Take Home Tips: Sexually Transmitted Infections

ACP Virginia Scientific Meeting
March 8, 2019

Michael F. Rein, MD, MACP

Professor Emeritus

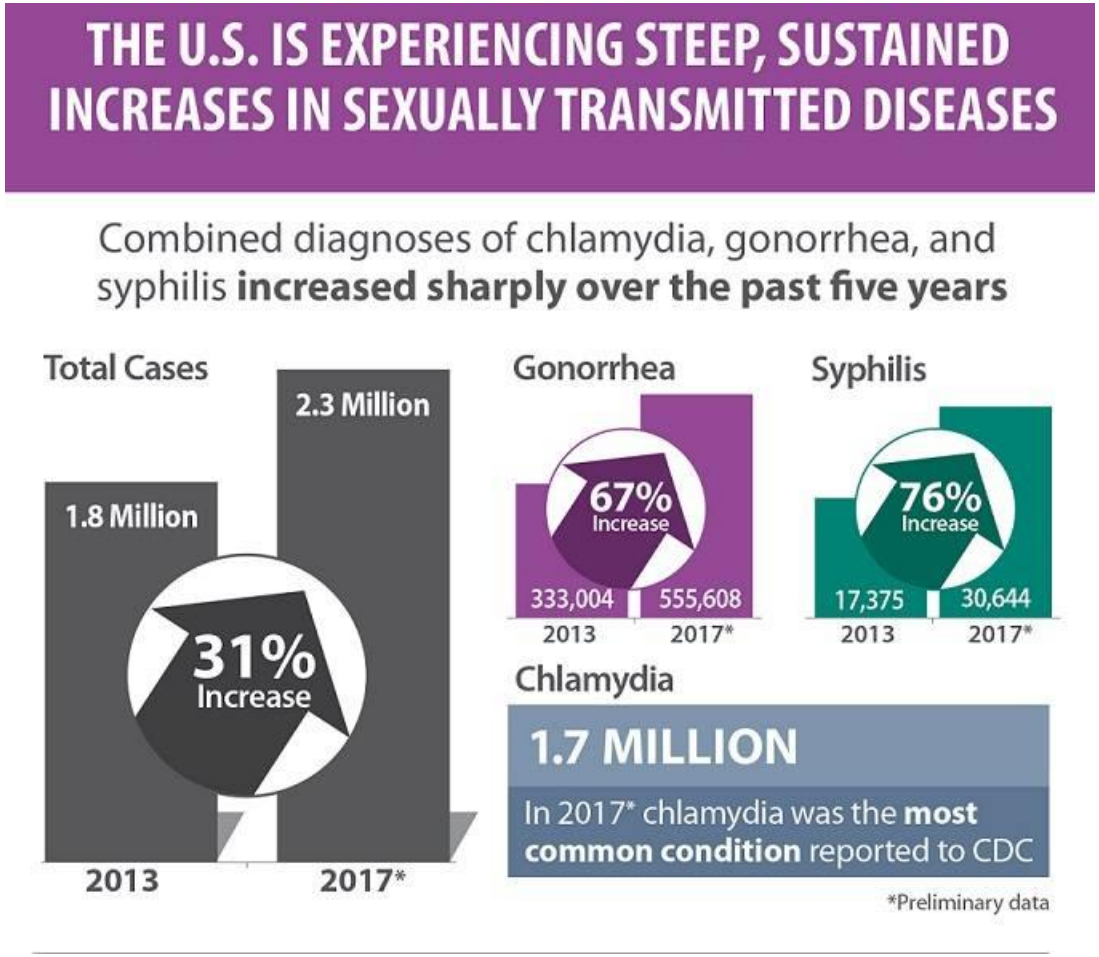
Harrison Distinguished Educator

Division of Infectious Diseases and International Health

University of Virginia

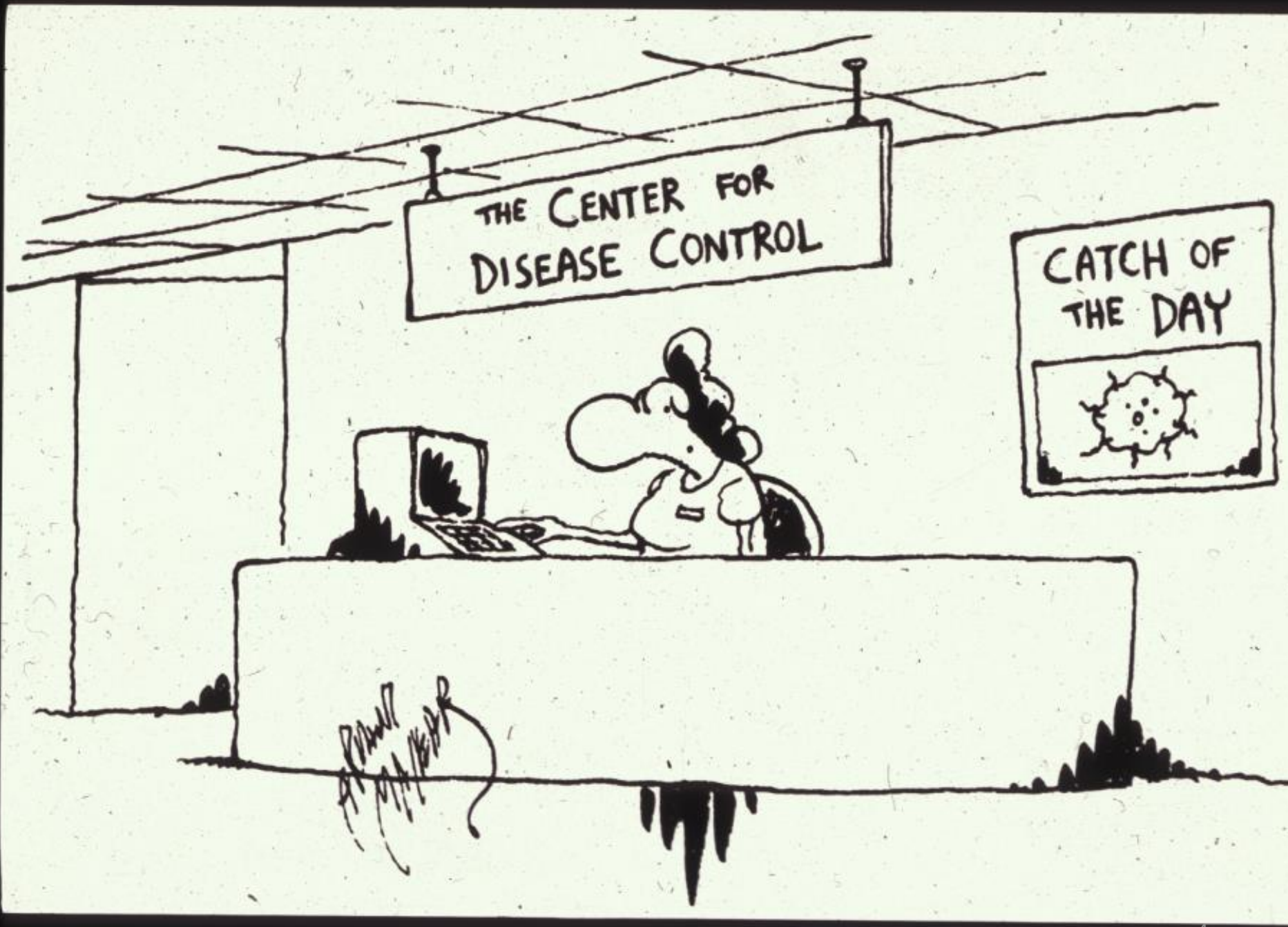
Dr. Rein has no conflicts of interest to declare

CDC: September 2018



Experimental Approach

- Not approved by Human Experimentation Committee
- Please make sure you have the one-page handout with (useful) tips
- Rapid (really rapid) presentation of some supporting data: average 2 minutes/tip
- Slide deck available for more detailed review
- Please provide evaluation of this approach
- Unanswered Questions: mfr6t@virginia.edu


THE CENTER FOR
DISEASE CONTROL
CATCH OF
THE DAY

Tip 1:

Oral and anal sex are common and must be part of the sexual history and the results acted upon:

History must be obtained in terms the patient can understand. This requires some desensitization.

The only sexually transmitted condition that absolutely cannot be acquired through oral or anal sex is "pregnant"

Heterosexual anal and oral sex (older data)

- National Survey of Family Growth
- 12,571 men and women age 15-44 years
- 1/3 have had anal sex at least once
- 3/4 have had oral sex at least once

Leichliter, JS, et al: J Infect Dis 2007;196:1852-9

Pharyngeal gonorrhea

- N = 245, 56% female, public STD clinics, all reporting oral sex in past 3 months
- Gonorrhea 27% (64)
  - 45% urogenital only (29)
  - 28% pharyngeal only (18)
  - 27% both sites (17)
- ≥ 5 partners vs 1 partner: GC aOR 5.7 (1.2-25.6)

Scherer l, Univadis; Javenbakht H, et al: Sex Transm Dis 2018 Feb 26, epub

Transmission from Oropharynx to Penis

- San Francisco STD Clinic, MSM, insertive fellatio only in 3 months
- *Chlamydia trachomatis* N = 397
  - 4.8% Ct positive
    - HIV positive 16.0%
    - HIV negative 3.0%
- *Neisseria gonorrhoeae* N = 395
  - 4.1% GC positive
    - HIV positive 10.0%
    - HIV negative 3.0%

Bernstein KT et al: *Clin Infect Dis* 2009; 49:1793–7

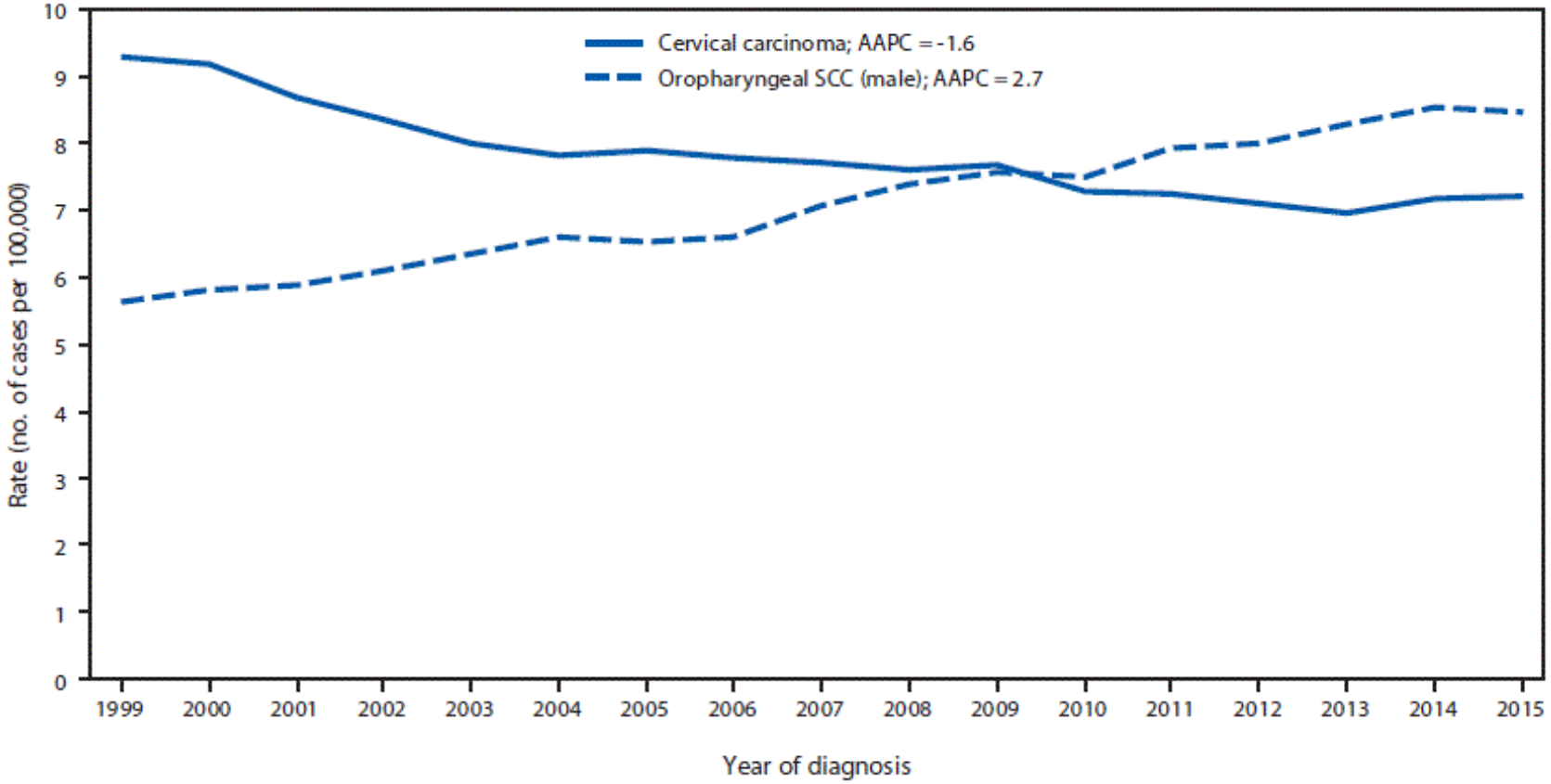
Oral HPV Prevalence

- NHANES 2011-2014: M=4493, F=4641
  - Oral samples, PCR: HPV 37 types including HR HPV 14 types
- Prevalence of oral HPV:
  - Men: Overall 11.5%, HR 7.3%
  - Women: Overall 3.2%, HR 1.4%
- Risk factors:
  - Smoking ≥ 20/day
  - ≥ 16 sexual partners
  - Same sex partners
  - Coincident genital infection
- Quadrivalent vaccine reduced prevalence of vaccine types, but not overall
- Review article: Overall prevalence: 7.7%, 1.4% HR
- Message: oral sexual history and oral exam are an important part of management

Sanawane K, et al: Ann Intern med 2017;167:714-24; Tam S, et al: Oral Oncol 2018;82:91-9

HPV-associated cancer rates (CDC)

Van Dyne EA et al: MMWR 2018;67:918-24



Anal Intercourse

- Nationally representative survey N=5162 age 18-50
  - Women 37%, 12% in past 3 months
  - Condom use: 9% anal, 16% vaginal
- 7.4% of STD Clinic women endorsed anal intercourse in the past 3 months N=2818

	Genital only	Rectal only	Both sites
N. gonorrhoeae (128)	31	23 (18%)	74
C. trachomatis (292)	61	60 (21%)	171

- Message: Anal sexual history and testing are an important part of management

Benson L, et al: Obstet Gynecol 2016;doi:10.1097/01.AOG.0000483642.35361.2d (abstract);Llata E, et al: Obstet Gynecol 2018;132:692-7

Tip 2:
Serological tests for HSV *genital* infection are almost always useless, do not use for screening

Okay, of very, very limited utility

HSV-1 Genital Infection

- Overall prevalence: at least 35% of genital herpes
- In newly acquired cases among young people: about 70%

Ryder: Sex Transm Infect 2009, online; Pena KC, et al: *J Clin Microbiol* 2009; E publication, November 17, doi:10.1128/JCM.01336-09

HSV Types in Cervical Specimens

- HSV PCR on 60,000 cervical specimens Jan-Dec 2007
- 14% positive for HSV
  - 32% HSV-1
  - Among women <24 years old: 47% HSV-1

Pena KC, et al: *J Clin Microbiol* 2010;*48(1):150-3*

HSV in genital specimens

- Vaginal swabs from 800 women collected for GC/CT testing
  - Average age 29.8+/- 9.2 years
- Among 13-30 year-olds
  - HSV-1 5.26%
  - HSV-2 4.31%

Vahidnia A, et al: Clin Microbiol Infect 2012;doi:10/1111/1469-0691.12105

% of Genital Herpes Due to HSV-1

- University of Wisconsin (shhhh)
- First episode
- Culture, monoclonal antibody typing.
- 1993-2001
- 2.5 fold increase in percentage of genital isolates that were HSV 1 (30.9% □ 77.6%)
- Especially among younger students (16-21 yo)

Sex Transm Dis 2003;30:947-800

Against screening for HSV in the general population

- HSV-1 antibody may result from genital or orolabial infection
- Huge stigma associated with putative infection
- Many people HSV 1 positive, and even if HSV 2 Ab negative, cannot rule out genital infection
- Serology useful in some settings (beyond the scope of this discussion)

Hook EW: JAMA 2016;316:2493-4; Bibbins-Domingo K and USPSTF: JAMA 2016;316:2525-30; Rein MF: Curr Infect Dis Rpts 2006;8:1-2

Tip 3:
Suppressive Rx of genital HSV reduces symptomatic recurrences and reduces but *does not eliminate* transmission of infection to partners

HSV-2 Suppressive Therapy

- Crossover studies: 4-7 weeks each arm
- Swabs 4X/day, quantitative PCR: 5.4% +
- Bottom Lines
  - Suppressive therapy better than no treatment
  - No significant differences among treatment groups: high dose no better than standard dose
  - Suppressive therapy reduces but does not eliminate shedding

Johnston C, et al: Lancet 2012; online publication

HSV-2 Suppressive Therapy

	% swabs+	Episodes/P-Y
No treatment	18.1%	28.7
Acyclovir 400 mg bid	4.2%	10.0 - 14.9
Acyclovir 800 mg tid	4.5%	16.5 - 20.2
Valaciclovir 500 mg qd	3.3% - 5.8%	22.6
Valaciclovir 1 gm tid	5.4%	

- Johnston C, et al: Lancet 2012; online publication

Suppressive Therapy: *Reduction of Risk of Transmission of Virus to Partner*

- International, randomized, double-blind, placebo-controlled trial
- 1488 couples with one partner with symptomatic recurrent genital herpes (4-9 episodes per year) and one susceptible
- Symptomatic partner randomized to valaciclovir 500 mg per day or placebo
- Couples followed monthly for 8 months for symptoms or seroconversion
- Safer sex counseling done on enrollment and monthly during study

Corey L et al: New Engl J Med 2004;350:11-20.

Suppressive Therapy: *Reduction of Risk of Transmission of Virus to Partner*

- 743 source partners received valaciclovir; 741 received placebo.
- Valacyclovir reduced overall acquisition of genital HSV-2 infection (laboratory-confirmed symptoms or seroconversion) by [only] 50%:
  - 3.8% placebo versus 1.9% valaciclovir, p=0.039
- Valaciclovir reduced the acquisition of symptomatic genital infection by ~80%
  - 2.3% placebo versus 0.5% valacyclovir, p=0.006

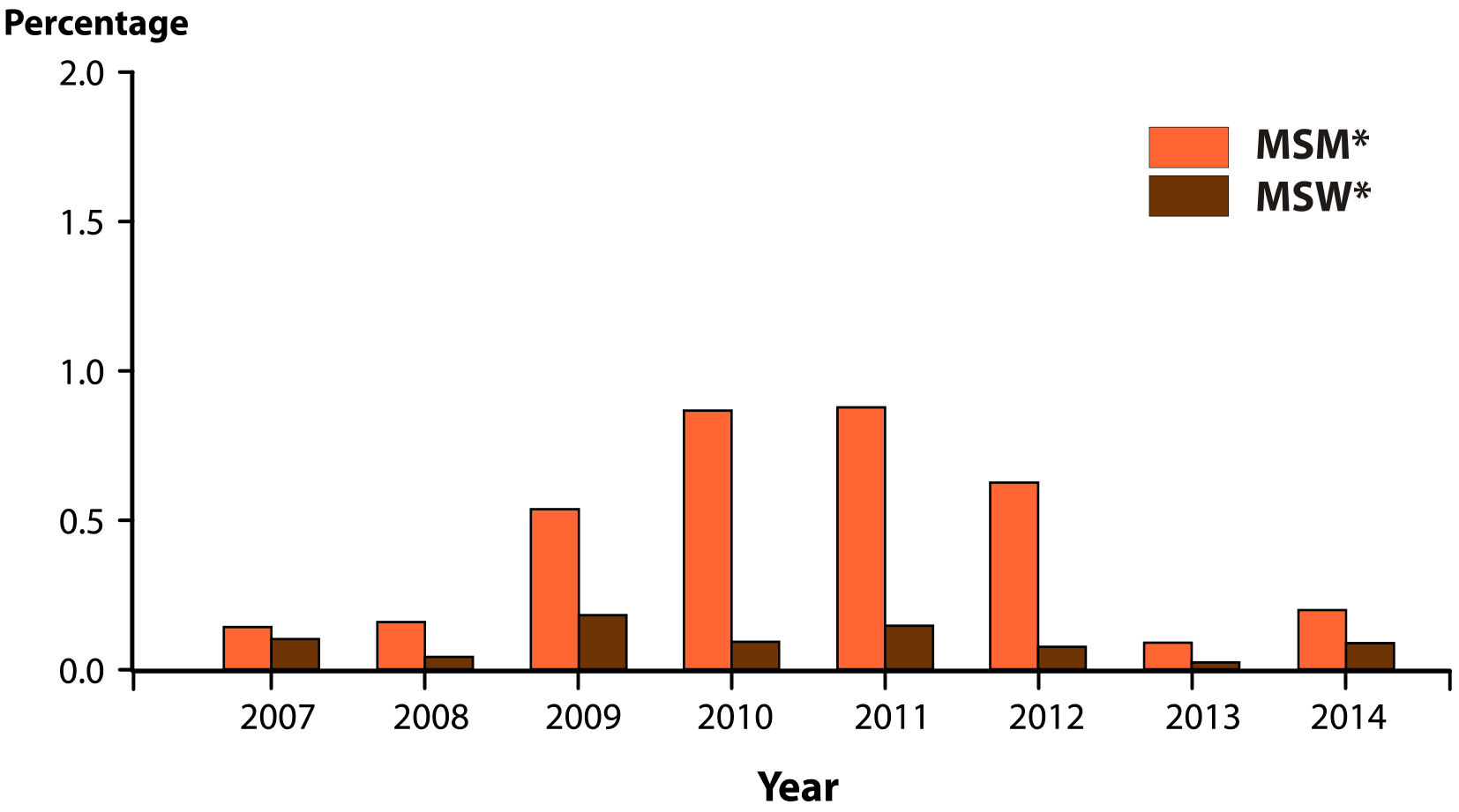
Corey L et al: New Engl J Med 2004;350:11-20.

Tip 3.1
If/when suppressive Rx discontinued, expect a flare of frequency and severity of outbreaks

Tip 4: Always treat gonorrhea with two drugs

- Provides double coverage for GC
  - CDC: Rate of increase in resistance to β-lactams appears to have slowed since the widespread acceptance of dual therapy
  - And also with the cessation of use of oral cephalosporins and single dose fluoroquinolones (don't use these)
- Treats coincident chlamydial and *nonchlamydial* NGU

Neisseria gonorrhoeae — Percentage of Urethral Isolates with Elevated Ceftriaxone Minimum Inhibitory Concentrations (MICs) (≥0.125 µg/ml) by Reported Sex of Sex Partner, Gonococcal Isolate Surveillance Project (GISP), 2007–2014



***MSM**=men who have sex with men; **MSW**=men who have sex with women only.

2013-Fig Z. SR. Pg. 75.

Rx of GC
(for now)

Ceftriaxone 250 mg im

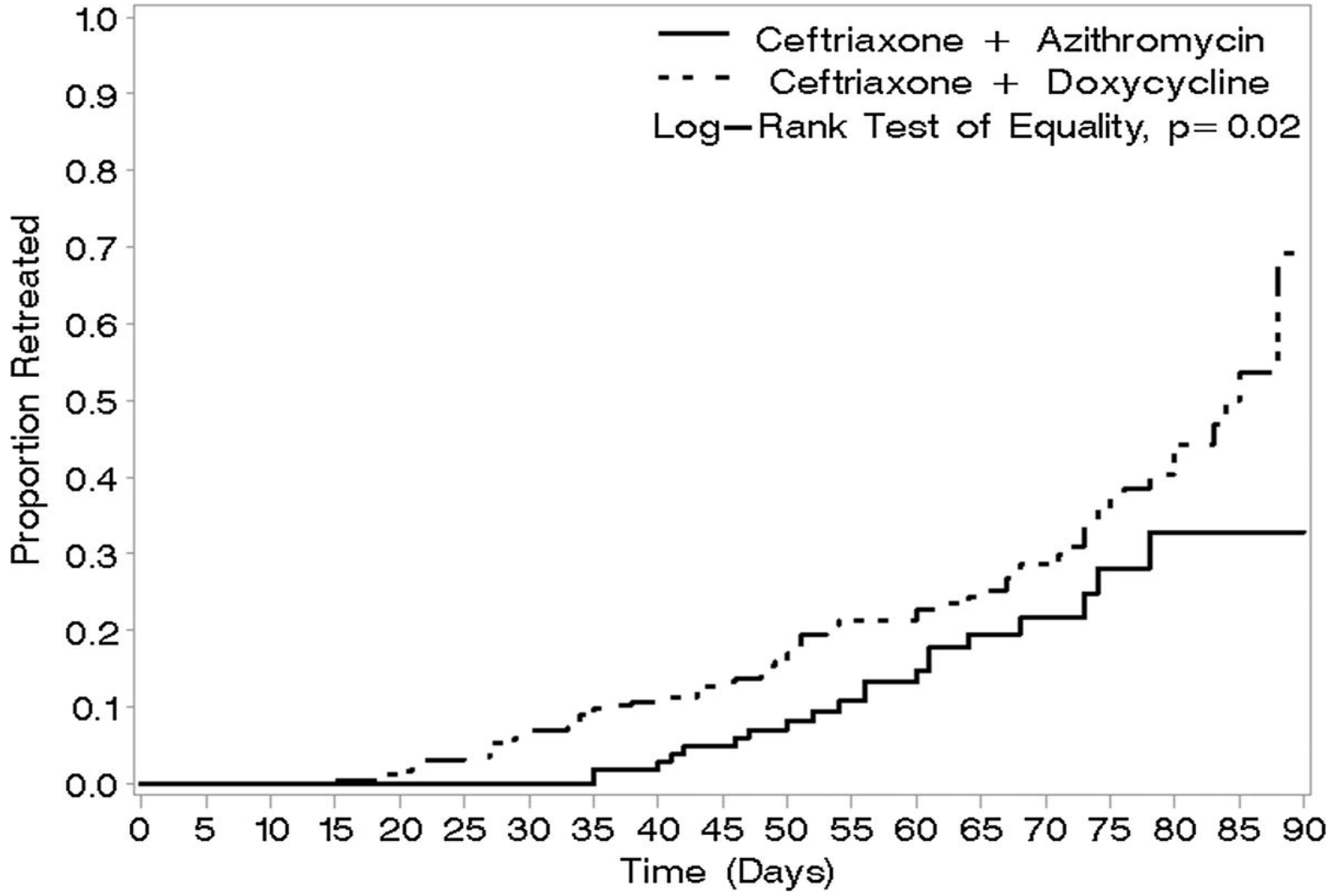
Plus

Azithromycin 1 gm po

- A number of groups have called for increasing doses of ceftriaxone
- Do not use oral therapy for GC
  - Except for expedited patient therapy (EPT)
  - Do not use single-dose fluorquinolones pretty much for anything (uhhh, still used for *N. meningitidis* prophylaxis?)

Gonorrhea retreatment rates: reexamined in 90 days

Schumacher CM, Ghanem KG: Sex Transm Dis 2013;40;539-545



Treat all gonorrhea cases for coincident NGU

- Patients with gonorrhea are likely to be carrying one of the other causes of NGU, like *M. genitalium*
- Use dual therapy even if negative for *C. trachomatis*
- If you don't use dual therapy:
  - Beware of postgonococcal urethritis
    - Patient treated for gonococcal urethritis with β-lactam alone
    - Partial response or response with relapse in absence of reexposure
  - Treat for agent of NGU
- Treat partners as well

Tip 5:Followup tests for GC and CT

- Retest at 3 months to detect reinfection
- Dead organisms can be detected by NAATs
  - Dead organisms may persist for:
    - 3 weeks for *Chlamydia trachomatis*
    - 3 (rarely 9) days for *Neisseria gonorrhoeae*
- *Chlamydia trachomatis* may form so-called aberrant bodies
  - Metabolically inactive
  - Detectable by NAATs
- For gonorrhea treatment failures, do culture as well, so organisms can be tested for antimicrobial susceptibility

CDC: MMWR 2015 Recomm Rep 2015;64(RR#3); Renault CA, et al:Sex Hlth 2011;8:69-73; Bachmann LH, et al: J Clin Microbiol 2002;40:3596-601; Ampel NM, et al: Clin Infect Dis 2016;62:1356

Tip 6: Salvage treatments for resistant gonorrhea

- CDC/NIH study: heterosexual men and women and MSM, randomized, open-label, 2010-2012
  - Negative urogenital culture 10-17d post-Rx
- 240 mg gentamicin IM + 2 gm azithromycin po
  - Cured 202/202 (≥98.5%) anogenital infections
  - Cured 10/10 pharyngeal infections
- 320 mg gemafloxacin po + 2 gm azithromycin po
  - Cured 198/199 (≥97.6%) anogenital infections
  - Cured 15/15 pharyngeal infections
- Lots of GI side effects
  - Mentioned in 2015 CDC guidelines and later publications
  - Not (yet) FDA approved

Kirkcaldy RD,et al: Clin Infect Dis 2014;59:1083-91; Rice PR: Clin Infect Dis 2014;59:1092-4; CDC: MMWR Recomm Rep 2015;64(No. RR-3):65.

Tip 7:
You can *probably* get away with expedited partner therapy

Providing medication or prescription for partner of patient with an STI.

It should never be your first approach

Expedited Partner Therapy

- Providing a patient with a prescription or medication to give to sexual partner(s)
- Supported by CDC, AAFP, ACOG, VDH
- CDC: Not recommended for MSM (high rate of coprevalence)
- ACOG: Carefully consider:
  - High risk of intimate partner violence
  - Suspected child abuse
  - Suspected sexual assault

ACOG: Committee Opinion 632, June, 2015; CDC: MMWR 2015;Recomm Rpts 64:3

EPT (slightly) Reduces Reinfection Rate in STD Clinic

Study 1: Baltimore STD Clinic, retrospective

Reinfection rate:

With EPT: 2.1%

Without EPT: 3.4%

Note: very small absolute difference; historical controls

Study 2: Also Baltimore STD Clinic, retrospective

9.9% (4457) of patients were retreated within 2 years of initial treatment

Patients received EPT were less likely to be retreated compared to patients treated before EPT became available

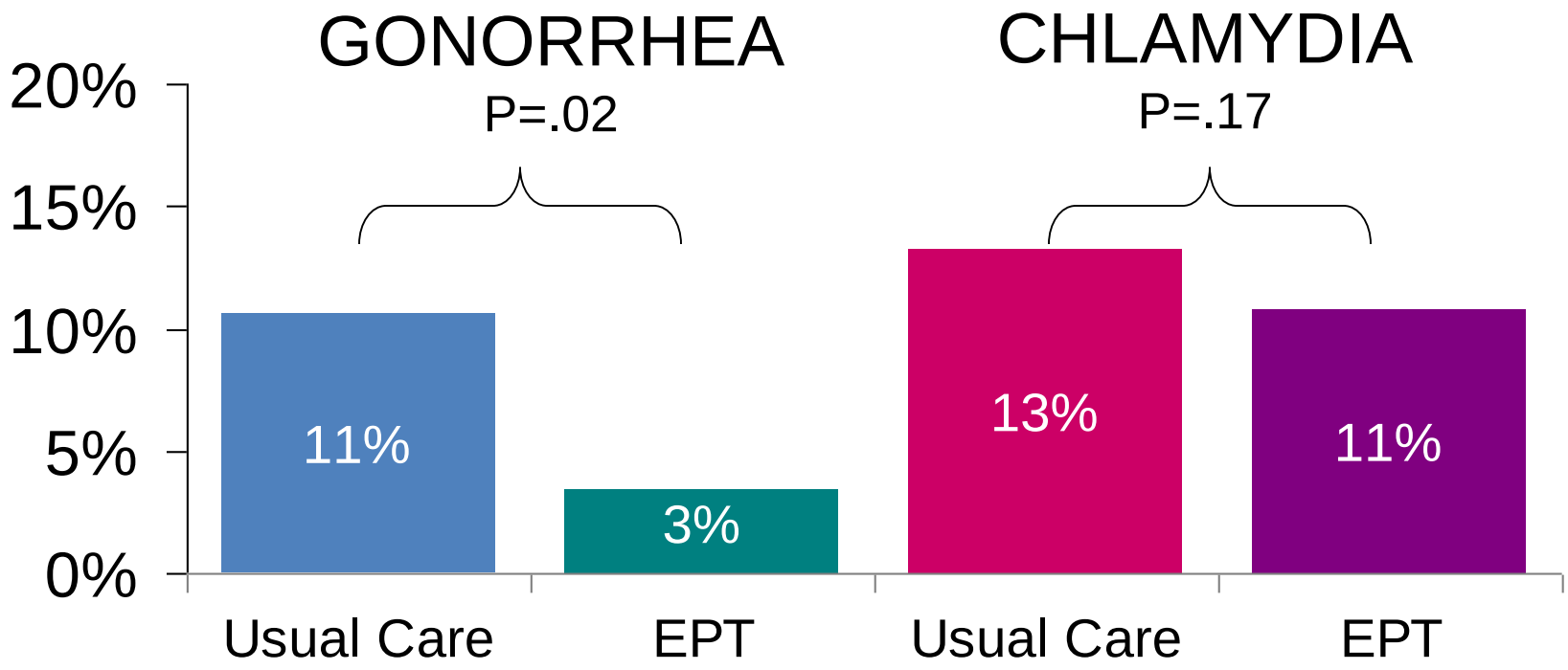
aHR 0.55 (0.31-0.96)

BUT: patients treated after EPT became available but who did not get EPT were 40% less likely to be retreated

aHR 0.60 (0.34-1.03)

2010 National STD Prevention Conference (NSTDP): Abstract P86. Presented March 10, 2010;
Schumacher CM, Ghanem KG: Sex Transm Dis 2013;40;539-545

The Effectiveness of Expedited Partner Treatment on Re-Infection Rates



Usual care = patient refers partner(s)

Golden M, et al. N Engl J Med 2005 Feb 17;352(7):676-85.

Expedited Partner Rx (EPT) in Virginia

House Bill 1054 (2018)

- EPT is “potentially allowable”
- Only for gonococcal and chlamydial infection
  - Not if other STI are also diagnosed (coprevalence)
    - Not recommended for MSM
- Only by Health Department clinicians (?)
- Only using CDC-recommended regimens
  - (Not Rx of choice for gonorrhea)
- Must call the recipient(s)
  - Obtain history of drug sensitivities
  - Recommend test of cure at 3 weeks

Recommended by CDC for expedited therapy

Cefixime 400 mg po

plus:

Azithromycin 1 gm po

Note that this is not first-line therapy

Is expedited patient therapy ethical?

- Must use oral therapy, not the first choice for gonorrhea
- Does a patient have the right to know why he or she is being treated?
- Does patient have the right to counseling and examination for coprevalent STI
- Cannot actually document that partner got treatment

Tip 8: Sexual contacts to NGU should be epidemiologically treated

- Epidemiological treatment: provide Rx on basis of contact (risk) before diagnosis
  - For: GC, NGU, Ct, Syphilis, Trich, Chancroid
- Epi-treat even if chlamydia negative
- NGU is a syndrome with multiple etiologies
  - *Chlamydia trachomatis* is not the only cause (~25%)
  - *Mycoplasma genitalium* is an important etiology (~25%)

Etiologies of NGU

- *Chlamydia trachomatis* 25%
- *Mycoplasma genitalium* 10%-25%
- *Ureaplasma urealyticum* 16-26%
- *Trichomonas vaginalis* ~1%
- *Neisseria meningitidis**
- Herpes simplex*
- Enterobacteriaceae
- *Hemophilus influenzae**
- Adenovirus*
- “Idiopathic” (so far)

*Associated with insertive fellatio

Ct Rx: Azithro vs Doxy

- Meta-analysis: 14 studies, 2147 men, 568 women:
  - Azithromycin: single dose 1 gm
  - Doxycycline: 100mg qd or bid X 7da
  - Mean followup 30 days
- Failure rates: Azithro *vs* Doxy

	Microbiological	Clinical
Men (N=891)	2.45 (1.36-4.41)	0.94 (.43-2.95)
Women (N = 338)	1.71 (0.48-6.16)	NA

[The difference in clinical results may result from coprevalence with *M. genitalium,* against which Azithro is much more active]

Paez-Canro C et al: Cochrane Database Syst Rev 2019;1

Tip 9: *M genitalium* is a bad actor

- First recognized 1981
- Women, men, including MSM
- Important diseases
- Becoming resistant to standard therapy
- Commercial diagnostic test FDA approved in February 2019

M. genitalium in sexual partners

- Melbourne Sexual Health Center, 2008-2016
- Vaginal or anal contact of known case
- PCR targeting16s rRNA: urine, vaginal swab, anal swab
- Prevalence of *M. genitalium*
  - Women: 48% (67/139)
  - Heterosexual men: 31% (39/126)
  - MSM: 27% (30/112)
- [This is high enough to warrant epidemiological treatment]

Slifirski JB, et al: Emerging Infect Dis 2017;23:1826-33

M. genitalium in women

- Meta-analysis
- Pooled odds ratio (# of studies)
  - Cervicitis (20) 1.66 (1.35-2.04)
  - Pelvic inflammatory disease (4) 2.53 (1.03-6.06)
  - Female infertility (5) 2.43 (.93-3.64)
  - Adverse pregnancy outcomes
    - Preterm birth (6) 1.89 (1.25-2.85)
    - Spontaneous abortion (3) 1.89 (1.10-30.3)

Lis R, et al: Clin Infect Dis 2015;61:418-26

M genitalium in men

- Meta-analysis
- NGU
  - Median prevalence among men with nonchlamyidal NGU = 25% (10%-38%)
  - Prevalence *vs* asymptomatic control group
    - Statistically significant in 16/22 studies (73%)
    - Odds ratios: 2.2 -20.3
  - Dose-response relationship to severity
  - Clinical resolution associated with elimination of organism

Manhart LE, et al: Clin Infect Dis 2011;53(S3):S129-42

Anorectal *M genitalium* in MSM

- Melbourne STD clinic with Sx of proctitis N=166
  - Prevalence
    - Gonorrhea 54%
    - Chlamydial infection 38%
    - *M. genitalium* 31% *Mg* only: 17%
  - Less painful than GC or Ct
  - Cure rates:
    - Azithromycin 38%
    - Moxifloxacin 92%
    - Pristinomycin 79%
- Primary care clinic, Birmingham 157 MSM
  - Prevalence: 17.2% (27/157)
    - Genital: 10.8%
    - Anorectal: 6.4%
  - Resistance mutations
    - Macrolide: 80% (8/10)
    - Fluoroqinolone: 74% (20/27)

Ong JJ, et al: Sex Transm Dis 2018;45:522-6;Dionne-Odom J, et al: Clin Infect Dis 2018;66:796-8

Commercial test for *M genitalium*

- Aptima *Mycoplasma genitalium* Assay (Hologic Inc)
- NAAT, 16s rRNA; vs "validated reference alternate TMA assays" (?)
- Performance:

	Sensitivity	Specificity
– Urine	F:78% M:91%	F:99% M:99%
– Urethral	98%	99.6%
– Meatal	88%	98%
– Endocervical	82%	98%
– Vaginal	92%-99%	98%-99%

- PV+ and PV- depend on prevalence (*a priori* probability)
- Effect of douching and tampons unclear

Hologic: Package Insert 2019

Tip 10:
M. genitalium is rapidly becoming resistant to azithromycin

M genitalium resistance over time

- Meta-analysis, ~1500 pts, most observational, 1 gm azithromycin
- Cure rates:
  - Before 2009 (12 studies) 85.3% (82.3-88.3)
  - 2009-2015 (9 studies) 67.0% (57.0-76.9)

Lau A, et al: Clin Infect Dis 2015; 61:1389-99

Standard NGU Regimens

- Azithromycin: 1 gm single dose
- Doxycycline: 100 mg twice daily for 7 days
  - Compliance!!
- Metronidazole 2 gm single dose
- Tinidazole: 2 gm single dose
- Metronidazole 500 mg bid for 7 days
  - Compliance!!

- Workowski KA, Bolan GA: CDC Rx Guidelines 2015: MMWR Recomm Rep 2015;64 (RR-3): 1-137;Schwebke JR, et al: Clin Infect Dis 2011;52:163-70

Tip 11: Approach to NGU treatment failures

- Current CDC approach
- Tetracycline failure:
  - Metronidazole/Tinidazole for trichomoniasis
  - Azithromycin for mycoplasmas
- Azithromycin failure:
  - Metronidazole/Tinidazole for trichomoniasis
  - Moxifloxacin 400 mg orally daily for 10 days
    - Also covers *C. trachomatis*
    - *Not FDA approved*
  - Gatifloxacin 200 mg orally twice daily for 7 days
    - Also covers C. trachomatis
    - *Not FDA approved*

CDC: 2015 STD Rx Recs; Hamasuna et al: Sex Trans Infect 2011

M genitalium: Lab-guided sequential therapy for *M genitalium*

- N = 244, Melbourne, 2016-2017
- Doxycycline 100 mg bid X 7 days
  - Reduced bacterial load by 2.6 logs (N = 56)
- Test for 5 macrolide-resistance mutations
  - MRM +: Sitafloxaciine 100 mg bid X 7 d
    - Cure 154/167 (92.2%)
  - MRM -: Azithromycin 2.5 gm, then 500 mg qd X3
    - Cure 73/77 (94.8%)
    - Selection of macrolide resistance: 2/76 (2.6%)
- [I would seriously consider using this regimen for all NGU – recommended by Britain and Australia, not yet by CDC]
  - Will compliance be an issue???

Read TRH, et al: Clin Infect Dis 2019;68:554-60

Tip 12:
Seriously consider treating trichomoniasis with the 7 day rather than the single dose regimen of metronidazole

2 gm single dose

500 mg bid X 7 day

Treat sexual partners with same dose

Treatment of trichomoniasis

- Prospective, open-label, 3 STD clinics, N = 623
- Metronidazole: single 2 gm dose *vs* 500 mg twice daily for 7 days
- F/U at 4 weeks with culture and NAAT
- Compliance 2gm: 99%; 7d: 96%
- Failure rates

	Overall	Compliant/No reexposure
2 gm	19%	20.8%
7d	11%	9.8%

[I am not sure how these data apply to single dose treatment with tinidazole]

Kissinger P, et al: Lancet Infect Dis 2018;18:1251-9; Kissinger P, Munzy CA: Lancet Infect Dis 2019;19:20-1

Tip 13:
Always obtain a nontreponemal test for syphilis (e.g. RPR)

- Follow for 4X drop in 3 months as indication of adequate Rx
- Follow annually for seroconversion or stabilization
- Subsequent 4X rise: relapse or reinfection. Consider CSF examination

RPR titers following Rx

- CDC Recommendations – HIV negative
  - Primary and secondary syphilis: 6 months and 12 months
  - Early latent syphilis: additional at 24 months
- Interpretation
  - ≥ 4X drop: cure
    - Independent of initial titer
  - ≥ 4X rise: relapse or reinfection (consider CSF examination)
  - ≤ 2X drop or rise: serofast

CDCP: MMWR 2010;58(RR-12):26-34; CDC: Sexually Transmitted Diseases Treatment Guidelines, 2015. MMWR Recomm Rep 2015;64(No. RR-3).

RPR titers following Rx (MFR)

- Consider initial followup at 3 months
  - Eliminate 85% of patients requiring additional acute follow-up
  - Reduce loss to follow-up
  - Reinforce safe-sex practices
  - Check for chlamydial/gonococcal reinfection
  - Evaluate for HPV
  - Patients with previous syphilitic infection may show a slower drop in titer
- Still want to do long term serological follow-up to document lowest titer
  - Test q3mo until 4X drop
  - Test annually until seronegative or persistent titer stabilizes

Serologically defined cure

- All treatments: penicillin and azithromycin
- ≥ 4X drop in RPR titer

	3 months	6 months
Primary (N=116)	85.5%	87.0%
Secondary (N=217)	82.5%	85.8%
Early latent (N=132)	54.5%	62.1%

- Little increase between 3 and 6 months
- Early latent less responsive (Followup at 24 months)

Seña AC, et al: Clin Infect Dis 2011;53:1092-9

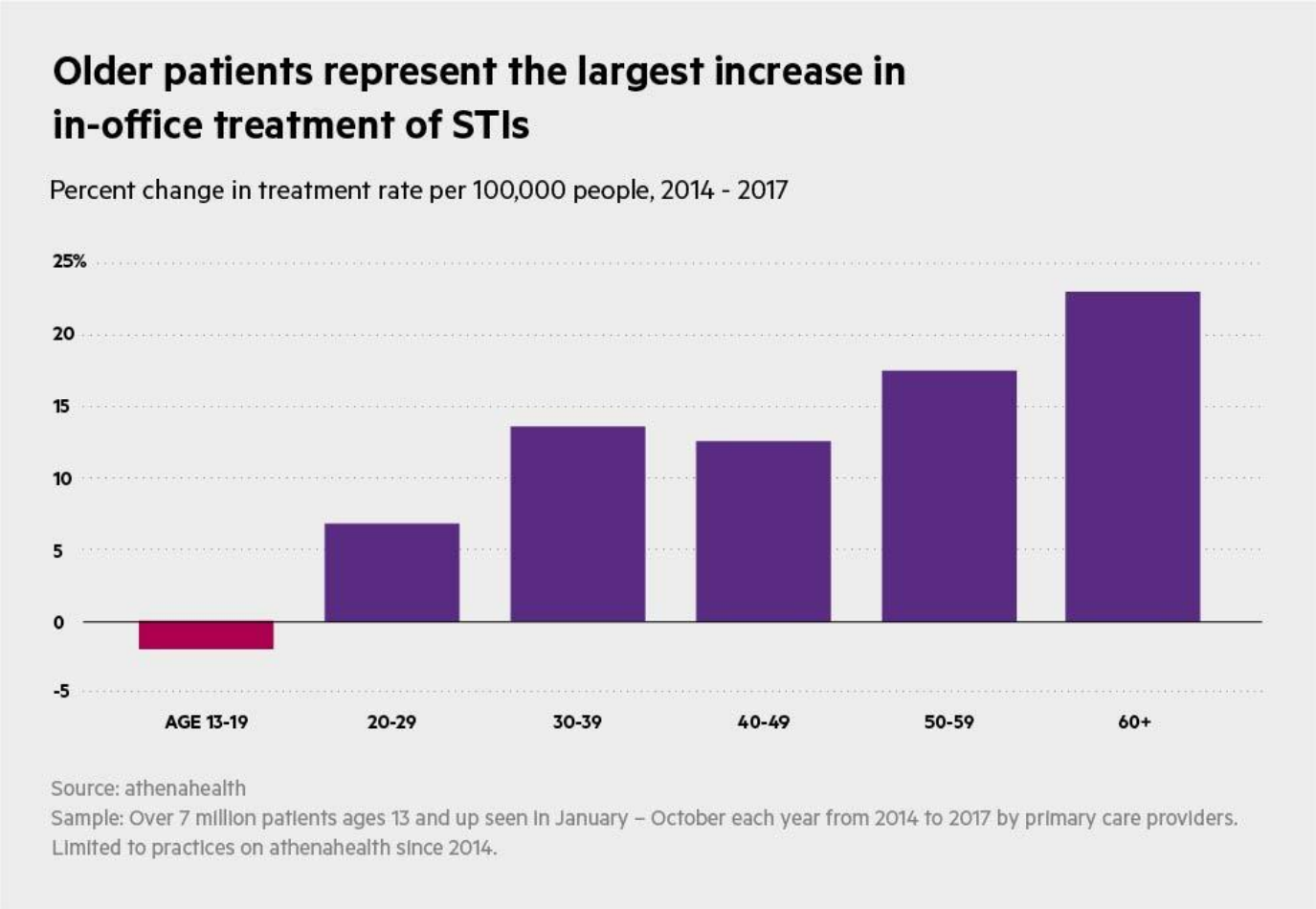
Tip 14:
Screen “seniors” (> 60 yo) for STI

- Up 23% vs 11% in general population
- Take a sexual history in patients over 60
  - Heterosexual and homosexual
  - Inform regarding safer sex practices
  - Consider the female condom

Pereto A: Athenahealth; 2018:May 16; Howly EK: US News 2018;Dec 10;
Emanuel EJ: NY Times; 2014: January 18 Sunday Review

Seniors with STI

(Herpes, Gonorrhea, Syphilis, Hepatitis B, Trichomoniasis, Chlamydial Infx)



Pereto A: Athenahealth; 2018:May 16

Are seniors concerned about STD?

Tests used by Medicare Recipients 2011-2012 (millions)

Mammography	8.4
Bone Mass	5.1
Prostate	4.1
Diabetes	3.8
Pap (without physician)	2.6
Pelvic exam	2.4
STD screening and counseling	2.2
Colonoscopy	2.2
Pap (physician interpreted)	2.1
Stool heme	1.8
Tobacco counseling	0.1
Depression screening	0.1
HIV	**0.07**
Alcohol abuse	0.06
Obesity screening or therapy	0.03

Emanuel EJ: NY Times 2014; January 18 Sunday Review

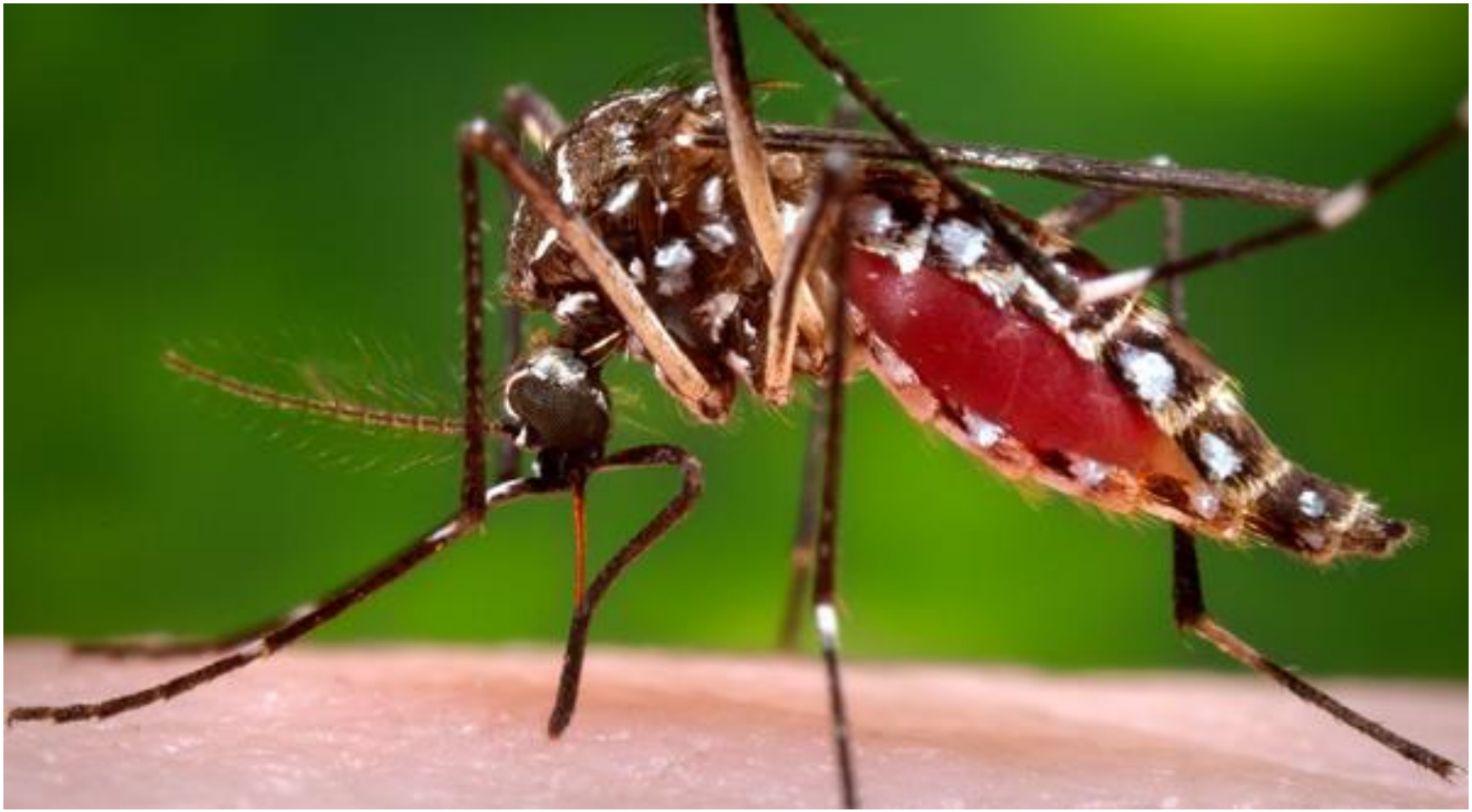
Tip X: Get tested

Actually, get treated

Tip 15:
Sexual transmission of Zika is real

If there is time

Aedes aegypti



Possible epidemiological consequence of sexually transmitted Zika

- Comparing incidence of Zika (ZIKV) and dengue (DENV), Rio de Janeiro, 2015-2016.
  - DENV not sexually transmitted
  - Both mosquito borne
- Cases reported late 2015
  - Overall:
    - ZIKV: 20K women, 9K men
    - DENV: 56K women , 46K men
  - Ages 15-65 y/ per 100,000
    - ZIKV: 5383 women, 2855 men, risk ratio: 1.88
    - DENV: 16128 women , 13941 men, risk ratio: 1.19
    - P = .006
- Suggests sexual transmission epidemiologically important
  - Possible biases: women seeking medical care more than men

Coelho FC et al: Int J Infect Dis 2016;epub doi:10.1016/j.ijid.20167.08.023

Sexually transmitted Zika

(Variations in data)

- Literature review up to April 2018: 128 papers, 77 in humans
  - Rhesus data: Sexual transmission in pregnancy may pose higher risk than mosquito tramnsmission
- 36 human cases, 34/36 male to female
  - Median incubation period: 12d (max 44d)
  - Note: 56 confirmed cases reported to CDC by 7/3/18
- Semen:
  - Median duration of RNA in semen: 40d (max 370d)
    - Note: Median time to clearance 54 days (CDC)
    - Note: ≤ 7% at > 90 days (CDC)
  - Median duration of infectious virus 12d (max 69d)
  - Testicular reservoir in animal studies
- Vaginal fluid:
  - Median duration of RNA 14d (max 37d)

Counotte MJ, et al: PLOS Med July 24, 2018 doi:10.1371/journal pmen.1002611; Polen KD, et al: MMWR 2018;67:868-71;

Sexually transmitted Zika - USA

- 10 reported cases as of May 2016
  - Areas without endogenous mosquito transmission
  - Symptoms 8 d before to 10 d after return
  - All male to female
    - Onset 8 – 21 d after 1st sexual contact
    - Condomless sexual exposure:
      - 10 penile vaginal
      - 4 fellatio
      - 1 anal

Russell K et al: Clin Infect Dis 2017;64:211-3

Zika: homosexual transmission

Dallas, Texas

- Patient A:
  - I w visit to Venezuela, many cases of Zika present
  - 2 d after return: Fever, pruritic rash, conjunctivitis
  - 1 d before and 1 day after symptom onset, condomless insertive anal sex with Patient B
  - Semen RT-PCR equivocal
  - IgM positive
- Patient B
  - Day 7: fever, myalgia, headache, lethargy, rash, arthritis
  - IgM positive

Deckard DT, et al: MMWR 2016;65:372-4

Female to male transmission fo Zika

- Woman returns from Zika+ area to NYC
  - Condomless vaginal sex with man
  - Next day, develops signs and symptoms of Zika
  - Zika RNA in serum and urine
- Male partner
  - 7 days later: rash, joint pain, conjunctivitis
  - RT-PCR positive from serum and urine

Davidson A, et al: MMWR Morb Mortal Wkly Rep 2016;65:716–717

Zika: *Possible* oral sexual transmission

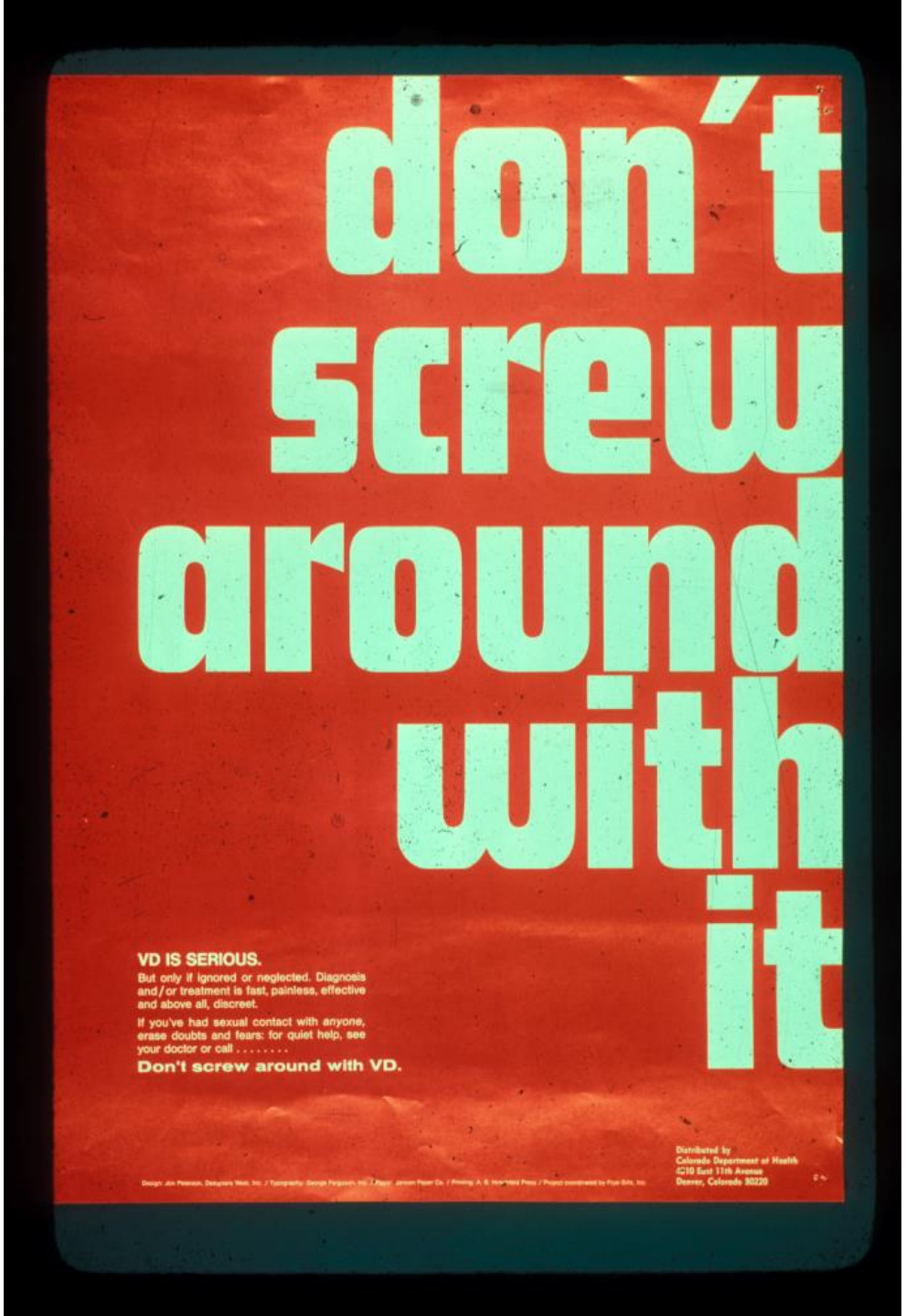
- Paris, France
- 46 yo man with symptoms while in Rio de Janeiro, resolved the day after his return
- Next 9 days: 7 sexual exposures to healthy woman
  - Oral sex without condom and with ejaculation
  - Vaginal: no condom but without ejaculation
  - Urine and semen positive for Zika
  - Saliva (10 days later) negative for Zika
- Woman experienced 7 days of illness
  - Positive for Zika in urine and saliva
  - Plasma and vaginal swabs negative
- No cases of transmission in which kissing the only contact

D'Ortenzio E, et al: New Eng J Med 2016;374:2195-98

CDC: Updated Guidance for Zika

- Men with infection or possible exposure
  - Planning to conceive: Abstain or use condoms ≥ 6 mo after sx or last possible exposure before unprotected sex
  - Not planning to conceive: Abstain or use condoms ≥ 3 mo after sex or last possible exposure before unprotected sex
- Women: No unprotected sex for 8 weeks after exposure

Polen KD, et al: MMWR 2018;67:868-71


don't
screw
around
with
it
VD IS SERIOUS.
But only if ignored or neglected. Diagnosis and/or treatment is fast, painless, effective and above all, discreet.
If you've had sexual contact with anyone, erase doubts and fears: for quiet help, see your doctor or call . . . . . .
Don't screw around with VD.
Distributed by
Colorado Department of Health
4210 East 11th Avenue
Denver, Colorado 80220