A Pain in the Rectum

Case Conference

Megan Alexander, PA-C
Southeast AETC
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AETC AIDS Education & Training Center Program Southeast

Disclosures

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AETC Program National Centers and HIV Curriculum

- **National Coordinating Resource Center –** serves as the central web –based repository for AETC Program training and capacity building resources; its website includes a free virtual library with training and technical assistance materials, a program directory, and a calendar of trainings and other events. Learn more: https://aidsetc.org/
- **National Clinician Consultation Center –** provides free, peer-to-peer, expert advice for health professionals on HIV prevention, care, and treatment and related topics. Learn more: https://nccc/ucsf.edu
- **National HIV Curriculum –** provides ongoing, up –to-date HIV training and information for health professionals through a free, web –based curriculum; also provides free CME credits, CNE contact hours, CE contact hours, and maintenance of certification credits. Learn more: www.hiv.uw.edu

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Learning Objectives

- *Develop differential diagnosis for outpatient case.*
- *Identify pertinent patient history and important components for diagnosis of [mystery illness].*
- *Indicate pathophysiology and epidemiology of [mystery illness].*
- *Report diagnosis and treatment considerations of [mystery illness].*
- *Outline benefits and limitations of Doxy PEP.*

Meet our patient

40-year-old male who presents to clinic for primary care follow up. On an ART regimen for 5 years with fair to moderate adherence. Today he reports not taking medication for past month while hosting company.

Chief Complaint: “I’ve seen blood in the toilet for two weeks.”

Acute concern

- Intermittent rectal bleeding x2 weeks - bright red blood
- Painful bowel movements (tenesmus)
- Eating less to reduce stooling - lost 12lbs in two weeks
- Endorses some abdominal fullness and constipation

Patient history

Medical History

- HIV
- LSIL on anal pap
- Essential hypertension
- Seizure disorder
- Anxiety/Depression
- Alcohol Use Disorder

Surgical History

- Wisdom tooth extraction
- Anoscopy- identified anal lesions consistent with HPV

Medication List

- Amlodipine 5mg daily for hypertension
- Levetiracetam 500mg daily for seizure disorder
- Sertraline 50mg daily for depression/anxiety
- Hydroxyzine 25mg TID PRN for anxiety
- Darunavir 800mg daily for HIV
- Elvitegravir-cobicistat-tenofovir-emtricitabine daily for HIV

Sexual history
In the past 3 months….

- Partners: multiple; cisgender males
- Practices: anal receptive, anal insertive, oral intercourse
- Protection: sporadic condom use
- Past STI history: Primary syphilis s/p IM Benzathine-LA
- Pregnancy intention: Partners do not have uteruses

Differential?

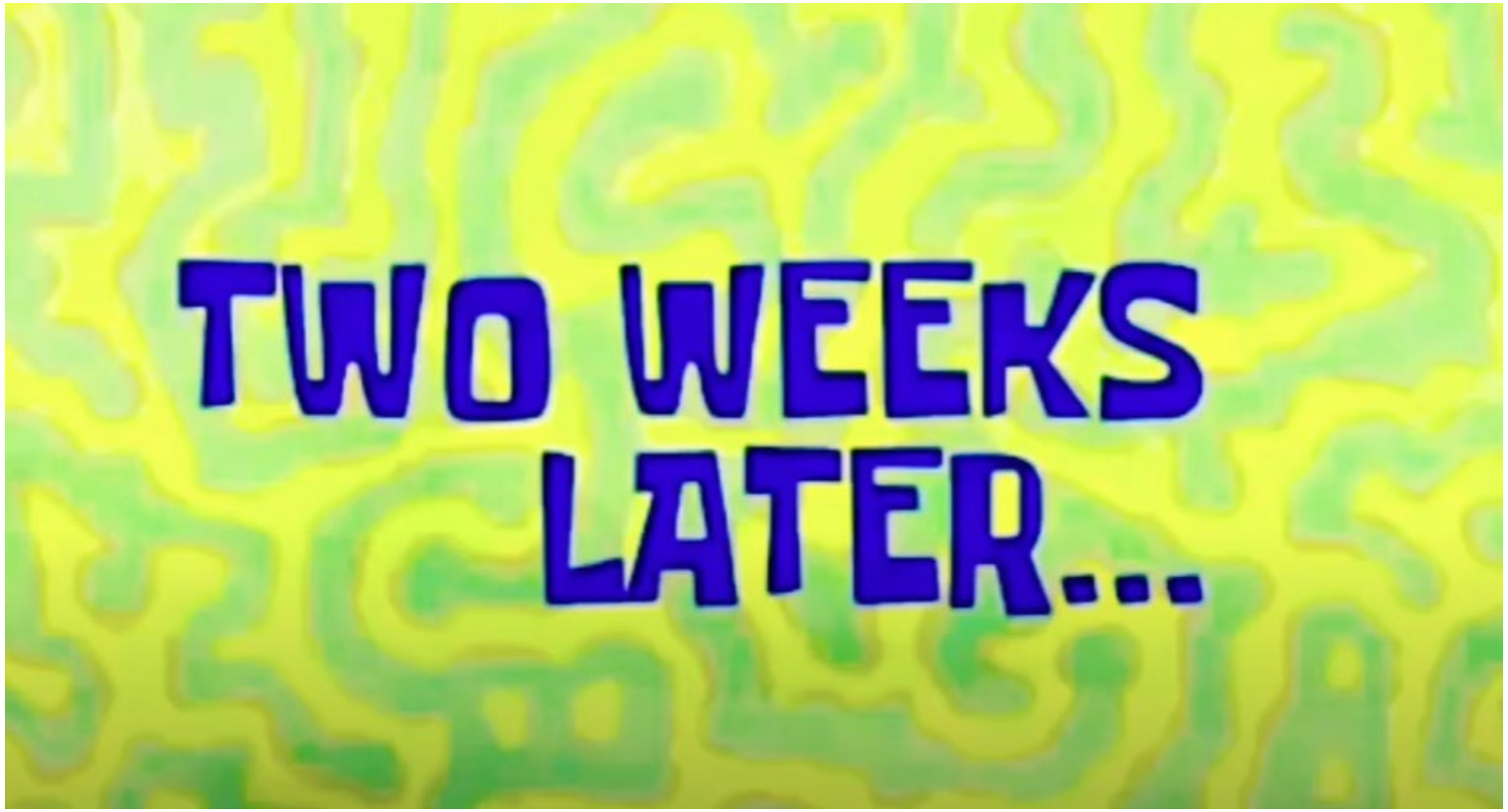
- HPV
- Mpox
- Proctitis
- Gonorrhea
- Chlamydia
- Syphilis
- HSV
- Anal fissure
- Hemorrhoid(s)
- IBD
- Anal malignancy

What would you like to order?

Outpatient interventions

- DRE: normal
- Constipation treatment: psyllium and polyethylene glycol
- Urgent referral to colorectal surgery
- Labs ordered: CBC, CMP, HIV Viral load, Lymphocyte enumeration panel
  - STI Screening: RPR, NG x 3 sites, CT x 3 sites

Patient unfortunately did not complete labs after visit.


TWO WEEKS
LATER...

Patient presents to ED

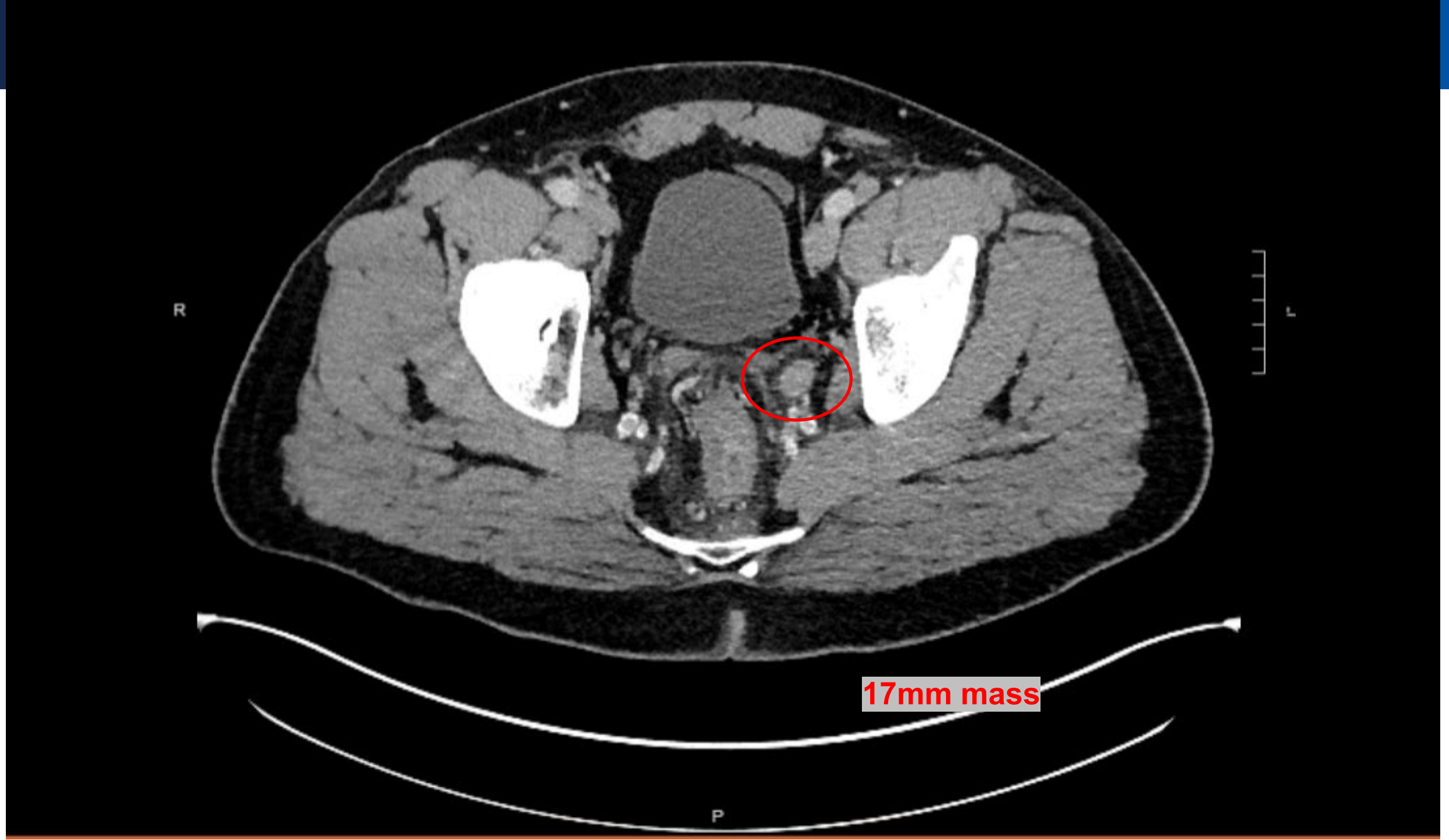
- Continued concerns of rectal bleeding.
- Now having loose BMs 5-6x daily.
- Endorses use of stool softeners and primarily liquid diet.

ED Course

WBC Count	3.70 - 10.30 10*3/uL	9.90
RBC Count	4.60 - 6.10 10*6/uL	4.72
HGB	13.7 - 17.5 g/dL	13.7
HCT	40.0 - 51.0 %	41.5
Platelet Count	155 - 369 10*3/uL	287
MCV	79 - 98 fL	88
MCH	26.0 - 32.0 pg	29.0
MCHC	30.7 - 35.5 g/dL	33.0
RDW	11.5 - 14.5 %	13.2
MPV	8.8 - 12.5 fL	9.1
nRBC	<=0.0 per 100 WBCs	0.0

Glucose, Plasma	74 - 99 mg/dL	86
BUN, Plasma	7 - 21 mg/dL	5 ↓
Creatinine, Plasma	0.80 - 1.30 mg/dL	0.71 ↓
BUN/Creatinine Ratio		7
Sodium, Plasma	136 - 145 mmol/L	136
Comment: na abl		
Potassium, Plasma	3.7 - 4.8 mmol/L	6.6 ↑↑
Comment: Hemolyzed		
Chloride, Plasma	97 - 107 mmol/L	102
CO2, Plasma	22 - 29 mmol/L	22
Anion Gap	6 - 16 mmol/L	12
Total Calcium, Plasma	8.9 - 10.2 mg/dL	8.7 ↓
Total Protein	6.3 - 7.9 g/dL	8.8 ↑
Albumin, Plasma	3.5 - 5.2 g/dL	3.4 ↓
AST, Plasma	10 - 50 U/L	70 ↑
Comment: Hemolyzed		
ALT, Plasma	10 - 50 U/L	21
Comment: Hemolyzed		
Alkaline Phosphatase, Plasma	40 - 115 U/L	85
Comment: Hemolyzed		
Total Bilirubin, Plasma	0.2 - 1.1 mg/dL	0.7
eGFRcr	mL/min/1.73m*2	118.9

No acute anemia, labs hemolyzed- otherwise not requiring intervention


R
L
17mm mass
P

ED Course (cont.)

CT A/P Impression:

1. Sequela consistent with proctitis with reactive lymphadenopathy.
2. Nonspecific enhancing mass in the left internal iliac chain. This may represent pseudoaneurysm of the adjacent internal iliac artery or abnormally enhancing lymph node.

Patient self-directed discharge from ED due to anxiety.

1 week later….

Colorectal surgery appointment

- Reassured patient for no discrete masses noted on CT
- Proceeded with anoscopy
  - Noted to have purulence of the anal canal but no evidence of ulcerations
- Recommended to proceed with colonoscopy to identify cause of proctitis

Revisit to clinic

- Tearful on exam, with continued intermittent rectal bleeding and pain.
- Offered support for mental health with behavioral health counseling and increased dose of sertraline - patient declined both, focused on resolution of symptoms.

Lab results

HSV PCR (rectal swab): negative

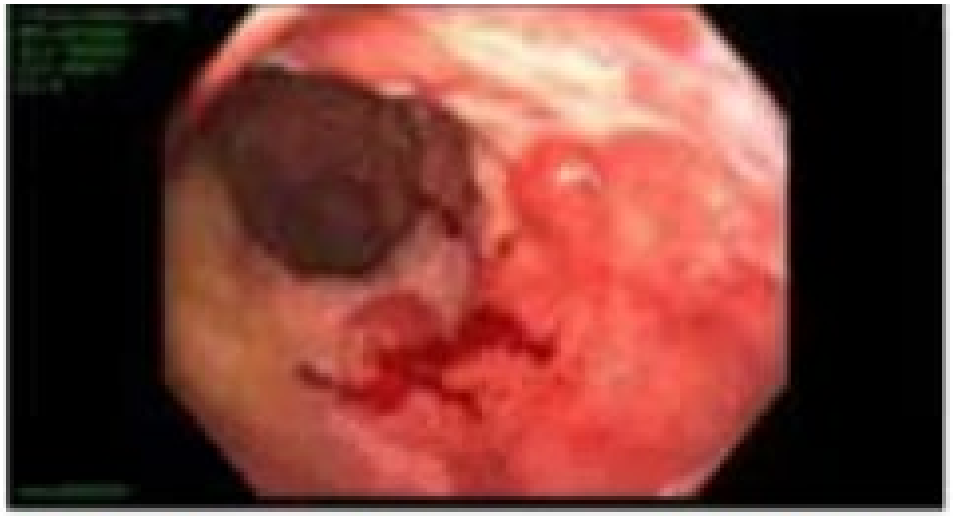
Neisseria gonorrhea DNA PCR (rectal swab): negative

Chlamydia trachomatis DNA PCR (rectal swab): positive

Treatment

Doxycycline 100mg BID x 7 days for rectal chlamydia infection

Colonoscopy



Erythematous and friable mucosa; Rectum

Surgical pathology results

Colorectal mucosa histology: “ulceration, granulation tissue and associated acute inflammation”

Immunohistochemical stains:

GMS: Negative for fungal organisms.

T. Pallidum (Spirochete): Negative.

Herpes Simpex I&II: Negative.

CMV: Negative.

Back to clinic

Endorses improvement of symptoms

More labs completed…

Lymphogranuloma venereum antibody

C. Trachomatis (L1) IgG	>=1:1024	C. Pneumoniae IgG	1:64
C. Trachomatis (L1) IgA	1:128	C. Pneumoniae IgA	1:16
C. Trachomatis (L1) IgM	<1:10	C. Pneumoniae IgM	<1:10
C. Trachomatis (D K) IgG	>=1:1024	C. Psittaci IgG	<1:64
C. Trachomatis (D K) IgA	<1:16	C. Psittaci IgA	<1:16
C. Trachomatis (D K) IgM	<1:10	C. Psittaci IgM	<1:10

Lymphogranuloma Venereum

- Ulcerative STI caused by Chlamydia Trachomatis serovars L1, L2, L3
- Can cause more severe, invasive infection than C Trachomatis serovars D-K
- Traditionally seen in tropical/subtropical regions: India, Africa, Southeast Asia, and the Caribbean region
- Increasing number of cases have been reported since 2004 in western Europe and North America. These outbreaks have been associated with MSM and HIV.

Epidemiology

- Globally, LGV is estimated to affect males and female equally, though is more frequently associated in males because of earlier manifestations.
- In North America, disproportionately affects MSM community.
- Prevalence of HIV among LGV cases is estimated to be 67-100%.

Pathophysiology

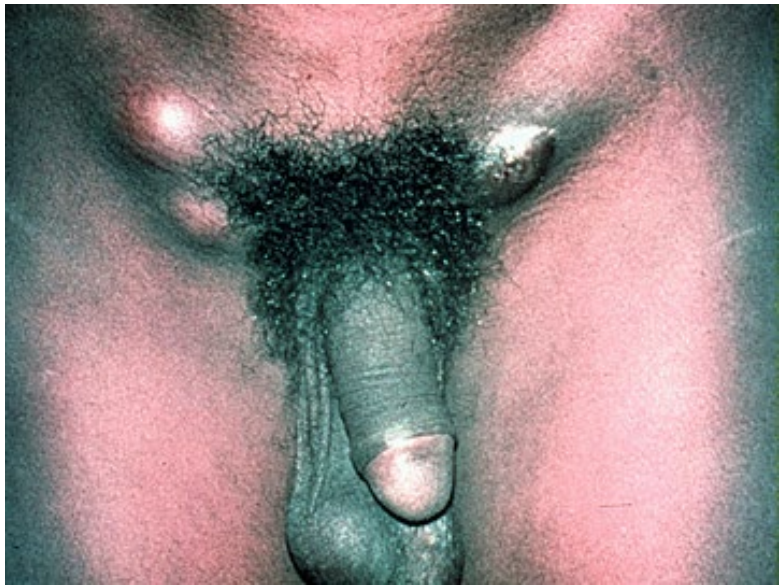
- LGV infects lymphatic tissue
- Chlamydia serovars D-K primarily limited to mucosal tissue, serovars L1-L3 thought to travel to lymph system via lymphatic drainage of the primary infection site.
- Once the lymphatic tissue is inoculated, areas of necrosis can occur in the lymph nodes, causing abscesses.

Primary stage

- Occurs 3-12 days after exposure
- Painless ulcer at site of inoculation (mouth or genitals)
- Lesions often go unnoticed
- Self-resolves within days

Secondary stage

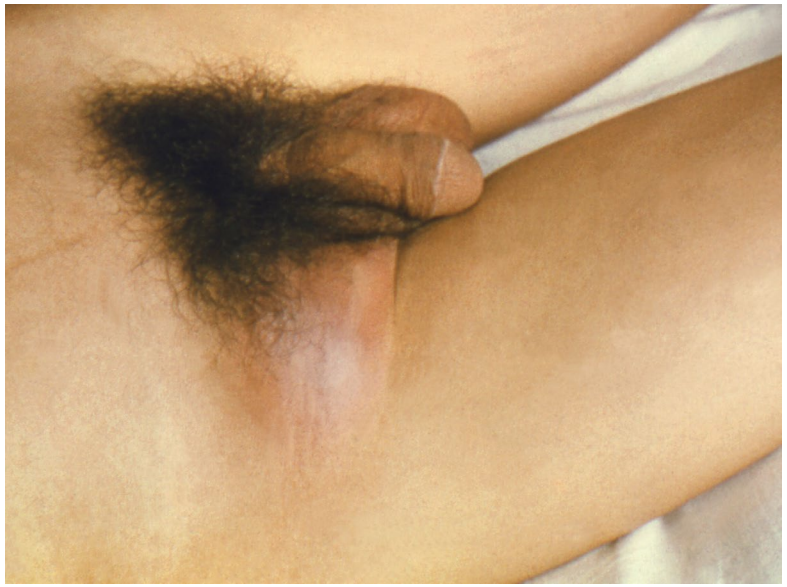
- Occurs 2-6 weeks after exposure
- **Inguinal Syndrome:**
  - Unilateral or bilateral tender inguinal/femoral lymphadenopathy
  - Development of “buboes”- inflamed lymph nodes which can rupture
  - Groove sign- separation of the inguinal lymph nodes from the inguinal ligament



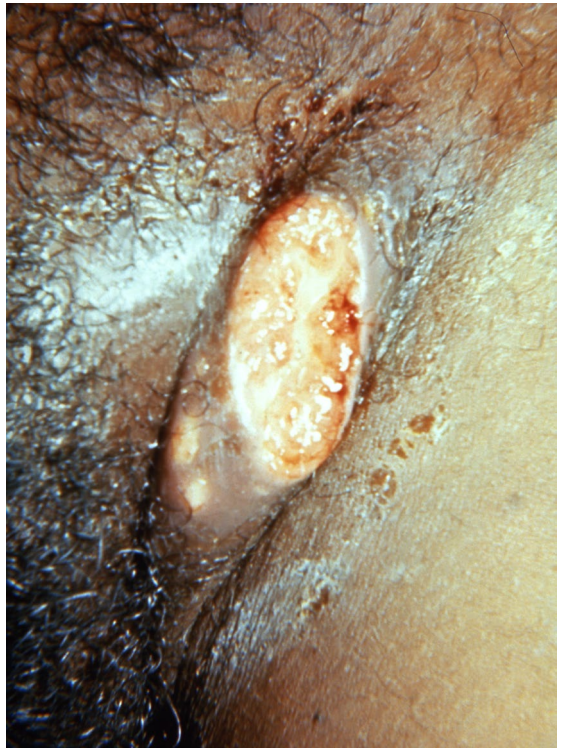
"Groove sign"

Figure 1. [InguinalsyndromeinLGV.jpg (360×270) (uptodate.com)]CDC, n.d. Public domain

Painful inguinal buboe



[*https://phil.cdc.gov/Details.aspx?pid=20866*] by CDC/ O.T. Chambers, 1966. Public Domain



Ulcerative buboe- ruptured

Figure 3 [*https://phil.cdc.gov/Details.aspx?pid=18034*] by CDC/ Renelle Woodall, 1969. Public Domain.

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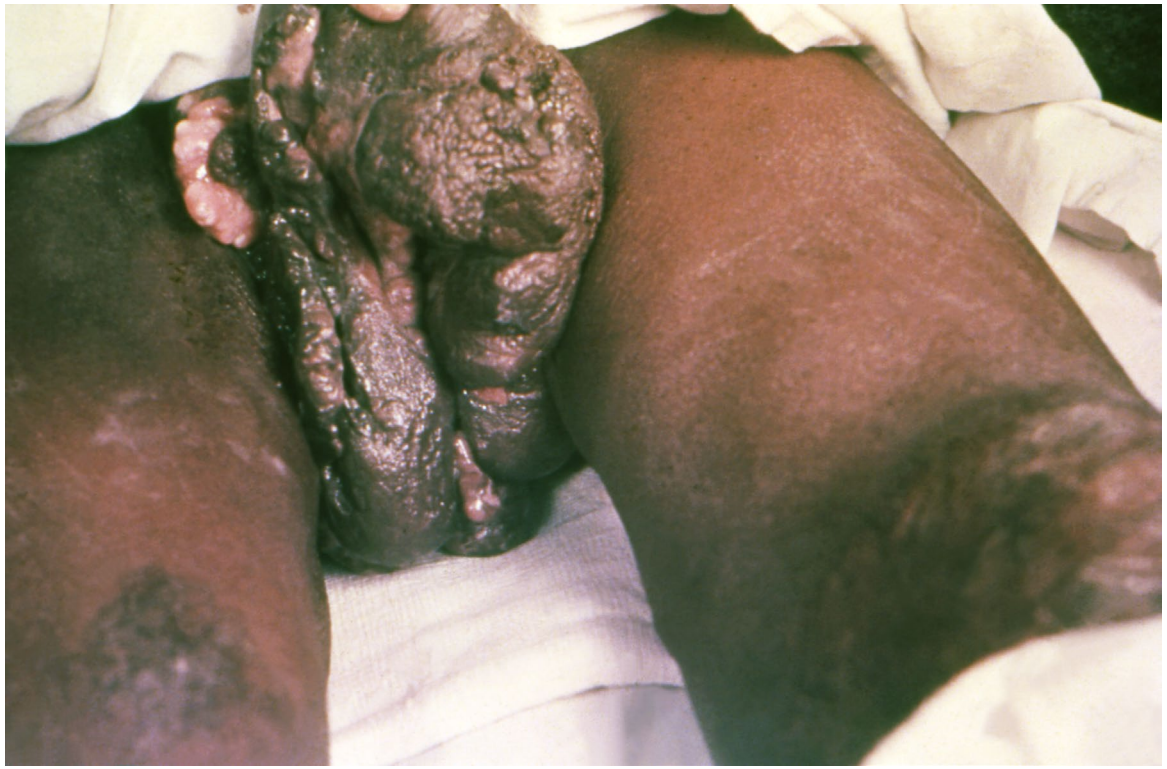
Secondary stage (continued)

- **Anorectal syndrome**
  - Rectal bleeding, pain, tenesmus, constipation
  - Can develop inflammatory mass of rectum[4]
  - Generalized aches
  - More often associated with the anal route

- **Oral syndrome**
  - Cervical lymphadenopathy
  - Associated with oral route of transmission

Late LGV

- Occurs if earlier stages remain untreated or undertreated
- Necrosis/rupture of lymph nodes
- Anal strictures/fibrosis
- Anal fistula
- Genital elephantiasis
- Esthiomene: chronic genital ulceration and elphantiasis of female genitals
  - Very rare complication, but very disfiguring



Esthiomene: elephantiasis and ulceration of labia and vulva

Figure 4 [*https://phil.cdc.gov/Details.aspx?pid=18051*]. CDC/ Renelle Woodall, 1969. Public domain.

Diagnosis

Clinical diagnosis: positive C. trachomatis NAAT + clinical/epidemiological findings consistent with LGV, when other etiologies for genital ulceration and inguinal lymphadenopathy can be excluded

- Limitations: if patient presents in late disease, there may not be enough material to send for NAAT

LGV-specific molecular testing – only definitive diagnostic test, but PCR testing is not widely available

LGV serology – can help retrospectively identify/confirm LGV in a suspected case, however is not definitive and are not well standardized.

Culture – Will need to be obtained from site of infection (genital ulcer) in primary disease, or from affect lymph node in secondary disease.

Treatment

First line treatment	Alternative therapy
Doxycycline 100mg PO BID x 21 days	▪ Azithromycin 1g PO once weekly x3 ▪ Erythromycin 500mg PO QID x 21 days

Prevention

- Abstain from sexual activities until symptoms resolve AND treatment is completed (day 21 of doxycycline/ 7 days after last dose of azithromycin).
- Minimize reinfection:
  - Clean fomites (sex toys)
  - Notify all sexual partners in past 60 days – have tested/treated
  - Asymptomatic partners can be treated with doxycycline 100mg PO BID x 7 days (Grade 2C recommendation)

Test of cure

- CDC recommends test of cure with chlamydia NAAT at 3 months after treatment
- If 3 month follow up is not possible, retest within 12-month period
- Pregnant persons should have test of cure performed 4 weeks after treatment

Public health considerations

- Chlamydia is the most frequently reported bacterial STI in the United States.
- Strong association of LGV and HIV: HIV shedding can increase during acute proctitis, increasing potential transmission to uninfected partners
- 34% of LGV cases can be asymptomatic
- Strong association with other STIs
  - Ensure screening for additional STIs
  - HIV PrEP should be offered to those not living with HIV

What about our patient?

- He reported improvement of symptoms after 7 days doxycycline
- Treated with definitively (21 days doxycycline) after last visit.
- Test of cure completed and confirmed negative on C. Trachomatis NAAT.
- Discussed initiating DoxyPEP

DoxyPEP – doxycycline post-exposure prophylaxis

- Administration of 100mg of doxycycline within 72 hours of condomless intercourse
- Found to significantly decrease rates of chlamydia and syphilis
- Literature varies regarding decrease in incidence of gonorrhea

Limitations with DoxyPEP studies

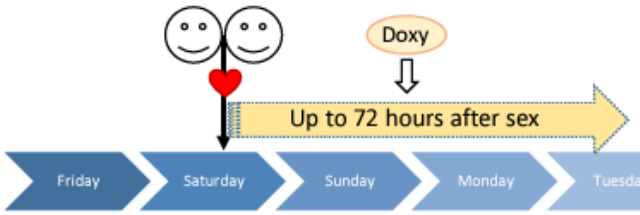
- Most studies supporting use of DoxyPEP involved cisgender men and transgender women.
- One study done in Kenya involved cisgender women
  - STI incidence was not significantly different in PEP group vs. standard care.
  - Researchers used hair analysis to look at actual use of doxycycline in the treatment group - found low usage.

Doxy PEP – How to Take

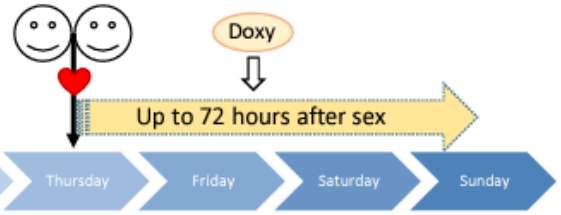
= sex without a condom, including oral sex

Two 100 mg pills of doxycycline ideally <u>within 24 hours</u> but no later than 72 hours after condomless oral, anal or vaginal sex

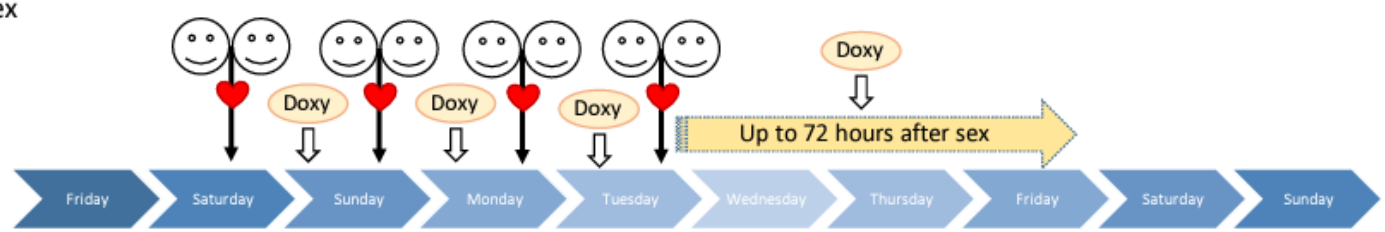
Example: Sex on Sat; take dose of doxy by Tues



Example: Sex on Thursday; take dose of doxy by Sunday



Example 2: Daily (or more) sex Sat-Tues; take daily dose of doxy and last dose within 24 hours *but not later than 72 hours* after last sex



***No more than* 200 mg every 24 hours**

Figure 5. "DoxyPEP dosing instructions." [*https://www.sfcityclinic.org/providers/guidelines/hiv-and-sti-prevention*] San Francisco City Clinic.

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