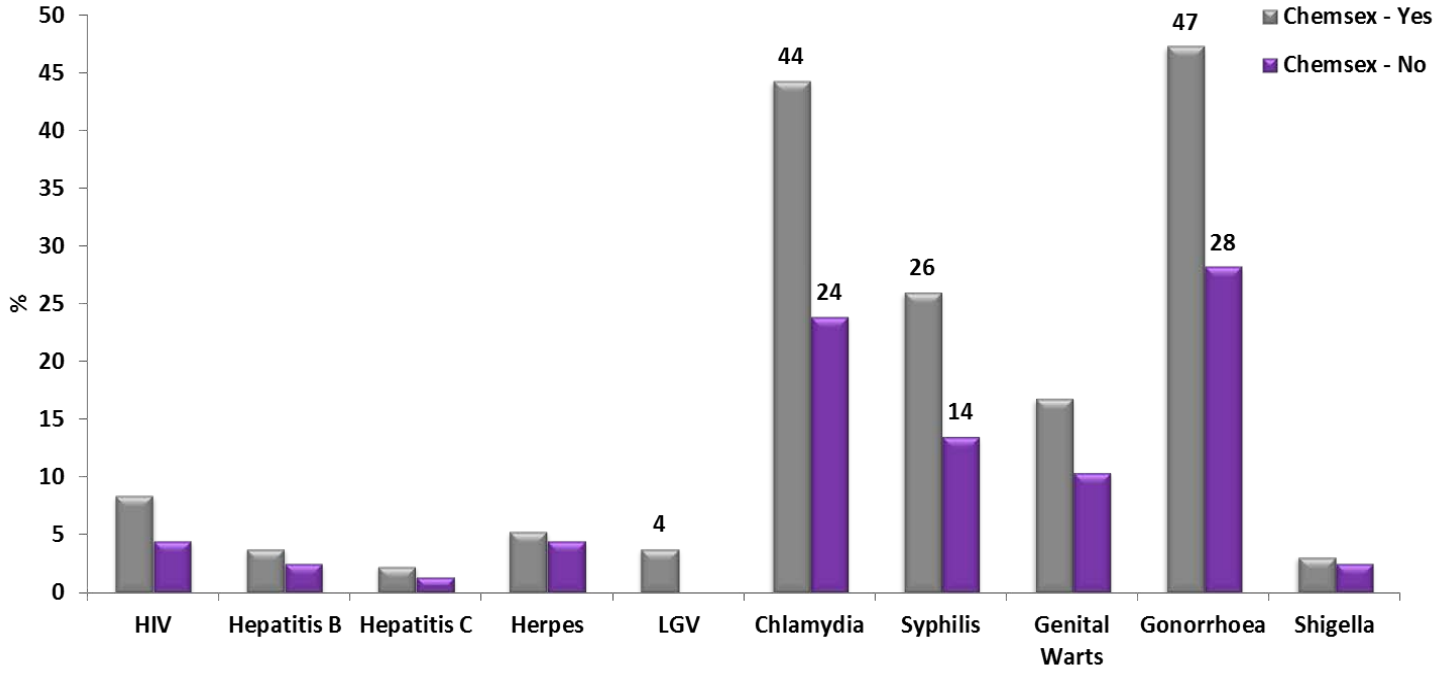
Sexual risk behaviours associated with chemsex

- **Anal Sex**
  - Half of those engaging in chemsex had ≥6 partners for anal sex in previous 12 months
  - Compared to 30% of those who had not engaged in chemsex ($p<0.001$)
- **Unprotected Anal Sex**
  - Overall, 32% had had UAI at last anal sex
  - No significant difference seen according to whether men did (39%) or did not engage (29%) in chemsex ($p=0.073$)

Chemsex, STIs and HIV

Significant positive association seen between engagement in chemsex and EVER having had

- LGV OR 1.04, 95% CI 1.01-1.08
- *Chlamydia* OR 2.53, 95% CI 1.66-3.85
- Syphilis OR 2.24, 95% CI 1.37-3.68
- *Gonorrhoeae* OR 2.30, 95% CI 1.52-3.46

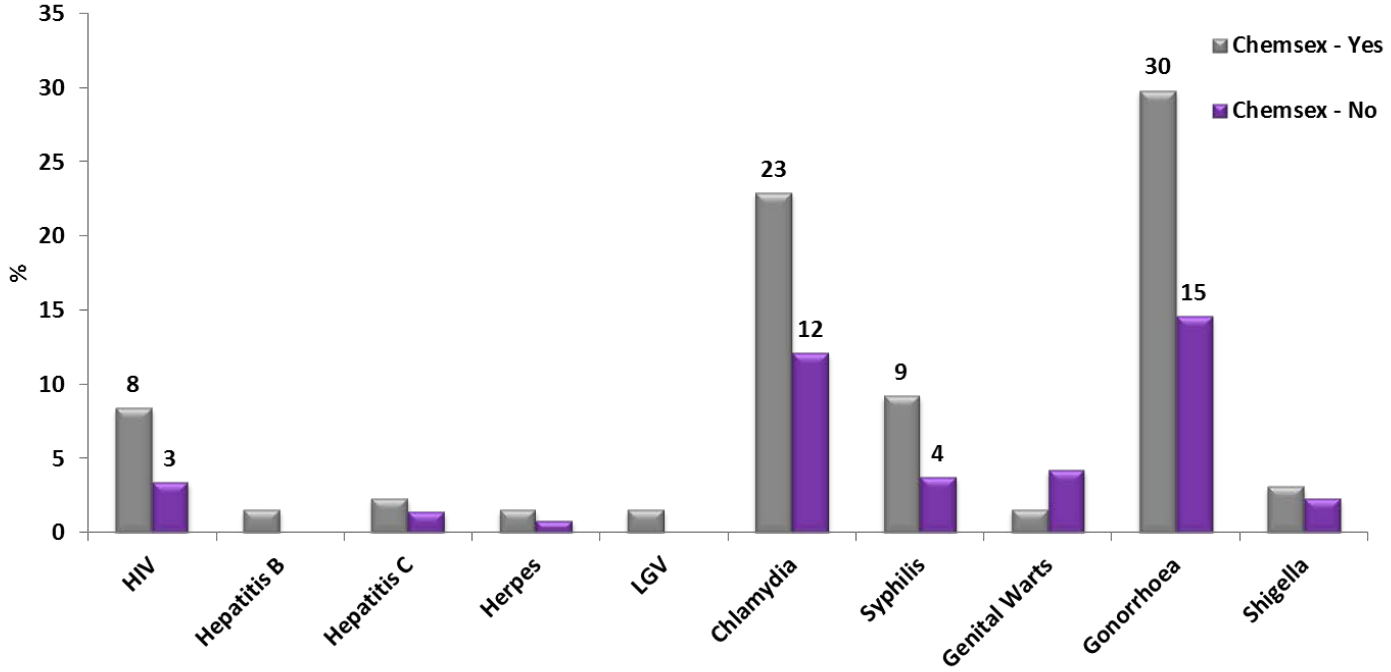


Have you EVER been diagnosed with…

Chemsex, STIs and HIV

Significant positive association seen between engagement in chemsex and having had treatment in the last year for

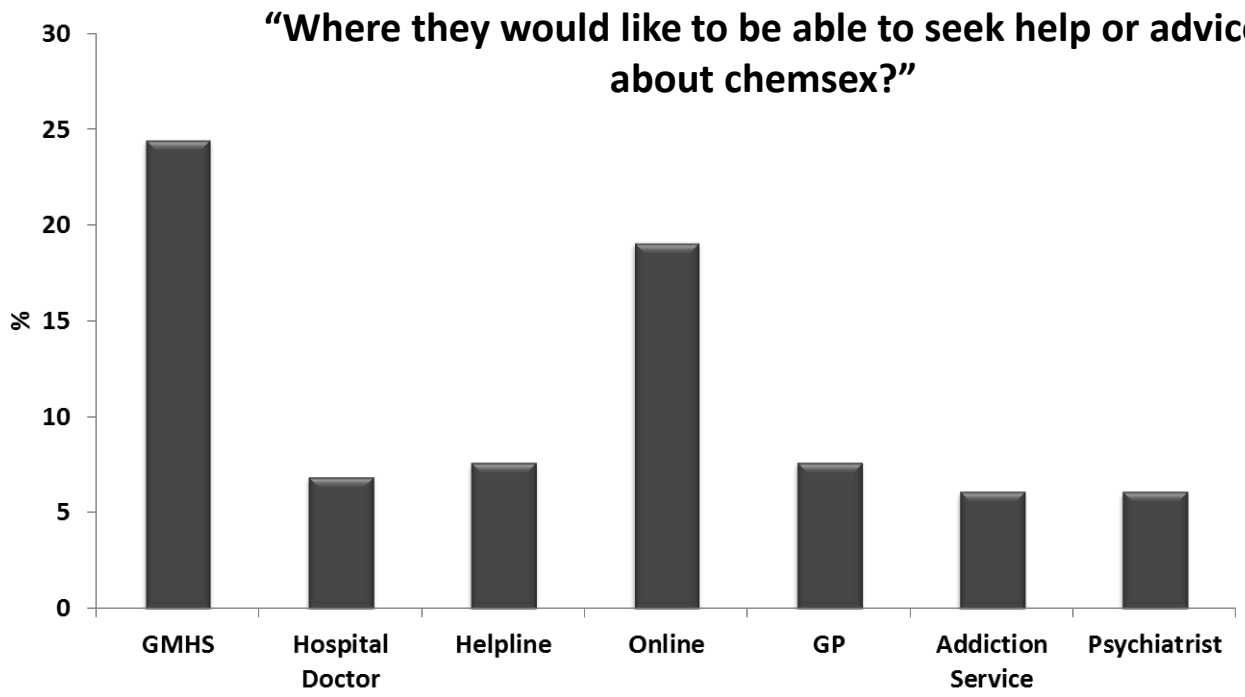
- HIV OR 2.62, 95% CI 1.23-6.10
- *Chlamydia* OR 2.16, 95% CI 1.29-3.61
- Syphilis OR 2.65, 95% CI 1.18-5.99
- *Gonorrhoea* OR 2.47, 95% CI 1.53-3.98



In the PAST YEAR, have you been treated for…

Help seeking and chemsex

- 1/3 would like help or advice regarding chemsex
- 2/3 agreed that a drugs advisor should be available for attendees at GMHS



Summary of Findings

- 1 in 4 men
  - Attending GMHS have engaged in chemsex
  - Who engage in chemsex (or their partners) has lost consciousness
  - Who engage in chemsex say it is impacting negatively on their lives
- There appears to be an association between chemsex &
  - Sexual risk taking behaviours
  - STIs and HIV
- Those engaging in chemsex are not a “hidden population”
- A substantial number of men want help + would like to receive this advice within sexual health clinics and online

Which one of these drugs is NOT a chemsex drug?

A. Mephedrone

B. Cocaine

C. Crystal methamphetamine

D. GHB

Take Home Messages

- Very specific drugs used, not classical recreational ones
- Addiction potential/ behaviours becoming ↑ recognised
- Assault / lack of recognition
- Different SE group to usually found with drug dependency issues, often injecting also – JOE
- Who/where will they present to?

- Provider knowledge can be poor
- Entire loss of weekends, binges can last 48-7 hours, major work, family, relationship fall out
- Depression
- €€€€€
- Pyschosexual morbidity-sexual experiences “will never be as good without chems”

2ND EUROPEAN CHEMSEX FORUM WEBSITE LAUNCHED

11/12/2017

The website of the 2nd ChemSex Forum is now live in English, German and Russian. It contains detailed information about the Forum, registration, abstract submission, the venue, accommodation, and the Forum Scholarship Fund (for Russian speakers from Eastern Europe, Central Asia and the Caucuses regions).

The 2nd ChemSex Forum will take place on 22 – 24 March 2018 in Berlin, Germany.

News categories: Substance use

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A Whole New Problem

Questions ?