



EM CASES SUMMARY

Episode 183 PID & Genital Lesions

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Pelvic Inflammatory Disease (PID) – an often elusive diagnosis

PID encompasses a wide spectrum of upper genital tract infections including endometritis, salpingitis, oophoritis, myometritis, tubo-ovarian abscess, and perihepatitis (Fitz-Hugh Curtis syndrome) and ranges in clinical presentation from acutely severely ill patients with intra-abdominal sepsis to those with mild abdominal pain and more indolent presentations over weeks to months.

Why should we care about making the diagnosis of pelvic inflammatory disease (PID) in the ED?

The long-term consequences of untreated PID include:

- Infertility
- Chronic pelvic pain

- Ectopic pregnancy (10% risk)

The diagnosis of PID is frequently missed in the ED due to:

- Sometimes vague and indolent presentation with mild or nonspecific symptoms or signs (e.g., abnormal bleeding, dyspareunia, and vaginal discharge)
- Poor accuracy of laboratory testing and imaging
- Unrecognized organisms besides gonorrhea and chlamydia (which comprise only 50% of PID cases) such as mycoplasma genitalium
- Increasing multi-drug resistant gonorrhoea with incomplete treatment

Pelvic Inflammatory Disease (PID) diagnostic criteria

PID should be considered in all sexually active females presenting with abdominal/pelvic pain where other causes have been excluded plus one or more of the following minimum diagnostic criteria:

1. Adnexal tenderness
2. Cervical motion tenderness
3. Lower abdominal tenderness

A presumptive diagnosis should be made *and treatment initiated* with any one of the above present after other causes of abdominal/pelvic pain are ruled out.

Additional diagnostic criteria can increase specificity for PID including:

1. Fever
2. Abnormal cervical mucopurulent discharge or cervical friability on pelvic exam
3. Elevated ESR/CRP
4. Laboratory documentation of cervical/vaginal infection with gonorrhea or chlamydia

Definitive diagnosis is made with:

1. Transvaginal ultrasound findings in keeping with PID including tubo-ovarian abscess
2. Biopsy
3. Laparoscopy

In summary, there is not one historical feature, physical exam or lab test that definitively rules in the diagnosis of PID. A low threshold for presumptive diagnosis should be employed in sexually active women with unexplained abdominal/pelvic pain and significant tenderness on pelvic and abdominal exam. A combination of features should increase one's pre-test probability for PID.

Imaging in pelvic inflammatory disease: Do all patients in whom you suspect PID require ultrasound imaging? What about CT and MRI?

While a normal transvaginal/abdominal ultrasound does not rule out PID with certainty, ultrasound is often done to rule out alternative diagnoses, and there are several findings that are suggestive of the diagnosis including:

- Fallopian tube wall thickness >5 mm
- Incomplete septae within the fallopian tube
- Fluid in the cul-de-sac
- [Cogwheel sign](#) (a cogwheel appearance on the cross-section tubal view)
- Tubo-ovarian abscess

The addition of color Doppler flow, in one small study, was found to be 100% sensitive for the diagnosis of PID however large RCTs are required to use this in practice.

Our experts recommend ED ultrasound imaging in those patients with severe disease, those in which the diagnosis is unclear, and in those whom you suspect tubo-ovarian abscess. Clinical findings to suggest tubo-ovarian abscess and hence consideration for ultrasound include unilateral adnexal tenderness, hemodynamic instability, fever or those requiring IV opioids for pain control.

Abdominal ultrasound in patients with Fitz-Hugh-Curtis Syndrome as well as PID may be normal. Findings suggestive of Fitz-Hugh-Curtis include a thickened hepatic capsule and ascites.

CT of the pelvis may show signs of PID including:

- Subtle changes in appearance of the pelvic floor fascial planes
- Thickened uterosacral ligaments
- Inflammatory changes of the tubes or ovaries
- Abnormal fluid collection

In a recent study of CT and MRI for the diagnosis of PID, CT with contrast had a pooled sensitivity of 79% and a specificity of 99%, and MRI had a sensitivity of 95% and a specificity of 89%.

***Pitfall:** One common pitfall is assuming that Fitz-Hugh-Curtis Syncrome has been ruled out when ultrasound of the abdomen/pelvis is normal. While a thickened hepatic capsule and ascites is sometimes seen, a normal abdominal ultrasound does not rule out the syndrome.*

Treatment of pelvic inflammatory disease (PID)

Empiric, broad-spectrum coverage of likely organisms should be initiated as soon as the presumptive diagnosis has been made as prevention of long-term sequelae is dependent on early treatment. Consult your local resources as treatment for this disease changes frequently. All regimens used to treat PID should be effective against gonorrhea and chlamydia regardless of screening test results for these organisms, as negative endocervical swabs/urine testing do not rule out upper genital tract infection.

Mild-moderate PID antibiotic treatment (CDC)

Consider IM or oral antibiotics for patients with mild-to-moderate acute PID as the clinical outcomes are similar when compared to IV regimens.

Ceftriaxone 500 mg IM in a single dose* + **Doxycycline** 100 mg orally 2 times/day for 14 days + **Metronidazole** 500 mg orally 2 times/day for 14 days

Or

Cefoxitin 2 g IM in a single dose and **Probenecid** 1 g orally administered concurrently in a single dose + **Doxycycline** 100 mg orally 2 times/day for 14 days + **Metronidazole** 500 mg orally 2 times/day for 14 days

Or

Other parenteral third-generation **cephalosporin** (e.g., ceftizoxime or cefotaxime) + **Doxycycline** 100 mg orally 2 times/day for 14 days + **Metronidazole** 500 mg orally 2 times/day for 14 days

*For persons weighing >150 kg (~300 lbs.) with documented gonococcal infection, 1 g of ceftriaxone should be administered.

Severe PID antibiotic treatment (CDC)

Ceftriaxone 1 g IV every 24 hours + **Doxycycline** 100 mg orally or IV every 12 hours + **Metronidazole** 500 mg orally or IV every 12 hours

Or

Cefotetan 2 g IV every 12 hours + **Doxycycline** 100 mg orally or IV every 12 hours

Or

Cefoxitin 2 g IV every 6 hours + **Doxycycline** 100 mg orally or IV every 12 hours

Disposition of patients with pelvic inflammatory disease (PID)

For patients with mild to moderate PID, most RCTs suggest that there is no difference in outcomes if patients are discharged home with the appropriate oral regimen vs. admitted to hospital for parenteral antibiotics. Patients with severe disease and pregnant patients require admission to hospital and consultation with gynecology.

CDC suggested admission criteria for PID include:

- Surgical emergencies (e.g., appendicitis) cannot be excluded
- Tubo-ovarian abscess
- Pregnancy
- Severe illness, nausea and vomiting, or oral temperature >38.5°C (101°F)
- Unable to follow or tolerate an outpatient oral regimen
- No clinical response to oral antimicrobial therapy

Does an IUD need to be removed in patients with PID?

IUD can be safely left in place unless there is no clinical improvement in 48-72h after starting treatment and you suspect that the IUD is the source of infection. Generally, the risk of PID from IUD insertion is isolated to the first 3 weeks post insertion.

Pearl: The risk of PID after IUD insertion is generally isolated to the first 3 weeks post insertion. There is no requirement for removal of

an IUD in a patient diagnosed with PID unless there is no clinical improvement in 48-72hrs after initiating of treatment.

Fitz-Hugh-Curtis Syndrome – an often elusive diagnosis of perihepatitis as a complication of PID

Fitz-Hugh-Curtis Syndrome is a complication of PID characterized by liver capsule inflammation leading to adhesions. Incidence ranges from 4% to 14% in women with PID, but is as high as 27% in adolescents with PID. Definitive diagnosis can only be made by direct visualization of the liver by laparoscopy or laparotomy, however a presumptive diagnosis can be made in the ED in the patient who presents with right upper quadrant (RUQ) abdominal pain several days after, or coinciding with, PID symptoms, and after other causes of RUQ have been ruled out. Rarely, patients present with isolated RUQ pain making the diagnosis even more elusive. If alternate causes of RUQ pain have been ruled out in a patient at risk for PID, a pelvic exam and consideration for the diagnosis should be made.

Pearl: In female patients presenting with right upper quadrant pain and negative work up for biliary, gallbladder and hepatic pathology consider PID and a pelvic exam. Liver enzymes are not always elevated and ultrasound may be normal in patients presenting with this syndrome.

Genital lesions and ulcers – a 3-step approach and specific recommendations

The vast majority of genital lesions seen in the ED will be secondary to Herpes Simplex Virus (HSV) however there is a differential to keep in mind especially considering the increasing incidence of syphilis, which carries a significant morbidity and mortality rate. While a definitive diagnosis of genital lesions cannot always be made in the ED it is useful to have a general approach to narrow your differential diagnosis and consider lesions that are often missed in the ED.

A 3-step approach to the identification of genital lesions

1. Are the lesions painful?

Painful: HSV or chancroid

Painless: Syphilis, LGV, granuloma inguinale

2. Are there multiple lesions?

Solitary: Syphilis, LGV, chancroid, granuloma inguinale

Multiple: HSV, chancroid, granuloma inguinale

3. Is there tender regional lymphadenopathy?

Tender lymphadenopathy: HSV, chancroid, LGV

Non-tender lymphadenopathy: Syphilis

Genital Herpes (HSV) – the most common sexually transmitted genital lesions

Presentation: Pruritic/painful lesions that evolve from clustered vesicles on an erythematous base, then crust over, lasting about 1-2 weeks, with history of recurrence.

Test: direct swab of vesicular lesions sent for HSV NAAT

Treatment of acute episode: acyclovir 400mg PO TID x 7 days or valacyclovir 1g PO BID x 7 days



Typical clustered vesicles on erythematous base of genital herpes

Syphilis – increasing incidence of a potentially deadly disease

Syphilis is on the rise with the majority of cases among men who have sex with men (MSM) aged 25–35, of whom 40% are HIV positive. Congenital syphilis is also on the rise. There is overlap in the presentations of syphilis and HIV, so it is recommended to test for both in patients presenting with either. Syphilis typically presents with a genital ulcer or a rash but its manifestations are many as it can affect any organ. Symptoms typically occur 9-90 days (median 3 wks) after direct contact with an infectious lesions.

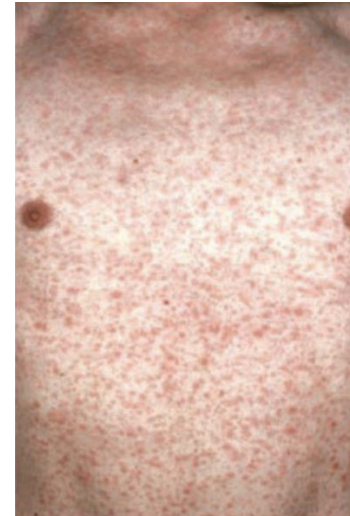
Primary syphilis presents with a genital, rectal or oral papule that breaks down into a 0.5-2cm firm, rubbery ulcer (chancre). However because they are typically painless and usually solitary (70%), they are often missed by the patient. The ulcer typically heals over 4-6 weeks.

Secondary syphilis is the stage that typically begins 4–10 weeks after the ulcer has healed and at which time the ED diagnosis is most likely to be made. **Generalized painless/nontender lymphadenopathy** is present in 85% of cases. Syphilis can be thought of as generalized painless/nontender lymphadenopathy + 1 of 3 key presentations.

There are **3 key presentations of secondary syphilis**:

1. **Rash** – the hallmark sign of syphilis is a non-pruritic maculopapular rash (seen in 50–70% of patients) that may affect the palms and soles

2. **Neurologic**– a variety of neurologic presentations including meningitis, infectious thrombosis/ischemia, hearing loss with or without tinnitus, general paresis
3. **Ocular** – uveitis, iritis, optic neuritis



Macopapular rash of syphilis which may involve the palms of the hands and soles of the feet

***Pearl:** a non-pruritic maculopapular rash of the palms and soles in a patient at risk for STIs should be considered to be syphilis until proven otherwise.*

Testing for syphilis

Any patient presenting with ulcer: perform direct swab of the ulcer for NAAT/PCR

For patients presenting with anogenital lesions/other STIs/or you have a suspicion for syphilis obtain serologic testing:

- First perform nontreponemal test (e.g. VDRL or rapid plasma reagin), *if* this is positive then this is confirmed with treponemal test such as the Treponema pallidum particle agglutination (TPPA) assay or the IgM/IgG enzyme immunoassay (EIA). If both are positive the patient is considered syphilis positive.
- There is possibility of false negative in the first 2-4 weeks of disease due to lack of serological conversion and testing needs to be repeated.
- False positive tests are possible with previously treated infections or autoimmune disease.

Treatment of syphilis: long acting benzathine penicillin G 2.4 million units IM x 1

Pearl: Syphilis can be thought of as generalized painless/nontender lymphadenopathy + 1 of 3 key presentations – non-pruritic rash (esp with involvement of palms and soles), neurologic including meningitis, ischemia and paresis and ocular such as uveitis. Patients who present with one of these 3 presentations should be checked for generalized lymphadenopathy.

Lymphogranuloma venereum (LGV)

- May present with proctitis or rectal bleeding and may mimic IBD

- Initially, there is a self-limited painless single papule that may ulcerate
- Untreated can lead to tenosynovitis, fistulas and strictures

Testing: send a swab for chlamydia and gonorrhea and *specify* that you are concerned about LGV as this is a subtype of chlamydia.

Treatment of lymphogranuloma venereum: Doxycycline 100mg PO BID x 21 days

Granuloma inguinale – Klebsiella granulomatis

Granuloma inguinale presents as painless extensive ulcerative lesions that are highly vascular in appearance and bleed easily on contact. It is typically diagnosed after other STIs are ruled out and requires for referral for biopsy for definitive diagnosis.



Treatment of granuloma inguinale: Doxycycline 100mg PO BID x 21 days

***Pearl:** LGV is relatively common mimic of IBD. In patients at risk for STIs who present with a first episode of IBD, think about the possibility of LGV, test for it, and consider empiric doxycycline*

Chancroid – a diagnosis of exclusion

Presentation: Single or multiple necrotizing painful ulcers often with onset of painful regional lymphadenopathy (that can be suppurative) ~2 weeks after initial ulcer.

Ulcers are well demarcated, 1-2cm in diameter on erythematous base and located on areas subjected to friction from sexual activity (penis, introitus, labia).

This is a diagnosis of exclusion as it is difficult to culture. If swabs are sent for syphilis and HSV and these are negative treat for likely chancroid.

Treatment: single dose of ceftriaxone 500mg IM/IV

Genital lesions: summary

Any anogenital lesions/ulcers presenting to the ED:

- Swabs of lesions/ulcer should be sent for HSV and syphilis (direct)

- Serological testing for syphilis regardless of suspected stage should be completed starting with nontreponemal (e.g. VDRL).
- Test for other STIs as one STI is a biomarker for others including Chlamydia and gonorrhea, HIV, Hepatitis
- Consider chancroid, LGV and granuloma inguinale in those with risk factors and physical exam findings that are in keeping with their presentation.

Empiric treatment of genital lesions undifferentiated

- Treat for HSV with acyclovir or valacyclovir unless your index of suspicion is low
- Consider empiric treatment of syphilis and LGV with penicillin and doxycycline respectively if you suspect either and the patient has poor access to follow-up

Remember to always consider follow-up for patients for confirmatory testing and consultation with your local infectious disease colleagues to assist with empiric regimens.

Considerations for people who are transgender

In patients with gender affirming surgery the risk of STIs is the same depending on practices and site of inoculation. Keep in mind original graft tissue. For example, patients with vaginoplasty using an intestinal graft may come in with symptoms secondary to STI or disease primary to native tissue like IBD or colitis.