

Pelvic Inflammatory Disease

Learning Objectives:

Upon completion of this module, the learner will be able to:

1. Define Pelvic Inflammatory Disease (PID).
2. Discuss the epidemiology and risk factors associated with PID.
3. List the clinical and laboratory criteria for diagnosis of PID.
4. Discuss clinical management of PID to include treatment, follow-up, patient counseling, and partner management.
5. List the criteria for hospitalization referral and possible sequelae to PID.
6. Discuss the relationship and management of PID with co-infection with HIV.

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Definition

An acute clinical syndrome associated with ascending spread of microorganisms from the vagina or cervix to the endometrium, fallopian tubes, ovaries, and contiguous structures. PID is defined as any combination of endometritis-salpingitis, tubo-ovarian abscess, or pelvic peritonitis.

I. Epidemiology

A. Pelvic Inflammatory Disease: occurs in approximately 1 million U.S. women annually. Annual cost exceeds \$4.2 billion. Surveillance and reporting limited by insensitive and nonspecific diagnosis and underreporting.

B. Risk factors/risk markers for PID:

1. Young age, adolescence: increased age-related chlamydia (CT)/gonorrhea (GC) rates.
2. History of prior PID: damaged fallopian tube mucosa may be more susceptible to recurrent infection.
3. History of prior GC or CT: increased likelihood of recurrent GC or CT.
4. Male partners with GC, CT, or multiple partners.
5. Current douching: probable contributions of vaginal flora changes, epithelial damage, and disruption of cervical mucous barrier.
6. Presence of IUD within the first 21 days of placement; after 21 days, risk returns to baseline.
7. Bacterial vaginosis: role in the development of PID is controversial.
8. Demographics (socioeconomic status).
9. Oral contraceptive use: may increase the risk of cervical chlamydial infection, but decrease the risk of clinically apparent symptomatic PID (mechanisms unclear).

C. Recent trends suggest a decrease in numbers of hospitalized cases of PID in USA, Sweden, and other industrialized countries coincident with decreases in incidence of gonorrhea and chlamydia. In the U.S., this trend may be due to

increasing rate of outpatient treatment at the expense of hospitalization rather than an actual decline in the incidence of PID.

II. Pathogenesis

A. Pathway of ascendant infection: Cervicitis--> Endometritis--> Salpingitis/oophoritis/tubo-ovarian abscess--> Peritonitis.

B. Microbial etiology:

1. Most cases of PID are polymicrobial in etiology.
2. Most common pathogens: GC and CT are present alone or in combination in approximately 20-60% of patients; relative prevalence of these and other organisms depends on population studied. With decreasing prevalence of GC and CT, these estimates may be lower.
3. *N. gonorrhoeae*: recovered from cervix in 30-80% of women with PID.
4. *C. trachomatis*: recovered from cervix in 20-40% of women with PID; recovered from endometrium and/or tubes in a majority of women with cervical chlamydia infection. Also, especially associated with perihepatitis (Fitz-Hugh-Curtis syndrome).
5. Aerobic Gram-negative rods (e.g. *E. coli*).
6. Anaerobes (*Bacteroides* spp., *Prevotella* spp., *Peptostreptococcus* spp.); especially those associated with BV.
7. Mycoplasmas, ureaplasmas: particularly important in pregnancy and procedure-related infections.
8. Gram-positive organisms, streptococcus spp.
9. Possible role of CMV under investigation.

C. Immunopathology of re-infection:

1. Role of chlamydia heat-shock proteins.
2. Local immune changes and deficits.

III. Clinical Manifestations

- A. When present, symptoms often include lower abdominal pain, cramping, dysuria, intermittent or post-coital bleeding, vaginal discharge, fever.
- B. "Silent" PID-diagnosis is difficult. Often asymptomatic or with atypical presentation in the setting of upper tract inflammation +/- infection, such as dyspareunia, irregular bleeding, urinary or gastrointestinal symptoms. Mild abdominal or uterine tenderness on exam has been associated with asymptomatic endometritis.
- C. Approximately 25% of women with a single episode of symptomatic PID will experience sequelae, including ectopic pregnancy, infertility, or chronic pelvic pain.
 - 1. The risk of ectopic pregnancy is increased 6-10-fold.
 - 2. Tubal infertility occurs in 8% of women after one episode of PID, in 20% after two episodes, and in 40% after 3 episodes.

IV. Diagnosis

- A. CDC recommends empiric treatment of PID if these minimum criteria are met in the absence of any other explanation.
 - 1. Uterine/adnexal tenderness; or
 - 2. cervical motion tenderness.
Under some circumstances, a clinician may choose to treat with even less specific findings. In patients with both pelvic tenderness and signs of lower genital tract inflammation, the diagnosis of PID should be considered. Acute adnexal tenderness may be the most sensitive sign of upper genital tract infection. The general recommendation is to err on the side of over treatment given the high incidence of adverse outcomes with untreated PID.
- B. Additional criteria to increase specificity of diagnosis (but will decrease sensitivity):
 - 1. Temp >38.3C.
 - 2. Abnormal cervical or vaginal discharge.
 - 3. Elevated erythrocyte sedimentation rate (ESR).

4. Elevated C-reactive protein (CRP).
5. Gonorrhea or chlamydia test positive.
6. WBCs on microscopic evaluation of saline preparation of vaginal secretions, but utility is controversial.

C. Specific diagnostic measures include:

1. Endometrial biopsy.
2. Transvaginal sonography (may demonstrate TOA or thickened tubes with or without free pelvic fluid).
3. Laparoscopy is indicated for:
 - a) Severe peritonitis to exclude ruptured tubal abscess or ruptured appendix.
 - b) Patients with mild signs in whom the diagnosis is unclear.
 - c) Patients who fail to respond to antibiotic therapy.
 - d) Percutaneous drainage of an abscess.

V. Treatment

- A. Regimens must provide coverage of *N. gonorrhoeae*, *C. trachomatis*, anaerobes, Gram-negative facultative organisms, and streptococci.
- B. Although PID is frequently treated on an outpatient basis, there are no long term studies comparing the efficacy of outpatient and parenteral regimens in preventing sequelae.
- C. Treatment should be instituted as early as possible to prevent long-term sequelae.
- D. If IUD is present, removal depends on the initial severity and response to therapy.
- E. If BV is present, choose an antibiotic with good anaerobic coverage.
- F. Indications for hospitalization and parenteral treatment include:
 1. Inability to exclude surgical emergencies (i.e., appendicitis, ectopic pregnancy).
 2. Tubo-ovarian abscess.

3. Pregnancy.
4. Current immunodeficiency (HIV infection with low CD4 count, immunosuppressive therapy).
5. Inability to follow or tolerate an outpatient regimen.
6. Failure to respond clinically to outpatient antimicrobial therapy within 48-72 hours.
7. Severe illness, nausea and vomiting, or high fever.

G. Antimicrobial regimens:

1. Parenteral (inpatient or outpatient parenteral therapy): continue either of these regimens for at least 24 hours after substantial clinical improvement, then complete a total of 14 days therapy with Doxycycline (100 mg b.i.d.) with regimen A or with Doxycycline or Clindamycin (450 mg PO q.i.d.), if using regimen B:
 - a) Regimen A:
Cefoxitin 2 g IV q 6 hours, or Cefotetan 2 g IV q 12 hours PLUS Doxycycline 100 mg PO or IV q 12 hours. If patient is able to tolerate po, oral Doxycycline is well absorbed.
 - b) Regimen B:
Clindamycin 900 mg IV q 8 hours PLUS Gentamycin loading dose (2 mg/kg), followed by maintenance dose (1.5 mg/kg q 8 hours). Once-daily gentamicin dosing may be used.
 - c) Limited data exist on other parenteral regimens, including combinations of:
 - 1) Ofloxacin (or Levofloxacin) ± Metronidazole.
 - 2) Ampicillin/Sulbactam and Doxycycline.
2. Oral treatment: each of these regimens should be continued for a total of 14 days therapy. Patients on oral therapy ideally should be followed up within 72 hours, at which time they should show substantial clinical improvement. The role of anaerobes in mild/moderate PID as an outpatient is unclear; the routine use of metronidazole is controversial. If bacterial vaginosis is present, addition of metronidazole in the treatment regimen may be particularly compelling.
 - a) Regimen A:
Ofloxacin 400 mg orally 2 times a day or Levofloxacin 500 mg orally QD ± metronidazole 500 mg orally 2 times a day for 14 days. Routine

administration of metronidazole is controversial.

b) Regimen B:

Either Ceftriaxone 250 mg IM once OR Cefoxitin 2 g IM with Probenecid 1 gm orally in a single dose OR other parenteral third-generation cephalosporin (e.g., Ceftizoxime, Cefotaxime), PLUS Doxycycline 100 mg orally 2 times a day for 14 days.

c) At present, an appropriate oral Azithromycin regimen for the treatment of PID has not been established and is not recommended. Azithromycin lacks anaerobic activity and lacks optimal coverage of some Gram-negative organisms.

H. Follow-up:

1. Patient should be re-examined within 72 hours after initiation of therapy, and should demonstrate substantial clinical improvement. If no improvement is shown, consider other work-up/etiology or change to parenteral therapy.
2. Some experts recommend rescreening for *C. trachomatis* and *N. gonorrhoeae* after completion of therapy, if initially positive. The optimal time period for rescreening is controversial and ranges from 4-6 weeks to 3-6 months.
3. Patient counseling about risk of re-infection and sequelae.
4. Avoid douching.

I. Management of sex partners: sex partners (within 60 days prior to onset of symptoms) of women with PID should be evaluated and treated empirically with regimens effective against both *C. trachomatis* and *N. gonorrhoeae*.

VI. Prevention

A. Screening recommendations:

1. Prevention of gonorrhea and chlamydia infection by screening and treating high-risk women reduces the incidence of PID.
2. Although BV is associated with PID, it is not clear whether identifying and treating women with BV will reduce the incidence of PID.

B. Partner management:

1. Male sex partners of women with PID should be examined and treated if they had sexual contact with the patient during the 60 days preceding onset of symptoms in the patient. The evaluation and treatment are imperative because of the risk for reinfection and the strong likelihood of urethral gonococcal or chlamydial infection in the sex partner.
2. Male partners of women who have PID caused by *C. trachomatis* and/or *N. gonorrhoeae* are often asymptomatic. Sex partners should be treated empirically with regimens effective against both of these infections, regardless of the apparent etiology of PID or pathogens isolated from the infected woman.

C. Reporting: report cases to the local STD program in states where reporting is mandated.

D. Patient counseling and education:

1. Nature of the infection:
 - a) Risk of re-infection and sequelae
 - b) Avoid douching
2. Risk reduction:
 - a) Assess client's behavior-change potential.
 - b) Discuss prevention strategies (abstinence, monogamy, condoms, limit number of sex partners, etc.). Latex condoms, when used consistently and correctly, can reduce the risk of transmission of chlamydia and gonorrhea.
3. Develop individualized risk-reduction plans.

E. Other:

Treatment of BV prior to upper tract invasive or surgical procedures. Although BV is associated with PID, it is not clear whether identifying and treating women with BV will reduce the incidence of PID. The efficacy of treating asymptomatic pregnant women with BV and pregnancy outcomes is unclear.

IV. References

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