

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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Pelvic Inflammatory Disease Curriculum Module Contributors

Primary Editors 2011 Revision:

Mychelle Farmer, M.D., HIV AIDS Technical Advisor, Catholic Relief Services, Baltimore, MD;
Eumee Chun, M.D.,

Primary Editor 2001 Edition

John F. Toney, M.D., Associate Professor of Medicine, Division of Infectious Diseases and Tropical Medicine, University of South Florida College of Medicine, Director, Florida STD/HIV Prevention Training Center, Tampa, Florida, CDC National Network of STD/HIV Prevention Training Centers

Contributing Editors 2001 Edition

Heidi M. Bauer, MD, MS, MPH, Director, Office of Medical and Scientific Affairs, STD Control Branch, State of California, Department of Health Services, Berkeley, CA, Medical Co-director, California STD/HIV Prevention Training Center, Berkeley, CA, Clinical Instructor, Department of Obstetrics, Gynecology and Reproductive Health Sciences, School of Medicine, University of California, San Francisco, CA; **Gail A. Bolan, MD**, Chief, STD Control Branch, State of California, Department of Health Services, Berkeley, CA, Director, California STD/HIV Prevention Training Center, Berkeley, CA, Assistant Clinical Professor, School of Medicine, University of California, San Francisco, CA; **Helene Calvet, MD**, Medical Co-director, California STD/HIV Prevention Training Center, Long Beach, CA, Public Health Physician, Long Beach Department of Health and Human Services, Long Beach, CA; **Thomas Cherneskie, MD, MPH**, New York City Department of Health, STD Control Program, New York, NY; **John Douglas, MD**, Director of STD Control, Denver Public Health, Professor of Medicine and Preventive Medicine, University of Colorado Health Sciences Center, Denver, CO; **Charles L. Heaton, M.D.**, Professor of Dermatology, University of Cincinnati and Medical Director Cincinnati STD/HIV Prevention Training Center; Cincinnati, OH; **Kathryn Koski, MEd**, Public Health Advisor, CDC/Division of STD Prevention; Atlanta, GA; **James P. Luby, MD**, Professor of Internal Medicine, Division of Infectious Diseases, University of Texas Southwestern Medical School at Dallas, Medical Director, Dallas STD/HIV Prevention Training Center, Dallas, TX; **Jeanne Marrazzo, MD, MPH**, Assistant Professor, Infectious Diseases, University of Washington, Medical Director, Seattle STD/HIV Prevention Training Center, Seattle, WA; **Sylvie Ratelle, MD, MPH**, Director, STD/HIV Prevention Training Center of New England, Division of STD Prevention, Massachusetts Department of Public Health, Assistant Professor of Family Medicine and Community Health, University of Massachusetts Medical School, Boston, MA; **Anne Rompalo, MD, ScM**, Associate Professor, Division of Infectious Diseases, Joint Appointment, Department of OB/GYN, Johns Hopkins University School of Medicine, Associate Professor, Department of Epidemiology, Johns Hopkins University School of Hygiene and Public Health, Medical Director, Baltimore STD/HIV Prevention Training Center, Baltimore, MD; **Marianne Scharbo-DeHaan, PhD, CNM**, Training and Health Communications Branch, Division of STD Prevention, Centers for Disease Control and Prevention, Atlanta, GA; **Bradley Stoner, MD, PhD**, Associate Professor, Washington University School of Medicine, St. Louis, Medical Director, St. Louis STD/HIV Prevention Training Center, St. Louis, MO

Expert Reviewers 2001 Edition

Linda Eckert, MD, Assistant Professor of Medicine, University of Washington Medical School, Seattle, WA; **Sudha Mehta, MD**, Medical Director, Cincinnati Health Department STD Clinic, Cincinnati, OH; **Judy Shlay, MD, MSPH**, Attending Physician, STD Clinic, Denver Public Health Director, Teen Clinic, Denver Public Health, Denver, CO; **Andrea Stephens, MS, MD**, Assistant Professor of Obstetrics and Gynecology, Washington University School of Medicine, St. Louis, MO; **Kimberly A Workowski, M.D., FACP**, Chief, Guidelines Unit, Epidemiology and Surveillance Branch, Division of STD Prevention, CDC, Associate Professor Medicine, Division of Infectious Diseases, Emory University, Atlanta, GA

National Network of STD/HIV Prevention Training Centers

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Contributors to Previous Editions

James Alexander, MD, Associate Professor, Department of OB/GYN, UT Southwestern Medical Center at Dallas, Dallas TX; **Jandel Allen-Davis, MD**, Assistant Clinical Professor, Department of OB/GYN, University of Colorado Health Sciences Center, Staff Physician, Kaiser Permanente, Department of OB/GYN, Denver CO; **Linda Eckert, MD**, Assistant Professor of Medicine, University of Washington Medical School, Seattle, WA; **David Eschenbach, MD**, Professor, Obstetrics and Gynecology, University of Washington School of Medicine, Seattle, WA; **Jeanne Marrasso, MD, MPH**, Assistant Professor of Medicine, University of Washington School of Medicine, Medical Director, Seattle STD/HIV Prevention Training Center, Seattle, WA; **Lauren Mason, RN, BSN**, Clinical Training Coordinator, Denver STD/HIV Prevention Training Center, Denver Public Health Department, Denver, CO; **James McGregor, MD**, Senior Technical Physician, Denver Health Medical Center, Professor of Obstetrics and Gynecology, University of Colorado Health Sciences Center, Denver, CO; **Anne Rompalo, MD, ScM**, Associate Professor, Division of Infectious Diseases, Joint Appointment, Department of Obstetrics and Gynecology, Johns Hopkins University School of Medicine, Associate Professor, Department of Epidemiology, Johns Hopkins University School of Hygiene and Public Health, Medical Director, Baltimore STD/HIV Prevention Training Center, Baltimore, MD

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PELVIC INFLAMMATORY DISEASE

Clinical Definition:

A clinical syndrome associated with ascending spread of microorganisms from the vagina and/or the cervix, to cause inflammation and infection in upper pelvic structures, such as the endometrium, fallopian tubes, ovaries, and contiguous structures. Pelvic inflammatory disease (PID) is defined as any combination of endometritis-salpingitis, tubo-ovarian abscess, or pelvic peritonitis.

I. Epidemiology

- A. Pelvic Inflammatory Disease: occurs in approximately 750,000 U.S. women annually. Annual cost of care and treatment exceeds \$4.2 billion. Surveillance and reporting is limited by insensitive and nonspecific diagnostic techniques for PID. PID is not a reportable disease in most states, thus underreporting of PID is quite common.
- B. Risk factors/risk markers for PID:
 1. Adolescents, young adult women: 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 cervicitis: increased likelihood of recurrent GC or CT
 4. Male partners infected with GC, CT, or multiple partners
 5. Current douching: probable contributions of vaginal flora changes, epithelial damage, and disruption of cervical mucous barrier. The physical pressure created by douching may promote ascending genital tract infections.
 6. IUD placement within previous 21 days; after 21 days, risk of PID returns to baseline
 7. Bacterial vaginosis: role in the development of PID is controversial
 8. Demographics . Adolescent, young adult women, lower socioeconomic status, early sexual debut
 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 U.S.A., 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 of PID. Routine STI screening for women at risk for infection may also contribute to 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 *Organisms associated with bacterial vaginosis*: *G. vaginalis*, *M. hominis*, *Prevotella* spp., *Peptostreptococcus* spp., *Mobiluncus* spp., *Bacteroides* spp
- 6 *Ureaplasmas*: particularly important in pregnancy and procedure-related infections
- 7 *Mycoplasma genitalium*: associated with cervicitis, urethritis, and upper genital tract infections (PID)
- 8 Aerobic Gram-negative rods (e.g. *E. coli*)
- 9 Anaerobes: especially those associated with BV (see above)
- 10 Gram-positive organisms, streptococcus spp

11 Possible role of CMV

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. An estimated 50% of PID is "silent", or subclinical.
- 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 at least two-fold following pelvic inflammatory disease.
 2. Tubal infertility occurs in 18% of women after one episode of PID, in up to 25% 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 tenderness or adnexal tenderness; or
 2. Cervical motion tenderness.
 3. 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, particularly among women at high risk for STIs, 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*, Gram-negative facultative organisms, and streptococci. Regimens providing effective coverage against anaerobic organisms may also be considered.

- B. Treatment should be instituted as early as possible to prevent long-term sequelae.

- C. If IUD is present, removal depends on the initial severity and response to therapy.

- D. If BV is present, choose an antibiotic with good anaerobic coverage.

- E. PID is frequently treated on an outpatient basis, with comparable outcomes in comparison to in-patient treatment.

- 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. Inability to follow or tolerate an outpatient regimen
 5. Failure to respond clinically to outpatient antimicrobial therapy within 48-72 hours
 6. Severe illness, nausea and vomiting, or high fever

G. Antimicrobial regimens:

1. Oral treatment: each of the following 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 (i.e. when treated on an outpatient basis) is unclear, so that 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: Ceftriaxone- 250 mg IM in a single dose, PLUS Doxycycline- 100 mg po, twice a day, for 14 days, WITH OR WITHOUT Metronidazole- 500 mg orally twice a day for 14 days

b) Regimen B: Cefoxitin 2 g IM in a single dose, AND Probenicid 1 g, administered concurrently in a single dose. PLUS Doxycycline 100 mg orally twice a day for 14 days. WITH OR WITHOUT Metronidazole- 500 mg orally twice a day for 14 days

As a result of the emergence of quinolone-resistant *Neisseria gonorrhoeae*, regimens that include a quinolone agent are no longer recommended for the treatment of PID.

c) Regimen C: Azithromycin may be effective when used with ceftriaxone 250 IM single dose and azithromycin 1 g orally once a week for two weeks. Metronidazole 500mg twice daily should be considered when using this regimen, in order to improve anaerobic coverage.

2. Parenteral (inpatient or outpatient parenteral therapy): continue either of the following regimens for at least 24 hours after substantial clinical improvement, then complete a total of 14 days therapy with Doxycycline (100 mg orally twice daily) with regimen A or with Doxycycline or Clindamycin (450 mg po qid), 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

oral medications, then oral Doxycycline is preferred 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 (3-5 mg/kg/day)..
- c) Alternative Regimen: ampicillin/sulbactam- 3 g IV, q 6 hr, PLUS doxycycline 100mg orally q 12 hours.

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, and consider hospitalization and/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
5. Rescreening for chlamydia and/or gonorrhea using NAAT

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 chlamydia infection by annual screening of high-risk women and prompt treatment for those testing positive for chlamydia 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. Expedited partner treatment (EPT): This approach to treatment of asymptomatic male partners of women with cervicitis due to chlamydia or gonorrhea is legal in some states, when other strategies for treatment have been unsuccessful. Refer to the following website for state-by-state information:

<http://www.cdc.gov/std/ept/legal/>

F. 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 effect on pregnancy outcomes of treating asymptomatic pregnant women with BV is unclear.

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