STIs 103:
Epididymitis and Proctitis/Proctocolitis

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Disclosures

- The author and their spouses/partners wish to disclose they have no financial interests or other relationships with the manufacturers of commercial products, suppliers of commercial services, or commercial supporters.

PTC Disclaimer

Some terms in this presentation may have been modified to align with executive order requirements that this CDC-funded grant has received.

Objectives

- Briefly review the differential and workup for genital ulcer disease
- Describe genital herpes presentation and epidemiology
- Discuss HSV diagnosis, treatment strategies, and transmission prevention

Upstream Consequences

Josh is a 54M presenting with 3 days of testicular pain and swelling

- Onset over the course of a day, no preceding trauma
- + dysuria, no urethral discharge
- PMH: HTN, DM2 on metformin and empagliflozin, PrEP. No allergies
- MSM, insertive and receptive anal sex, gives and receives oral sex. 2 partners in last 6 months, uses condoms with new partners, not primary partner

Physical Exam

- R-sided scrotal erythema and swelling
- R testicle in normal vertical position
- Exquisitely tender with palpable localized swelling along posterior aspect and in spermatic cord
- Cremasteric reflex intact

Epididymo-Orchitis

Prostate gland
Ductus (vas) deferens
Suspensory ligament of penis
Urinary bladder
Pubic symphysis
Corpus cavernosum
Corpus spongiosum
External urethral opening
Ampulla of ductus deferens
Seminal vesicle
Ejaculatory duct
Prostatic urethra
Deep muscles of perineum
Bulbourethral gland
Muscles of perineum surrounding anus
Membranous urethra
Spongy urethra
Testis
Epididymis
Scrotum

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Epididymitis/Epididymo-Orchitis - Presentation

- Symptoms:
  - Unilateral testicular pain/swelling.
  - Onset typically acute, sometimes chronic, but not sudden.
  - Concurrent dysuria is typical
- Exam: hydrocele, swelling and tenderness of epididymis/testis (tail -> head -> testicle) and spermatic cord
  - Testicle in normal position (not horizontal)

What is the Most Likely Culprit?

Choose all that apply

A. Enteric bacteria (*E. coli, Proteus*)

B. Testicular torsion

C. *N. gonorrhea/C. trachomatis*

D. Trauma/contusion

E. *M. genitalium*

What Workup Will We Send for Josh?

Urine gonorrhea/chlamydia NAAT

UA with microscopy and reflex culture

Comprehensive STI testing

Epididymitis: Ddx by Age* and Acuity

- **Acute (<6 weeks)**
  - STI: N. gonorrhea, chlamydia, Mgen
    - Younger***, sexually active
  - Enteric pathogens: E coli, etc
    - Older***, urinary obstruction or instrumentation, insertive anal sex

- **Chronic**
  - Infections: MTB
  - Post-infectious pain
  - Drug-induced: amiodarone
  - Inflammatory: Behcet's

Hyperacute/sudden onset: don't forget to consider testicular torsion!

What is the Most Likely Culprit?

Choose all that apply

A. Enteric bacteria (*E. coli, Proteus*)

B. Testicular torsion

C. *N. gonorrhea/C. trachomatis*

D. Trauma/contusion

E. *M. genitalium*

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What Treatment Should We Start for Josh?

A. CTX 500 mg x 1 + doxycycline 100 mg BID x 7 days

B. CTX 500 mg x 1 + levofloxacin 500 mg daily x 10 days

C. Levofloxacin 500 mg daily x 10 days

D. CTX 500 mg + doxycycline 100 mg BID x 7d + levofloxacin 500 mg daily x 10d

E. No treatment, wait for results of testing

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What Treatment Should We Start for Josh?

A. CTX 500 mg x 1 + doxycycline 100 mg BID x 7 days
   - Sexually active, no risk for enteric pathogens (no insertive anal sex, no history or suspicion of urinary tract obstruction/instrumentation)

B. CTX 500 mg x 1 + levofloxacin 500 mg daily x 10 days
   - Sexually active ***with*** risk for enteric pathogen

C. Levofloxacin 500 mg daily x 10 days
   - Not sexually active (alt TMP-SMX 1 DS tab BID)

D. CTX 500 mg + doxycycline 100 mg BID x 7d + levofloxacin 500 mg daily x 10d
   - Duplicates therapy for chlamydia

E. No treatment, wait for results of testing
   - Empiric treatment recommended while awaiting results

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Josh's Test Results

Work-up:

Urine gonorrhea/chlamydia NAAT (-)

UA with microscopy and reflex culture: Proteus vulgaris, pan-susceptible

Comprehensive STI testing (-)

Follow Up/Supportive Care

- Tailor antibiotics to urine culture/NAATs
- Scrotal elevation, NSAIDs
- Counsel regarding potential for prolonged time to resolution of discomfort (up to weeks)
- Follow up testing for negative results with persistent symptoms (e.g. Mgen NAAT, urology referral)

What's New in Epididymitis?

Treatment of Acute Epididymitis: A Systematic Review and Discussion of the Implications for Treatment Based on Etiology

Louette, Aaron[*]; Krahn, Jessica[*]; Caine, Vera PhD[*]; Ha, Shalane MSc[†]; Lau, Tim T. Y. PharmD[‡]; Singh, Ameeta E. BMBS, MSc[§] Author Information

Sexually Transmitted Diseases

December 2018 , Volume 45 (12), p e104 – e108

- Systematic review of evidence around treatment of epididymitis from 2006-2017
- Included all experimental and observational studies that described etiology and treatment (French/English)
- **1 study met inclusion criteria**
- Retrospective review from 2 STI clinics in Ottowa of epididymitis due to G/C
- 57 patients, 42 chlamydia, 9 gonorrhea, 6 co-infection
- 2 NG treatment failure, no elevated MIC

Digging Into Etiology

European Urology
Volume 68, Issue 3, September 2015, Pages 428-435

Platinum Priority – Infections
Editorial by Jean-Nicolas Cornu and Franck Bruyère on pp. 436–437 of this issue

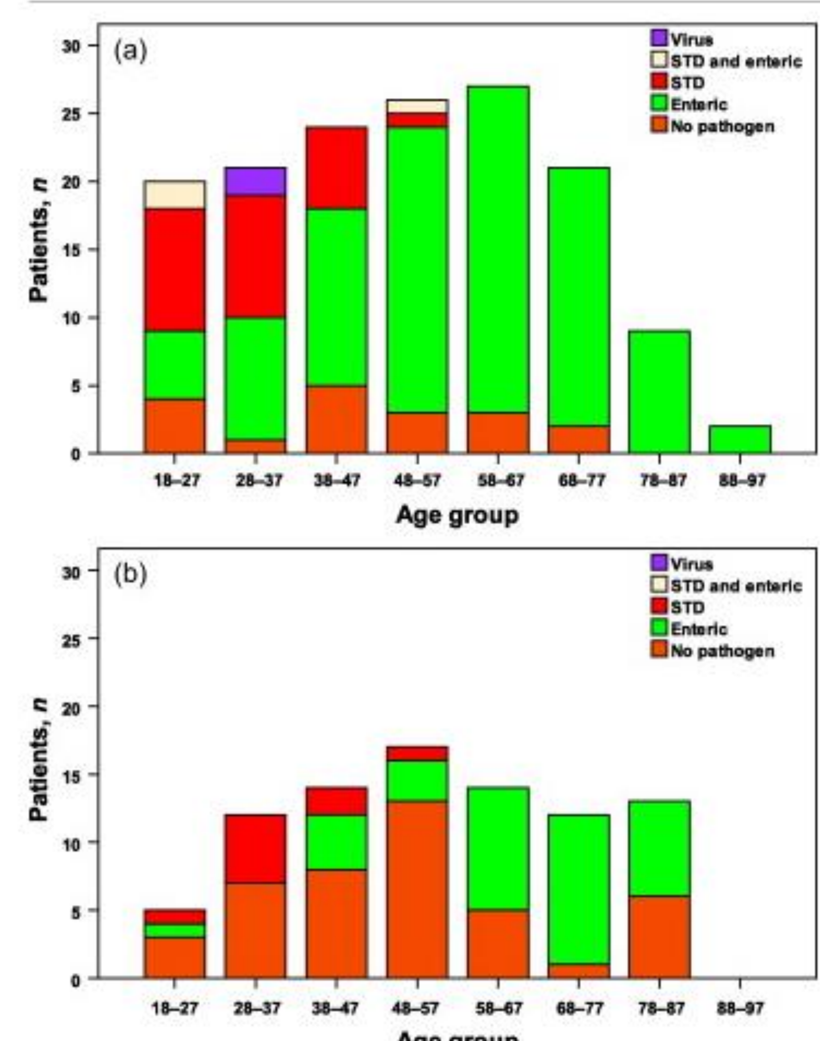
Acute Epididymitis Revisited: Impact of Molecular Diagnostics on Etiology and Contemporary Guideline Recommendations

Adrian Pilatz [a], Hamid Hossain [b], Rolf Kaiser [c], Annette Mankertz [d], Christian G. Schüttler [e], Eugen Domann [b], Hans-Christian Schuppe [a], Trinad Chakraborty [b], Wolfgang Weidner [a], Florian Wagenlehner [a]

- 2007-2013 137 patients with acute epididymitis
    - Compared 150 antibiotic-naïve, 87 pre-treated
- All with cultures, STI testing (if sexually active), 16s rDNA analysis if cx neg, and multiplex viral PCR if no other +
- Median age 50s, 55 vs 59% sexually active

Digging into Etiology (Cont.)

STI-PCR in all sexually active patients	*n* = 89	*n* = 48
Chlamydia trachomatis, *n*	20	5
Mycoplasma spp, *n*	7	1
Neisseria gonorrhoeae, *n*	2	4
Sexually active patients with positive STI, *n*	28	9[†]
Patients with negative culture and negative STI-PCR, *n*	29	57
16S rDNA analysis in culture- and STI-negative patients	*n* = 29	*n* = 57
Escherichia coli, *n*	0	8
Proteus spp, *n*	0	2
Staphylococcus epidermidis, *n*	0	1
Aerococcus spp, *n*	0	1
Propionibacterium spp, *n*	0	1
Haemophilus spp, *n*	5	1
Lactobacillus spp, *n*	2	0
Bacteroides spp, *n*	1	0
Eubacterium spp, *n*	1	0
Patients with positive 16S rDNA analysis, *n*	9	14[‡]



Epididymitis/Epididymo-Orchitis Take-Home

- Onset is acute, but not sudden (don't forget torsion!)
- Unilateral, often (but not always) with dysuria. Pain/swelling of epididymis +/- testicle
- DDx:
  - STI: GC, CT, Mgen
  - Enteric: E coli, Klebsiella, etc.
  - Others: H flu, enteroviruses?
- Testing: Urine G/C NAAT +/- Mgen NAAT, UA with microscopy and culture
- Treatment: add levofloxacin instead of doxy to CTX if suspicion for enteric + STI
- NSAIDs/scrotal elevation -- symptom resolution may be slow

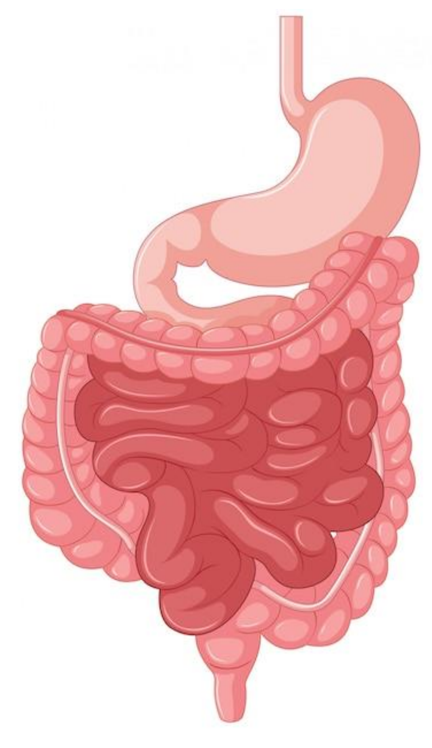
Questions?

Getting To The Bottom Of It

- 26 M presents with 2 days of rectal pain
- Notes associated tenesmus, mucoid/bloody anal discharge, and recently constipation with mild fevers
- PMH: no medical problems, no medications, no allergies
- Sexual hx: 10 cis-male partners in last 6 mo. Receptive anal, gives and receives oral. Does not use condoms. Hx syphilis, gonorrhea.
- Exam: Ill-appearing. Peri-anal skin mildly erythematous/tender, no ulcer, no fissure

Proctitis, Proctocolitis, Enteritis

- Proctitis: inflammation of rectum
  - Rectal pain
  - Tenesmus (persistent urge to defecate)
  - Rectal/anal discharge
- Proctocolitis: inflammation extending to colon
  - Often diarrhea and abdominal cramps
- Enteritis: inflammation of small bowel
  - Diarrhea and abdominal cramping without proctitis symptoms



Epidemiology

- People who have receptive anal sex
- Largely MSM
- Some implicated agents can cause outbreaks, especially in diarrheal presentations (proctocolitis, enteritis)

What Workup Would You Send for Jorge?

Choose all that apply

- A: Rectal GC/CT NAAT
- B: RPR
- C: HSV-1/HSV-2 lesion PCR
- D: Mpox PCR
- E: Stool culture
- F: Multiplex diarrhea PCR

Proctitis Differential

- Proctitis:
  - GC, CT, HSV, syphilis are most common (with mpox as a newer addition)
- Proctocolitis
  - LGV serovars of CT, Campylobacter, Shigella, syphilis. CMV among immunocompromised
- Enteritis
  - Shigella, Campylobacter, Cryptosporidium, microsporidia, Salmonella, Giardia
    - Outbreaks of first 4 have been described among MSM

What Workup Would You Send for Jorge?

Choose all that apply

- A: Rectal GC/CT NAAT
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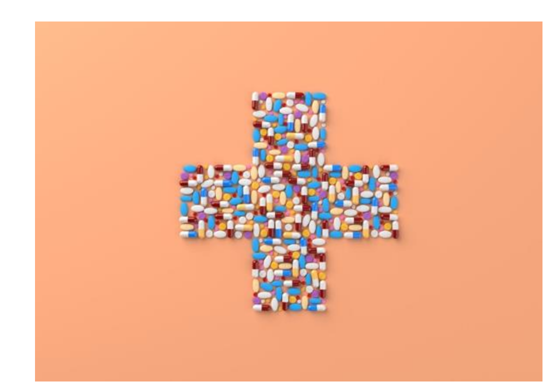
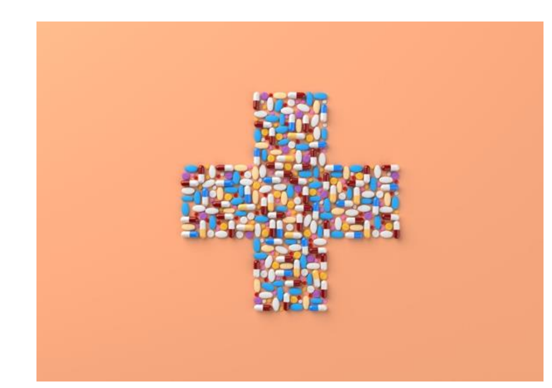
Would You Offer Jorge Any Treatment?



Choose all that apply

- A: Doxycycline 100 mg BID x 14 days
- B: Ceftriaxone 500 mg IM x 1 + doxycycline 100 mg BID x 7 days
- C: Valacyclovir 1 g BID x 7-10 days
- D: Levofloxacin 500 mg daily x 10 days
- E: Loperamide 4 mg, then 2 mg after each loose stool

Would You Offer Jorge Any Treatment?



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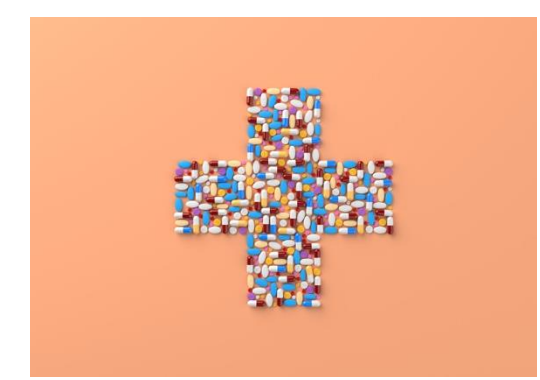
- E: Loperamide 4 mg, then 2 mg after each loose stool

Jorge's Results

- A: Rectal GC/CT NAAT: Chlamydia +
- B: RPR: non-reactive
- C: HSV-1/HSV-2 lesion PCR: negative
- D: Mpox PCR: negative
- E: Multiplex diarrhea PCR: negative

Would You Change Jorge's Treatment?



Choose all that apply

- A: Nope
- B: Change to levofloxacin 500 mg daily x 10 days
- C: Change to azithromycin 1 gram
- D: Extend doxycycline course to 21 days

Lymphogranuloma venereum (LGV)

- *C. trachomatis* serovars L1-3
- Historically: heterosexual individuals in East/West Africa, India, SEA, Caribbean
  - ”classic” genital ulcers, inguinal lymphadenopathy
- More recently: developed countries, MCM
  - Proctitis and proctocolitis
  - Crampy pain/tenesmus, rectal bleeding, rectal ulcers (not visible externally), systemic symptoms

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- Bradley P. Stoner, Stephanie E. Cohen, Lymphogranuloma Venereum 2015: Clinical Presentation, Diagnosis, and Treatment, *Clinical Infectious Diseases*, Volume 61, Issue suppl_8, December 2015, Pages S865–S873

LGV Continued

- Dx: Serovar-specific PCRs not widely available
  - CLINICAL

CDC Guidelines:

"Doxycycline course should be extended to 100 mg orally 2 times/day for 21 days in the presence of bloody discharge, perianal or mucosal ulcers, or tenesmus and a positive rectal chlamydia test."

Proctitis Take-Home

- Symptoms vary based on location of inflammation:
  - rectum (proctitis), rectum + large bowel (proctocolitis), or small bowel only (enteritis)
- Differential depends on symptoms--includes typical STIs, diarrheal pathogens, viral pathogens
- Empiric tx: CTX 500 mg x 1 + doxycycline 100 mg BID x 7 days
- If visible external ulcers: add HSV antiviral tx
- For rectal chlamydia with more severe sxs: doxy x 21 days for LGV
- In addition to treating infection, remember to provide good supportive care with analgesia +/- stool softeners +/- sitz baths!