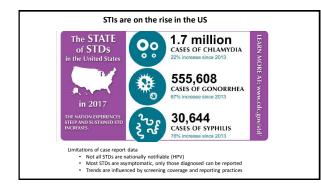
Sexually Transmitted Infections: Gonorrhea, Chlamydia, Trichomoniasis, and Human Papillomavirus

> Kimberly A. Workowski, MD Professor of Medicine Emory University School of Medicine Atlanta, Georgia

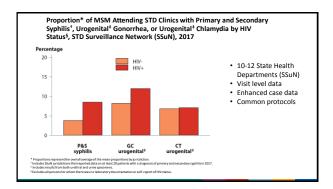
Learning Objectives

After attending this presentation, learners will be able to:

- Describe the current epidemiology of the most common STIs
- Identify current treatment recommendations for gonorrhea, chlamydia, trichomoniasis
- Describe the current trends in gonococcal antimicrobial resistance





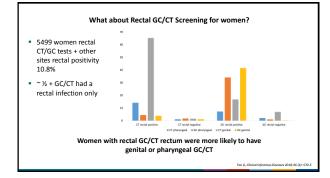


STI Testing during HIV care

- Initial care visit
 - Syphilis serology
- NAAT (gonorrhea, chlamydia) MSM (rectum, pharynx, urethra)
- Hepatitis A,B, C
- Women- Cervical pap test (HIV OI guidelines); Trichomonas (NAAT)
- Screening dependent on risk (3-6 mo)
 New sex partner, partner with concurrent partners or more than one partner, or partner with an STI

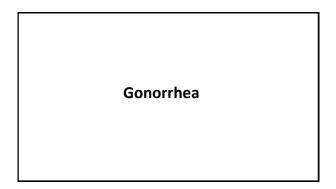
High risk behavior

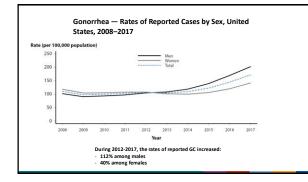
Partner services, prevention counseling

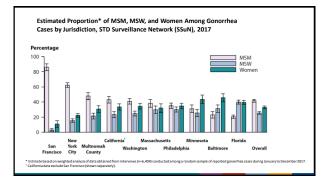


2015 Tre ent Guid nes, HIVMA 201











	Anatomic Site	Syndrome
Males	Urethra	Urethritis
	Epididymis	Epididymitis
	Pharynx	Asymptomatic, Nasopharyngitis
	Rectum	Asymptomatic, Proctitis
	Eye	Conjunctivitis
	Systemic	Disseminated Gonococcal Infection (DGI)
emales	Cervix	Cervicitis
	Fallopian tube	Salpingitis/Pelvic Inflammatory Disease
	Urethra	Urethritis
	Epididymis	Epididymitis
	Pharynx	Asymptomatic, Pharyngitis
	Rectum	Proctitis
	Eye	Conjunctivitis
	Systemic	Disseminated Gonococcal Infection (DGI)

Clinical Case—ARS Question 1

- 23 yo female G4P1
- Ankle swelling, pain, migratory polyarthritis, skin lesion left finger

What is the best method to make a diagnosis of DGI?

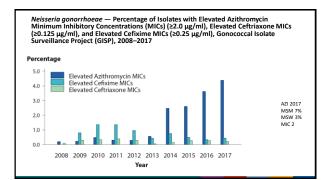
- 1. Joint aspiration
- 2. Blood culture
- 3. Lesion aspiration
- 4. Vaginal swab



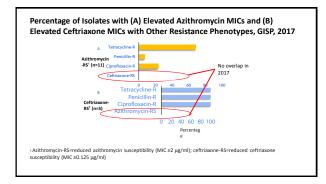
Disseminated Gonococcal Infection (DGI)

- Estimated to account for 0.5-3% of gonococcal infections
- Risk factors: female, menses, pregnancy, terminal complement
- deficiency
- Clinical presentation
 - Monoarticular arthritis
 - skin lesions (petechial or pustular) + tenosynovitis + polyarthralgia
 Perihepatitis, endocarditis, meningitis
- +Blood cx tenosynovitis/arthralgia > monoarticular arthritis
- Mucosal site infection often asymptomatic (NAAT)
- Antimicrobial susceptibility (AST) testing (culture)

Changing Patterns of DGI						Table 1 Epidemiologii characteristics of 21 Fre			iological	
						Years	2009	2010	2011	Total
						Patients (n)	2	9	10	21
						Epidemiological data				
DGLC	ases t	by Site	e in Al	BCs, 2	5 – 2017	Women	0	6	3	9 (43%)
						Men	2	3	7	12 (57%)
• Der	noars	nhice	. 12%	form	MSW 15.4%, Male 38%	MSM	1	1	3	5 (24%)
			427	reme	141344 13.470, 141816 3070	Median age (years) Paris area	54	20	35.5	30 10
 309 	6 >45	yrs				Paris area Other parts of France	2	4		10
						STI (excluding HTV)		2		
		GA-	GA-			STI (excuting miv) HIV infected		2	1	2 (9.5%)
		DPH*	MSA			Clinical data				\$ (4.3.9)
Year	CA	DPH-	IVISA	Total		loints	1	2	6	14 (56%)
2015	1		9	10		Knee	1	4	2	7
2016	0		5	5		Ebow	1	1	0	2
						Ankle	0	1	1	2
2017	1	3	7	11		Wrist	0	٥	2	2
Total	2	3	21	26		Hand	0	0	2	2
iotai	-	5		20		Кір	0	1	0	1
						TMJ	0	1	0	1
Site	Prop	ortion e	of DGI	Cases 1	eported GC Cases (in	Skin	1	0	3	4 (19%)
	Sun	eillance	Areal			Tenosynovitis	1	1	5	7 (33%)
_	_					Hands	1	•	1	2
CA	2/29	9,637 (0	0.007%)		Leg Four	0	1	2	3
GA-DPH*	3/9	770 (0.	031%)			Weigt	0		1	1
						Endocarditis	0			1(490
GA-MSA	21/2	29,323	(0.0729	%)		Genital signs		2	2	5 (23%)
Total	26/1	58,730	0 0 2 9 1	=)		Progatitis		1		1 (4%)
iotai	2070	36,730	(0.038.	5)		PID		1.1		1 (4%)
					Worker	Emerging ID		Belka	rem Sex T	rans infect 20:









Gonorrhea

- United States
- Ceftriaxone 250 mg IM in a single dose *PLUS*
- Azithromycin 1 g orally in a single dose
- United Kingdom Ceftriaxone 1 gram IM in a single dose
- Europe (European CDC)
- Ceftriaxone 500 mg IM in single dose PLUS
- Azithromycin 2 gm orally in a single dose
- Japan

Ceftriaxone 1 gm IV/IM in a single dose

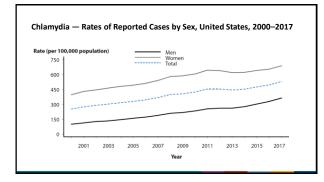
- Optimize therapeutic regimen
 - PK/PD (site of penetration) Concentration dependent vs independent
 - regimen
 Bacterial burden
 - Mutational frequency to resistance
- Resistance suppressive targets do not guarantee eradication
- Novel agents (Zoliflodacin, Gepotidacin) Treatment Failures
- Most apparent treatment failure likely due to reinfection
- If treatment failure suspect, obtain culture/susceptibility test + ensure partner treatment
- Dual therapy in UK (Fifer 2016)
 Ceftriaxone MIC of 0.5mg/L, azithromycin MIC of >256mg/L in UK, Australia (March 2018)

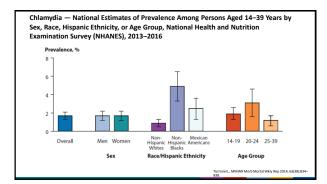
Alirol, PloS Med 2017

Global Antibiotic Research and Development Partnership

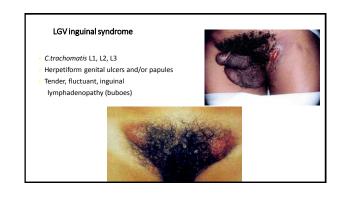
- Launched by WHO and Drugs for Neglected Disease Initiative in 2016
- Draft of acceptable GC target product profiles and timeline
- Research and Development plan
 - · Accelerate the development of a new clinical entity
 - Evaluate the potential of existing antimicrobials and combinations
 - Explore co-packaging and fixed dose combinations
 - · Development of simplified treatment guidelines

Chlamydia









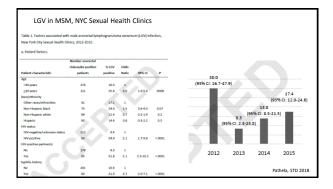
LGV Proctitis

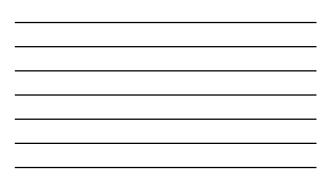
- MSM and women -+rectal chlamydia NAAT
- PCR based genotyping
- Protocolitis +/- perianal ulcersPresumptive tx (doxy 100 mg bid
- x 21 d)
- Painful perianal ulcers or mucosal ulcers presumptive therapy for HSV
- Short course therapy 7-14 d GUM clinic in UK (Simon, STD 2018)

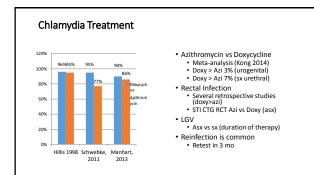


Notes from the Field: Cluster of Lymphogranuloma Venereum Cases Among Men Who Have Sex with Men — Michigan, August 2015–April 2016 Wexty/ systemies 2016 /659(3):2016

- 38 reports of LGV among MSM with HIV infection
- Median age 26 (19-60), median CD4 483 (270-1271)
- 21/38 confirmed by CDC (19 symptomatic proctitis, 2 penile ulcer)
- Concomitant infections
- 6/38 (16%) incident HIV
- 4/38 (11%) hepatitis C
- 6/38 (16%) syphilis
- 8/38 gonorrhea (8% oral, 13% rectal)







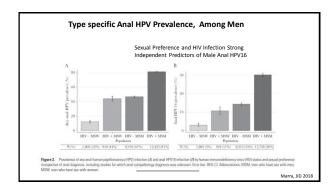
Human Papillomavirus

HPV Natural History

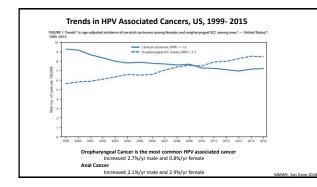
• HPV is the most common STI

- · The majority of sexually active people will become infected • Initially most persons have no symptoms
 - Ano-genital warts, low-risk (LR) HPV rarely cause cancer
- High-risk (16, 18) HPV infection may cause anogenital and oropharyngeal cancer

 - Most high risk HPV infection clears within 2 years Minority develop high-grade squamous intra-epithelial lesions
 - HSIL can progress to cervical cancer 1/80 per year



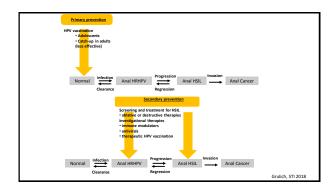






Women with HIV Aged <30 Years	
 A proop that ago 2, favore 11 also 410° takes more plasmost 48 MVL and assumpt active, screen within 1 year of most of its manual within application. The set of most of its manual within application. Henne with VVL ago 1-2: this has a the set of takes in a later displays. Henne with VVL ago 1-2: this has a later by 1 and 1 an	
Women with HTV Aged _30 Years	
Page Testing Dely:	
 Pag test should be done at backles and every 12 mosths (BB). Some experts recommend a Pag test of 8 mostles that (2010). If results of 12 mostles are constrained by test are constrained and page tables are backles to an be performed every 3 years (BB). 	
0r	
Page Text and HEV Co-Texting	
 Pop test and MPP cor builting totacids to show all baseline (BB). If show of the Pop test is normal and MPP contenting is negative, follow-up Pag test and MPP contesting can be performed every 3 years (BB). If the result of the Pop test is normal base MPP conducting is performed. 	
Ether	
Follow-up text with Pap text and HPV co-texting should be performed in 1 year. If the 1-year follow-up Pap text is abnormal or HPV co-texting is positive, whereal to opposcopy is recommended.	
0r	
"Instants HMP genetyping: If goalaws the PMP5 or IMP16, separate or water to recommended. If the fullow-up IMP1 test is positive or Pap test is atomical concerning in exercision and exercision.	
0r	
Pap Test and HPV16 or HPV16/18 Specified in Co-Testing	
 Pag test and HPV6 or 16/18 co-testing should be some at baseline (BB). If nearb of the Pag test is normal and HPV16 or 16/18 co-testing is negative, follow up Pag test and HPV co-testing can be prefitzment every 3 plens (BB). 	HIV OI Guidelines
 If initial test or follow up test is positive for HPV16 or 16/18, referral to colposcopy is recommended (BB). 	HIV OI Guidelines







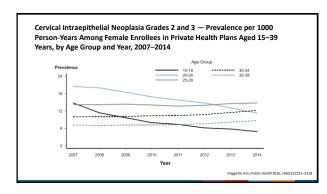
HPV Vaccine

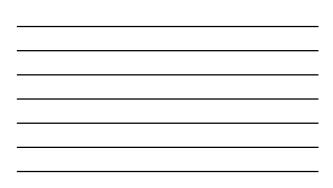
Nanovalent HPV Vaccine

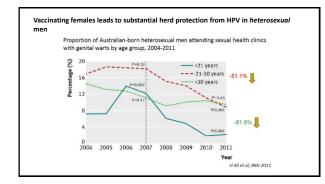
- Types 6, 11, 16, 18, 31, 33, 45, 52, 58
- FDA approved to prevent warts, cervical, vulvar, vaginal and anal cancer
 Mediativand Merality Weekly Report (MMMVR)

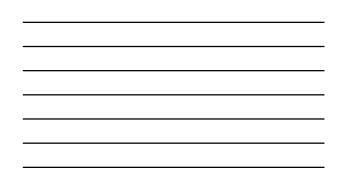
Use of a 2-Doire Schedule for Human Papillomavirus Vaccination — Updated Recommendations of the Advisory C on Immunization Practices Hereir Doorder 15.2051 (1989) 1495–1488

- 2 doses for males/females aged 9-14
- 3 doses for males/females aged 15-26
- Immunocompromised patients need 3 doses, regardless of age of initiation









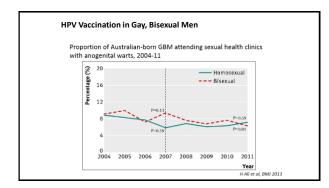




Table 2. Vaccine Efficacy Efficacy Population. ⁺	against HPV	/-6, 11, 16,	or 18-Relat	ed Anal Intra	epithelial No	roplasia (A	IN) and Ana	Cancer in t	he Per-Protocol
End Point	qHPV Vaccine (N=299)				Placebo (N = 299)				Observed Efficac (95% CI)?
	No. Included in Analysis	No. of Affected Partici- pants	Person-Yr at Risk	Events per 100 Person-Yr at Risk	No. Included in Analysis	No. of Affected Partici- pants	Person-Yr at Risk	Events per 100 Person-Yr at Risk	
									percent
By lesion type									
AIN grade 1	194	- 4	383.1	1.0	208	16	413.8	3.9	73.0 (16.3 to 93.4)
Condyloma acuminatum	194	0	386.8	0.0	208	6	418.2	1.4	100 (8.2 to 100)
Flat lesion	194	4	383.1	1.0	208	11	416.7	2.6	60.4 (-33.5 to 90.8)
AIN grade 2 or 3	194	3	383.9	0.8	208	13	417.2	3.1	74.9 (8.8 to 95.4)

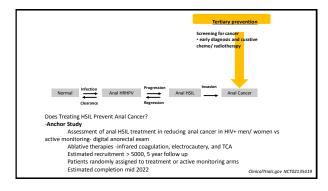


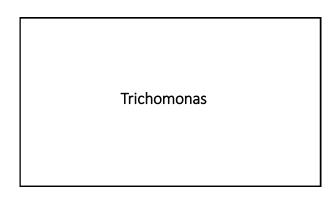
HPV Vaccination in HIV+ Adults >27 yrs

Table 2. Vaccine Efficacy for Persistent Anal Infection, Persistent Oral Infection, Anal High-Grade Squamous Intraepithelial Lesions on Anal Biopsy, and Abnormal Anal Cytology

Endpoint	Vao	Vaccine Group		trol Group	Efficacy (95.1% Confidence Interval
Persistent anal infection	n	Endpoint	n	Endpoint	
mITT-including single detection at final visit	286	27	283	33	22% (-31% to 53%)
mITT-persistent infection only	286	14	283	17	21% (-61% to 61%)
Per protocol analysis	276	7	277	10	31% (-82% to 74%)
Full ITT	288	28	286	41	35% (-5% to 60%)
Persistent oral infection					
mITT-including single detection at final visit	288	7	286	10	32% (-80% to 74%)
mITT-persistent infection only	288	1	286	8	88% (2% to 98%)
Per-protocol analysis	278	1	280	3	66% (-70% to 96%)
Full ITT	288	6	286	14	58% (-9% to 84%)
Improvement of anal high-grade squamous intraep	ithelial lesions o	n anal biopsy outcome	os ^a		
Full ITT	288	46	286	45	0% (-44% to 31%)
Abnormal anal cytology					
Week 52	231	123 (53%)	229	121 (53%)	0% (-19% to 16%)
Week 104	199	98 (49%)	198	108 (55%)	9% (-10% to 25%)
Week 156	130	58 (45%)	132	72 (55%)	17% (-6% to 35%)

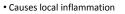




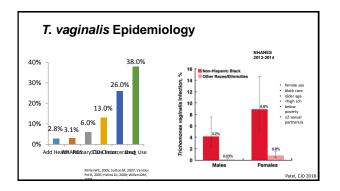


Trichomonas vaginalis

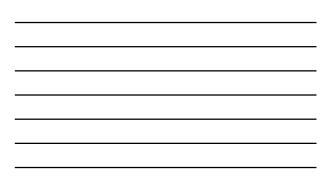
- Adheres to epithelial cells Male or female urethra • Female vagina, vulva



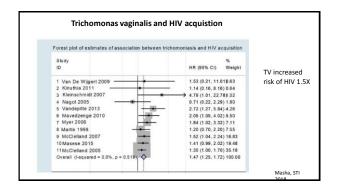
- Variable spectrum of disease
 - 70–85% of women and 77% of men are asymptomatic
 - Vaginitis, urethritis, prostatitis
 - Associated with increased susceptibility to other STIs (HIV), adverse pregnancy outcomes, low birth weight

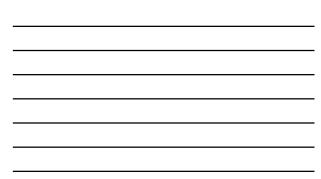


Infection		Prevalence, % (95%	Crude	Advand	Adjusted	
	Overall	Non-Hispanic Black	Other Races/Ethnicities	PR (95% CI)	Adjusted PR (95% CI)*	PR (95% CI) ^b
Males and females						
TV infection	1.2 (.6-2.1)	7.0 (4.4-11.1)	0.3 (.1-1.0) ^c	23.7 (7.2-78.1)	16.8 (5.4-52.7)	10.6 (2.9-38.7
CT infection	2.0 (1.3-3.0)	5.4 (3.7-7.9)	1.5 (.8-2.8)	3.6 (1.6-8.0)	2.6 (1.1-6.3)	2.1 (.8-5.4)
HSV-2 serostatus	10.7 (8.8-13.1)	31.3 (26.9-36.2)	8.0 (6.2-10.2)	3.9 (3.0-5.2)	3.8 (2.8-5.1)	3.8 (2.7-5.4)
Genital HPV infection	43.6 (39.0-48.2)	67.2 (60.3-73.5)	40.1 (35.4-45.0)	1.7 (1.4-2.0)	1.7 (1.4-2.0)	1.5 (1.3-1.7)
Males						
TV infection	0.3 (.19)°	2.7 (.9-7.9)°	0.0 ^d			
CT infection	1.8 (1.1-3.0)	5.4 (3.2-8.9)	1.3 (.6-2.9)*	4.0 (1.5-10.6)	3.8 (1.3-10.8)	2.3 (.6-8.6)
HSV-2 serostatus	7.2 (5.5-9.3)	20.9 (15.4-27.8)	5.5 (3.9-7.8)	3.8 (2.4-5.8)	3.9 (2.6-5.9)	3.5 (2.0-6.0)
Penile HPV infection	42.3 (37.5-47.2)	69.5 (61.1-76.7)	38.6 (33.4-44.0)	1.8 (1.5-2.2)	1.8 (1.6-2.1)	1.6 (1.3-1.9)
Females						
TV infection	2.0 (1.1-3.5)	10.5 (6.8-16.0)	0.6 (.2-2.0) ^e	17.6 (4.6-67.1)	14.0 (3.9-50.2)	8.3 (1.9-35.4)
CT infection	2.2 (1.4-3.4)	5.4 (3.2-9.1)	1.7 (.9-3.1)	3.2 (1.4-7.4)	2.0 (.9-4.4)	1.8 (.9-3.6)
HSV-2 serostatus	14.3 (11.1-18.1)	39.8 (34.9-45.0)	10.5 (77-14.2)	3.8 (2.7-5.4)	3.7 (2.7-5.2)	4.0 (2.8-5.7)
Vaginal HPV infection	44.8 (39.6-50.1)	65.3 (57.0-72.7)	41.6 (36.4-47.0)	1.6 (1.3-1.9)	1.5 (1.2-1.8)	1.4 (1.2-1.7)



• Single-celled protozoan parasite





Trichomonas

- Screen at initial visit HIV+ (NAAT)
- Rx: Metronidazole HIV+ 500 mg bid x 7 days (Kissinger, 1999)
- Options to Nitroimidazoles
- Single agent vs Combination therapy
- Intravaginal- paromomycin, boric acid
- Secnidazole
- Clinical treatment failure Re-infection, Nonadherence
 Antimicrobial resistance
- Retesting 3 months after treatment Management of persistent
- infection Up to 17% at 3 months Reinfection from untreated
- partner is common Infection with MTZ-resistant
- strain: ~4-10% Tinidazole-resistant ~1%
 No clear relationship to clinical
- treatment failure
- Susceptibility testing if resistance



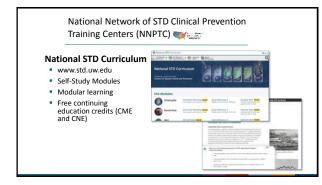


National Network of STD Clinical Prevention Training Centers (NNPTC)



- Clinical Training and Consultation Network

 Visit: www.STDCCN.org.
- Resources and tools for STD treatment
- STD Clinical Toolbox App
- Visit: www.nnptc.org





Sexually Transmitted Infections: Gonorrhea, Chlamydia, Trichomoniasis, and Human Papillomavirus

Kimberly A. Workowski, MD

SUGGESTED READINGS

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