Pelvic Inflammatory Disease

This is a PDF version of the following document:Module 2:Self-Study Lessons 2nd EditionLesson 6:Pelvic Inflammatory Disease

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Introduction

Pelvic inflammatory disease (PID) is a clinical syndrome characterized by infection and inflammation of the upper female genital tract. This process results from the ascending spread of microorganisms in the vagina or cervix to the structures of the upper female genital tract, with potential infection and inflammation of the endometrium, fallopian tubes, pelvic peritoneum, and, in some instances, formation of tubo-ovarian abscess.[1,2] In recent years, the range of microorganisms believed to play a major role in this process has expanded.[3] Typically, PID is classified either as acute (less than or equal to 30 days duration), subclinical (asymptomatic), or chronic (greater than 30 days duration) (Figure 1).[1] The diagnosis of PID may be challenging as women with PID often experience subtle clinical manifestations and precise diagnostic criteria are lacking.[4] Women who experience PID may have adverse reproductive sequelae, including infertility, ectopic pregnancy, and chronic pelvic pain.[5,6] Effective parenteral and oral treatments are available for PID that provide short-term clinical benefit and reduce the risk of developing long-term complications.[1,7] When considering the severe potential long-term consequences associated with PID, it is extremely important for clinicians to diagnose PID and promptly provide appropriate and effective antimicrobial therapy.

[Q] Definition of Acute PID

Epidemiology

Prevalence

It is difficult to accurately estimate the incidence and prevalence of PID in the United States as there is no single diagnostic test for PID, and it is not a reportable disease. In a comprehensive review of 6 national and 2 sentinel data sources, investigators summarized the burden of and trends in PID among reproductive-aged women (18 to 44 years of age) in the United States during 2006–2017; using a subset of data in this study from the 2013–2016 National Health and Nutrition Examination Survey (NHANES) and the 2015-2017 National Survey of Family Growth (NSFG), there was an estimated 4.1% self-reported history of PID in NHANES and 3.7% in NSFG, with an estimated 2 million or more reproductive-aged women in the United States having a diagnosis of PID in their lifetime.[8] For women with a previously diagnosed sexually transmitted infection (STI), the lifetime prevalence of PID has been estimated as even higher, at 10%.[9]

Trends in PID

Available data from national insurance claims, visits to office-based physicians, and emergency departments point to an overall trend of decline in the incidence of PID in the United States since the year 2000, although both office-based and emergency department visits showed slight increases from 2015 to 2016 (Figure 2) and (Figure 3).[8,10,11] In the NHANES and NSFG review, the data from the NSFG component of this study show a decline in the prevalence of PID from 4.9% in 2008 to 3.6% in 2017, representing an overall decrease of 26.5% during this time.[8] Though precise reasons for the overall decline in PID since 2000 are not known, there has been a major contribution from increased screening for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in young women, particularly with use of the more sensitive nucleic acid amplification tests (NAATs) for diagnosing chlamydia and gonorrhea.[12,13,14,15]

[Q] PID Trends in United States

Factors that Impact Risk for PID

Epidemiologic studies have revealed numerous factors associated with PID, and many of these factors overlap with those known to be associated with acquisition of infections that cause PID. Multiple sex partners, age younger than 20 years, and current or prior infection with gonorrhea or chlamydia have consistently been demonstrated as significant factors associated with women developing PID.[16] Other possible risk factors include a prior history of PID, male partners with gonorrhea or chlamydia, current douching, recent insertion of an intrauterine device (IUD), bacterial vaginosis, and oral contraceptive use.[17,18] The following provides greater detail on the major factors associated with risk of developing PID:

- Age and Age of Sexual Debut: Several studies have identified age less than 20 years as a major risk factor for the development of PID.[16,19] The increased risk of PID in younger women correlates with the high rates of chlamydia and gonorrhea in female adolescents and young adult women. In addition, cervical ectopy—the composition of the cervical epithelium that is often present in adolescents—allows for more efficient access of infectious pathogens to the vulnerable target cells. Younger age at sexual debut is also a risk factor for PID. In the NHANES 2013-2014, the lifetime PID prevalence in sexually experienced women aged 18 to 44 years was highest in those with the earliest sexual debut (Figure 4).[9]
- Number of Sex Partners: Several studies have shown a correlation with a greater number of sex partners and risk of PID. Most recently, in NHANES 2013-2014, the lifetime PID prevalence was approximately three times greater in women with 10 or more lifetime vaginal sex partners than in women with one partner (Figure 5).[9]
- **Condom Use**: In a study of 684 sexually active women with PID who were followed for a mean duration of 35 weeks, consistent condom use (about 60% of encounters) reduced the risk of recurrent PID, chronic pelvic pain, and infertility by 30 to 60%.[20]

- Screening for Chlamydia: Several studies have shown that screening young, sexually active women for cervical chlamydial infection, with treatment of chlamydia for those who test positive, can substantially reduce the incidence of PID.[21,22]
- **History of PID**: A prior history of PID increases the risk of developing recurrent infection.[23] The damage that occurs to the fallopian tube mucosa during an episode of PID makes women more susceptible to recurrent infection. Likewise, a history of a gonococcal or chlamydial infection increases the likelihood of recurrent disease, which then increases the risk for PID.
- Vaginal Douching: Douching is thought to increase the risk for PID because it contributes to vaginal flora changes, epithelial damage, and disruption of the cervical mucous barrier, all of which can increase the likelihood of developing PID.[<u>17,18</u>] The relationship between douching has been called into question in more recent studies, and the recommendation for or against vaginal douching is currently subject to debate.[<u>24</u>] The relationship of bacterial vaginosis to PID is similarly unclear. Although the anaerobic bacteria associated with BV have also been detected in the upper genital tract in association with PID, epidemiologic analyses have not consistently shown a clear association between BV and development of PID.[<u>24</u>]
- **Recent Placement of Intrauterine Device (IUD)**: The insertion of an intrauterine device (IUD) has been shown to increase the risk of PID approximately 6-fold within the first 21 days of placement, but after 21 days, the risk returns to baseline.[25,26,27] In 2016, the United States Medical Eligibility Criteria for Contraceptive Use (US MEC) recommended that mucopurulent cervicitis or current *N. gonorrhoeae* or *C. trachomatis* infection are contraindications to IUD insertion.[28] This recommendation has been controversial as several studies have noted rates of PID among new IUD users that were 1% or lower, regardless of whether they tested positive for *N. gonorrhoeae* and/or *C. trachomatis*.[29,30]

[Q] Factors Associated with PID

Microbiology and Pathogenesis

Organisms Associated with PID

The organisms associated with PID depend on whether the PID is acute (duration of 30 days or less) or chronic (duration of 30 days or more) (Table 1).[1] Most cases of acute PID are polymicrobial, but in many cases, no pathogen is identified.[3,19,31] The most common pathogens identified with acute PID are *N. gonorrhoeae* and *C. trachomatis*; earlier studies identified one (or both) of these pathogens in approximately 50% of cases of PID.[32,33,34] More recently, the spectrum of organisms identified that cause PID has expanded and the proportion of cases caused by *N. gonorrhoeae* or *C. trachomatis* has decreased to less than 50%.[3,35,36] Other microbes that likely cause PID include *Mycoplasma genitalium*, *Trichomonas vaginalis*, bacterial vaginosis-associated species (multiple anaerobic organisms), and, less frequently, bacteria associated with the gastrointestinal tract (*Bacteroides* species, *Escherichia coli*) or respiratory tract (*Streptococcus* species and *Haemophilus influenzae*).[2,3,37] Available data suggest some of these pathogens, particularly *M. genitalium*, cause less severe disease than *N. gonorrhoeae* or *C. trachomatis*.[3] Chronic PID is most often caused by *Mycobacterial tuberculosis* and *Actinomyces* species.[1]

[Q] Bacterial Pathogens and PID

Pathway of Ascendant Infection

The intermittent ascension of microorganisms from the lower genitourinary tract into the endometrial cavity and fallopian tubes likely occurs as a normal physiological phenomenon. Whether these organisms cause PID depends on their viability, number, pathogenicity, and immune defense mechanisms of the host. Host immunogenetic variations have been invoked as contributing factors since bacterial factors do not fully explain the differences observed between individuals in the development of symptoms, and complications are not fully explained by bacterial factors.[<u>38,39</u>]

Pathogenesis of Reproductive Damage

With acute PID, the ascending organisms trigger an inflammatory response that involves the endometrium, fallopian tubes, or the pelvic peritoneum.[1,5] The normal fallopian tube tissue has millions of tiny hair-like cilia that beat in waves that assist in transporting the egg through the tube to the uterine cavity. As a result of inflammation and tissue destruction, the fallopian tube may have a loss of cilia leading to dysregulation of egg transport and increased risk of ectopic pregnancy (Figure 6).[1] The damage and scarring caused by PID may lead to the described sequelae of infertility, ectopic pregnancy, and chronic pelvic pain (Figure 7).[1,40, 41] This can occur even in women who do not report a history of PID symptoms and is often referred to as subclinical PID.[6,42]

Clinical Manifestations

Signs and Symptoms

Women with acute or subacute PID present with a wide array of clinical manifestations that range from asymptomatic or subclinical infection to severe and debilitating symptoms. [1,6,43] Women with acute PID may experience subtle, nonspecific symptoms such as dyspareunia, dysuria, or gastrointestinal symptoms, which they may not attribute to pelvic infection. [44] In this situation, many women do not seek medical care, or they present with these nonspecific findings that may make it challenging for the medical provider to diagnose PID.[6,42] When mild to moderate symptoms of PID do occur, women may describe lower abdominal or pelvic pain that is accentuated with coitus. Other common symptoms include cramping, dysuria, urinary frequency, vaginal discharge, and intermittent or postcoital cervical bleeding. Systemic signs, such as fever, chills, nausea, and vomiting, are often absent in mild to moderate cases. Physical examination findings, if present, can include cervical motion, uterine, or adnexal tenderness.[1,5,7] In severe PID, women may appear very ill and may have additional findings of fever, chills, purulent vaginal discharge, nausea, and vomiting.

Alternative and Overlapping Diagnoses

Since many women with PID present with nonspecific clinical manifestations, it is important to consider other diseases that may overlap and appear similar to PID. The main considerations for alternative and overlapping diagnoses are appendicitis, ectopic pregnancy, endometriosis, endometritis, ovarian cyst (with or without rupture), nephrolithiasis, and urinary tract infection.[5] A thorough clinical evaluation with appropriate laboratory tests can usually differentiate these processes from PID.

Acute and Subacute Complications Associated with PID

Women with acute PID can develop a range of inflammatory complications, including local tissue damage, fallopian tube swelling, tubal occlusion, and development of adhesions (<u>Figure 8</u>).[<u>44,45</u>]

- **Fitz-Hugh-Curtis Syndrome**: The inflammatory process with PID can extend to the liver capsule, a process commonly referred to as perihepatitis or the Fitz-Hugh-Curtis syndrome.[5,46] The hepatic capsular inflammation can also be associated with adhesions. An estimated 1 to 30% of women with PID develop this complication.[47] Women with Fitz-Hugh-Curtis syndrome typically present with right upper quadrant pain that is usually accentuated with movement or inspiration. Abdominal ultrasonography or contrast computed tomography can support the diagnosis with a finding of increased perihepatic enhancement, usually of the right lobe of the liver; imaging can also help to rule out other causes of right upper quadrant pain.[46] Direct visualization with laparoscopy can confirm the diagnosis by showing characteristic violin string-like adhesions between the liver and the anterior abdominal wall.[47]
- **Tubo-ovarian Abscess**: Tubo-ovarian abscess is an inflammatory mass involving a fallopian tube, ovary, or both, that is characterized by the presence of abundant pus.[45] It is a known complication of PID and has been reported in approximately 30% of women hospitalized with PID.[48] The most common clinical manifestations associated with tubo-ovarian abscess are abdominal or pelvic pain, fever, vaginal discharge, nausea, and abnormal vaginal bleeding; approximately 25% will have a normal white blood cell count.[48,49] The reproductive outcome for women with tubo-ovarian abscess depends on whether surgical intervention is required and whether intraabdominal rupture occurs. If intraabdominal rupture is suspected, and women are treated with fertility-preserving, conservative surgery, the reported subsequent pregnancy rate is 25%. For women without rupture who are treated with medical management alone, reported pregnancy rates vary between 4% and 15%.[45] One retrospective cohort study of women hospitalized with PID or tubo-ovarian abscess found that 25.5% of women subsequently met the criteria of infertility, 16.0% had recurrent PID, and 13.8% reported chronic pelvic pain.[50]

Chronic Sequelae Associated with PID

The sequelae of PID, including ectopic pregnancy, infertility, or chronic pelvic pain, may occur after a single episode of symptomatic PID. In addition, available data suggest women with subclinical PID can develop long-term sequelae, including infertility.[6,42] The development of "silent PID" poses a major diagnostic and treatment challenge.[7] Appropriate therapy has been shown to significantly decrease the rate of long-term sequelae.[51] In contrast, delays in therapy for PID or repeated episodes of PID significantly increase the risk of developing long-term complications.[33,52,53]

- **Tubal Infertility**: Infertility is typically defined as the inability to conceive after 1 year of attempting to become pregnant. In several PID treatment studies that enrolled women with mild-to-moderate PID, 16 to 18% of women reported infertility.[33,53] Tubal infertility increases with multiple episodes of PID or more severe cases of PID.[53]
- **Ectopic Pregnancy**: In one PID treatment study, among women with documented salpingitis, the subsequent risk of ectopic pregnancy was 9%.[53]
- **Chronic Pelvic Pain**: Following treatment of PID, chronic pelvic pain is common; one large PID treatment study reported 29% of women had chronic pelvic pain (pain reported at two or more consecutive visits 3 to 4 months apart during a period of 2 to 5 years) after receiving treatment for PID.[<u>33</u>]

[Q] Chronic Sequelae of PID

Diagnosis

Due to the difficulty of diagnosis and the potential for damage to the reproductive health of women, health care providers should maintain a high index of suspicion for PID.[33] Acute PID is difficult to diagnose due to the wide range of clinical presentations associated with the illness. No single physical finding, image, or laboratory test can reliably make a definitive diagnosis.[54] Given the importance of prompt diagnosis and treatment of PID, the initial diagnosis is often made based on clinical findings.[7,55] Several studies suggest the sensitivity of a clinical diagnosis for symptomatic PID, when compared with laparoscopy, is in the range of 65 to 90%.[56,57,58,59]

Recommended Initial Diagnostic Evaluation

Routine initial laboratory testing for women with possible PID should include saline microscopy of vaginal fluid, nucleic acid amplification testing (NAAT) for chlamydia and gonorrhea, urinalysis (with culture if indicated), and pregnancy test.[7] If there is a need to increase the diagnostic specificity for PID, especially if using CDC criteria, additional initial studies should include a complete blood count, C-reactive protein, and erythrocyte sedimentation rate. The role of testing for *M. genitalium* infection in the initial evaluation of PID is unknown.[7] Radiographic imaging and laparoscopy can help to confirm a clinical diagnosis of PID, and obtaining samples for culture during laparoscopy can also provide a microbiologic diagnosis. In many situations, laparoscopy may not be indicated or available. In addition to the diagnostic evaluation, all persons who possibly have PID should have syphilis and HIV testing as part of their initial evaluation.[7]

Diagnostic Criteria

The following summarizes the main criteria recommended in the 2021 STI Treatment Guidelines for making a diagnosis of PID, including criteria for initiating presumptive treatment.[7]

Criteria for Initiating Presumptive Treatment for PID

- Presumptive PID treatment should be initiated for sexually active young women and other women at risk for STIs who are experiencing pelvic or lower abdominal pain unexplained by another illness **AND** they meet at least one of the following three clinical criteria on pelvic examination:
 - Cervical motion tenderness, or
 - Uterine tenderness or
 - Adnexal tenderness

Additional Clinical Criteria

- One or more of the following additional criteria can be used to enhance the specificity of the minimum clinical criteria to support a diagnosis of PID.
 - Oral temperature greater than 38.3°C (greater than 101°F)
 - Abnormal cervical mucopurulent discharge or cervical friability
 - Presence of abundant numbers of white blood cells on saline microscopy of vaginal fluid
 - Elevated erythrocyte sedimentation rate
 - Elevated C-reactive protein
 - Laboratory documentation of cervical infection with N. gonorrhoeae or C. trachomatis

Specific Diagnostic Criteria

• In some women with suspected PID, more extensive evaluation, such as radiographic imaging, biopsy, or laparoscopy, is warranted. Endometrial biopsy is indicated in women who are undergoing laparoscopy but do not have visual evidence of salpingitis; in this situation, endometritis may be the only objective sign of PID. The following summarizes specific criteria used to make a diagnosis of PID if

biopsy, radiographic, or laparoscopic procedures are performed.

- Endometrial biopsy with histopathologic evidence of endometritis, or
- Transvaginal sonography or magnetic resonance imaging techniques showing thickened, fluidfilled tubes with or without free pelvic fluid or tubo-ovarian complex, or Doppler studies suggesting pelvic infection (e.g. tubal hyperemia), *or*
- Laparoscopic findings consistent with PID.[7]

[Q] Minimal Clinical Criteria

Reporting Requirements

Although there is no specific reporting requirement for PID, laws and regulations in all states require that clinicians, laboratories, or both, report persons with PID who have a positive test for gonorrhea or chlamydia to public health authorities.

Treatment

General Considerations for Treatment

Clinicians should have a low threshold for diagnosing and promptly treating PID in sexually active women with pelvic or lower abdominal pain.[7] Treatment should not be withheld while waiting for STI testing results.[5] Timely administration of antimicrobial therapy improves outcomes and reduces the risk of long-term adverse sequelae. In a case-control study that included 443 women with PID, delayed care (treatment 3 or more days after onset of abdominal pain) was associated with a 3-fold increase in infertility or ectopic pregnancy.[52] The empiric treatment regimens should provide broad-spectrum coverage of the likely causative pathogens, most notably *N. gonorrhoeae*, *C. trachomatis*, and anaerobic organisms. A negative endocervical, vaginal, or urine screening for gonorrhea and chlamydia does not rule out upper genital tract infection with these pathogens. The importance of empirically treating *M. genitalium* is unknown, and most regimens do not provide reliable treatment for *M. genitalium*; if treatment for *M. genitalium* is indicated, moxifloxacin is the treatment of choice.[7] Multiple parenteral, oral, and parenteral-oral combination antimicrobial regimens have been effective in achieving clinical and microbiologic cure in clinical trials.[60,61,62,63,64,65] Depending on the severity of the clinical illness, there are sufficient data to support treatment of PID with oral regimens, parenteral antimicrobials, or a combination of both.[1,7,35,66]

Hospital Admission Criteria with Acute PID

The decision of whether to hospitalize for more intense monitoring and treatment can be challenging. This decision should be made based on the medical provider's clinical judgment in conjunction with assessment for criteria that strongly indicate a need for inpatient monitoring and care. The following are suggested criteria for the hospitalization of women with PID.[$\underline{7}$]

- Inability to exclude surgical emergencies (e.g. appendicitis, ectopic pregnancy)
- Tubo-ovarian abscess
- Pregnancy
- Severe illness, nausea and vomiting, or temperature greater than 38.5°C (101°F)
- Inability to follow or tolerate an outpatient oral regimen
- Nonresponse to oral therapy, as defined by failure to respond clinically to outpatient antimicrobial therapy within 48 to 72 hours

[Q] Criteria for Hospitalization

Parenteral Treatment

Multiple randomized trials have demonstrated the efficacy of parenteral regimens for treatment of acute PID.[35,63,65,66,67] For initial parenteral therapy for PID, there are three recommended and two alternative regimens (Table 2).[7] The three recommended parenteral regimens consist of a cephalosporin plus doxycycline, with or without metronidazole (depending on the cephalosporin):

- Ceftriaxone plus doxycycline plus metronidazole, or
- Cefotetan plus doxycycline, or
- Cefoxitin plus doxycycline

The ceftriaxone plus doxycycline regimen requires the addition of metronidazole to provide adequate activity against anaerobic organisms. With the other two recommended regimens (cefotetan plus doxycycline or cefoxitin plus doxycycline), the addition of metronidazole is not necessary because cefotetan and cefoxitin both have strong anti-anaerobic activity. If the person receiving treatment is able to reliably tolerate oral administration of medications, administering doxycycline orally is preferred over intravenously to avoid pain that can be associated with doxycycline infusions. Within 24 to 48 hours of clinical improvement, therapy can

be transitioned from parenteral to oral therapy to complete 14 days of antimicrobial treatment.[7] For persons with a severe cephalosporin allergy, the alternative regimen of clindamycin plus gentamicin is an option for parenteral therapy.

[Q] Parenteral Regimen for PID Therapy

Intramuscular/Oral Treatment

Intramuscular/oral therapy can be considered for women with mild-to-moderately severe acute PID because the clinical outcomes among women treated with the recommended regimens are similar to those treated with intravenous therapy (a cephalosporin plus doxycycline, with or without metronidazole depending on the cephalosporin) (Table 3).[33,62,67] Women receiving oral therapy for PID should have follow-up within 72 hours, at which time they should show substantial clinical improvement. If no improvement occurs by 72 hours, reevaluation should take place to confirm the diagnosis, and the oral regimen should be switched to parenteral therapy, usually in the inpatient setting.[7] There are published data for several alternative regimens, but these alternative regimens should only be considered for use if the person diagnosed with PID has a cephalosporin allergy, the community prevalence and individual risk for gonorrhea are low, and follow-up is likely.[68,69,70,71] If *N. gonorrhoeae* infection is identified on NAAT or is isolated in culture and shown to be fluoroquinolone-resistant, then consultation with an infectious diseases specialist is advised to guide therapy and follow-up. Limited data suggest options for alternative regimens in the setting of low risk for gonorrhea could include:

- Moxifloxacin 400 mg orally once daily for 14 days, [69,71,72] or
- Levofloxacin 500 mg orally once daily plus metronidazole 500 mg orally twice daily for 14 days, [69] or
- Azithromycin 500 mg daily intravenously for 1-2 days, followed by 250 mg orally daily to complete 7 days plus metronidazole 500 mg orally 2-3 times a day for 12-14 days[<u>68</u>], or
- Azithromycin 500 mg daily intravenously for 1-2 days, followed by 250 mg orally daily to complete 7 days[<u>68,73</u>]

Management of PID in Adolescents and Young Adults

There are no studies that have shown adolescents and young adults with PID have better outcomes with hospitalization versus management in the outpatient setting. In addition, available data suggest that adolescents with PID have similar clinical response rates as older women when both are treated in an outpatient setting.[7] Therefore, adolescents should receive the same treatment approach as older women, taking into account whether the adolescent can adhere to outpatient management and present to care for follow-up.[7] Although the treatment approach with adolescents is usually the same as with adults, it is important to consider adolescents may have barriers to diagnosis and care for PID, such as lack of awareness, confidentiality concerns, and difficulties accessing care.[74] Recently, the Technology Enhanced Community Health Nursing (TECH-N) model has been shown to be a feasible and acceptable intervention that can support precision PID management for adolescents and young adults.[75,76] This program provides community health nursing education, daily text medication reminders, and a follow-up visit by a community health nurse after 3 to 5 days of treatment.[75,76] The goal of this program is to provide adolescents and young adults with a cost-effective nursing approach to enhance PID care and reduce disparities.[75,76]

Management of PID in Women with HIV

The management of PID in women with HIV is generally the same as in women without HIV. Early observational study data suggest that some women with HIV and PID have an altered immune response to an upper genital tract infection, which may contribute to a reduced response to antimicrobial therapy, longer hospital courses, greater risk of tubo-ovarian abscess, and a higher rate of required surgical intervention.[77,78,79,80] Other studies, however, have indicated that women with HIV have similar symptoms, manifestations, and treatment responses as women without HIV.[80,81,82]

Management of Tubo-Ovarian Abscess

Women with suspected or diagnosed tubo-ovarian abscess should undergo hospitalization for intensive management, including prompt receipt of intravenous antimicrobial therapy and expert consultation. A minimum of 24 hours of inpatient observation is recommended for women with a tubo-ovarian abscess.[7] The antimicrobial regimens used to treat tubo-ovarian abscess are usually consistent with recommended parenteral PID regimens.[7] Radiographic imaging can confirm the presence of a tubo-ovarian abscess, and it can be used to track response to therapy. In some women, further intervention may be needed, particularly if there are signs of rupture, evidence of hemodynamic instability, the presence of a large tubo-ovarian abscess (7 cm or greater), or there is poor response to medical therapy. The most common indications for surgery (or image-guided drainage) are failure to improve clinically or evidence of a persistent abscess on interval imaging. Notably, 85% of abscesses with a diameter of 4 to 6 cm resolve with antibiotic therapy alone, whereas only 40% of those 10 cm or larger respond.[83] An estimated 15% of women with PID and tubo-ovarian abscess will experience spontaneous rupture of the abscess, which can be life-threatening and requires emergency surgery.[45,84]

Recent Placement of Intrauterine Device (IUD)

For women who develop PID after a recent IUD insertion, treatment for PID can be initiated without removal of the IUD if close follow-up is arranged.[7,28] If, however, there is no clinical improvement after 48 to 72 hours of antimicrobial treatment, then consideration should be given to removing the IUD.[7]

Follow-Up

Women with PID managed in the outpatient setting should be reexamined within 72 hours after initiation of therapy, and ideally, they should have a substantial clinical improvement in this time frame, typically manifested as resolution of fever, reduction in rebound or direct abdominal tenderness, and diminution in uterine, adnexal, and cervical motion tenderness. Women who do not improve usually require hospitalization, additional diagnostic tests, and possible surgical intervention. Women diagnosed with chlamydial or gonococcal infections have a high rate of reinfection within 6 months of treatment. Retesting of all women with PID who have been diagnosed with chlamydia or gonorrhea is recommended 3 months after treatment, regardless of whether their sex partners were treated.[7] If retesting at 3 months is not feasible, then retesting should at least occur within 1 year after their treatment.[7] There are no specific recommendations for follow-up regarding possible long-term sequelae after treatment for PID or tubo-ovarian abscess.

[Q] Follow-Up for PID

Management of Sex Partners

All sex partners during the 60 days preceding onset of the woman's PID symptoms or diagnosis should be examined, tested, and presumptively treated for gonorrhea and chlamydia, regardless of the pathogens identified.[7] If the woman's last sex partner was more than 60 days before onset of symptoms or diagnosis, then her most recent sex partner should be treated. Expedited partner therapy may be utilized if partner treatment is unlikely to occur. Such evaluation and treatment are imperative because of the risk for reinfection and the strong likelihood of gonococcal or chlamydial infection in the sex partner. Patients (and ideally partners) should be counseled that:

- Male partners of women who have PID caused by *C. trachomatis* or *N. gonorrhoeae* are often asymptomatic.
- Sex partners of women with PID should be treated empirically with regimens effective against both *C*. *trachomatis* and *N*. *gonorrhoeae*, regardless of the apparent etiology of PID or pathogens isolated from the woman with PID.

[Q] Management of Sex Partners of Women with PID

Counseling and Education

The following summarizes key counseling messages for women diagnosed with PID.

- **Resuming Sexual Activity**: Women treated for PID should receive instructions to abstain from sexual activity until all the following criteria are met: (1) they have completed treatment for PID, (2) symptoms have resolved, and (3) their sex partners have received appropriate treatment.
- **Partner Notification**: It is extremely important that women treated for PID understand the importance of partner notification (for all sex partners in the prior 60 days). Partner notification with evaluation and treatment can markedly reduce the spread of STIs in the community, and it also reduces the woman's likelihood of reinfection and recurrence of PID.
- **Follow-Up Testing**: It is important that all persons treated for PID have a follow-up visit in approximately 3 months for repeat STI testing.
- **STI Prevention**: At the time the woman is receiving treatment for PID, it is appropriate to provide counseling messages for her on how to prevent STIs in the future (e.g. limiting the number of sex partners and consistently using condoms).
- **Natural History Following Diagnosis of PID**: Women should receive counseling that recurrences of PID may occur. In addition, they should receive counseling that they may experience longer-term complications of PID, including ectopic pregnancy, chronic pelvic pain, and infertility.

Summary Points

- Pelvic inflammatory disease (PID) is a clinical syndrome comprising a spectrum of infectious and inflammatory diseases characterized by ascending spread of organisms from the vagina or cervix to the structures of the upper female genital tract, which may result in endometritis, salpingitis, tubo-ovarian abscess, or perihepatitis.
- Multiple sex partners, age younger than 25 years, and current or prior infection with gonorrhea or chlamydia have consistently been demonstrated to be significant factors associated with enhanced risk of developing PID. The trend of decreasing PID since the year 2009 is likely attributed to an increase in effective screening and treatment of chlamydial and gonococcal infections in adolescents and young women.
- Most cases of PID are polymicrobial, most commonly caused by *N. gonorrhoeae* or *C. trachomatis* (or both). Other microbes associated with PID include *M. genitalium*, *T. vaginalis*, bacterial vaginosis-associated species, and, less frequently, some gastrointestinal and respiratory organisms.
- Acute sequelae of PID include tubo-ovarian abscess and perihepatitis. Long-term sequelae include ectopic pregnancy, infertility, or chronic pelvic pain.
- No single physical examination finding, image, or laboratory test can reliably make a definitive diagnosis; a combination of clinical criteria and laboratory results should be utilized in making the diagnosis of PID.
- The evaluation for PID should include NAAT testing for chlamydia and gonorrhea, saline microscopy of vaginal fluid, urinalysis, and pregnancy testing. All persons diagnosed with PID should also have HIV and syphilis testing.
- Prompt presumptive PID treatment should be initiated for sexually active young women (and other women at risk for STIs) if they are experiencing pelvic or lower abdominal pain, if no cause for the illness other than PID can be identified, or if one or more minimum clinical criteria are met.
- Multiple effective oral, intramuscular, and intravenous treatment regimens are available for the treatment of PID.
- All women with PID should be reexamined within 72 hours after initiation of therapy, and they should ideally demonstrate substantial clinical improvement within that time frame.
- All recent sex partners of women with PID should receive evaluation and empiric treatment for chlamydia and gonorrhea, regardless of the pathogens identified in the woman with PID. Repeat testing for chlamydia and gonorrhea should be performed 3 months after PID treatment to screen for reinfection.

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Figures

Figure 1 Clinical Classification of Pelvic Inflammatory Disease

Source: Brunham RC, Gottlieb SL, Paavonen J. Pelvic inflammatory disease. N Engl J Med. 2015;372:2039-48.

Clinical Classification for Pelvic	Inflammatory Disease (PID)
PID Clinical Syndrome	Duration of Clinical Symptoms
Acute	Duration ≤30 Days
Subclinical	No symptoms and duration unknown
Chronic	Duration >30 Days

Figure 2 Pelvic Inflammatory Disease: Initial Visits to Physicians Offices

This graphic shows the initial visits to physicians' offices among women with PID 15-44 years of age in the United States, during the years 2006-2016. These visits exclude PID follow-up visits. These data are from the National Disease Therapeutic Index (NDTI) dataset.

Source: Kreisel KM, Llata E, Haderxhanaj L, et al. The burden of and trends in pelvic inflammatory disease in the United States, 2006-2016. J Infect Dis. 2021;224:S103-S112.

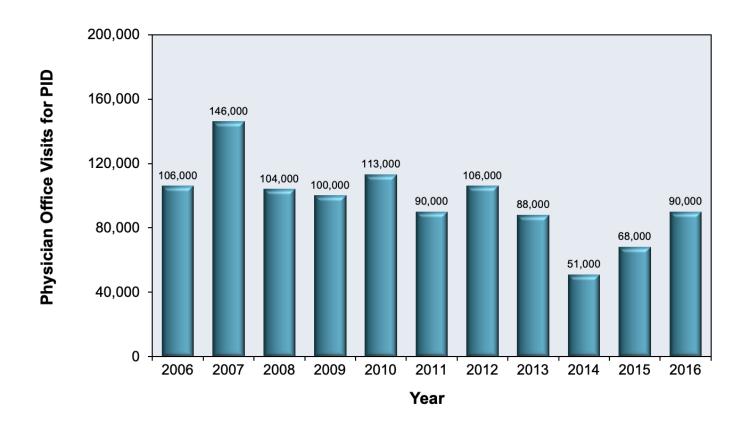


Figure 3 Pelvic Inflammatory Disease: Initial Visits to Emergency Departments

This graphic shows the initial visits to physicians' offices among women with PID 15-44 years of age in the United States during the years 2006-2016. These visits exclude PID follow-up visits. These data are from two nationally representative emergency department visit datasets (Healthcare Cost and Utilization Project-Nationwide Emergency Department Sample (HCUP-NEDS).

Source: Kreisel KM, Llata E, Haderxhanaj L, et al. The burden of and trends in pelvic inflammatory disease in the United States, 2006-2016. J Infect Dis. 2021;224:S103-S112.

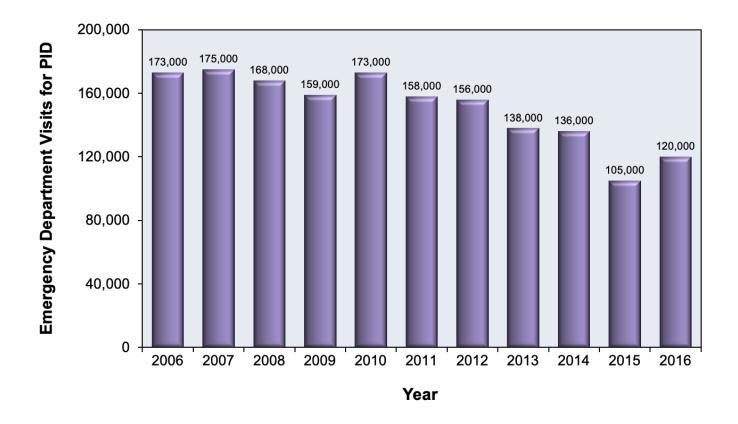
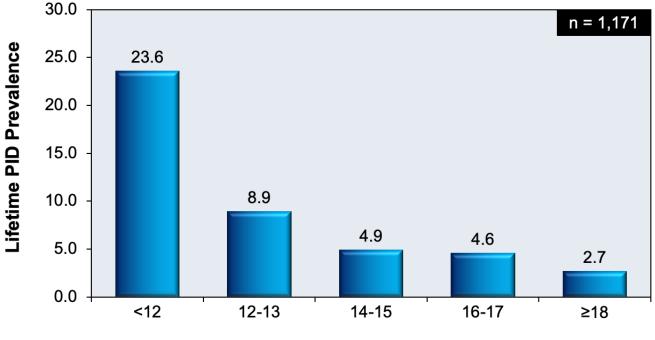


Figure 4 Prevalence of Self-Reported Lifetime PID and Age of Sexual Debut

In the National Health and Nutrition Examination Survey (NHANES) 2013-2014, a total of 1,171 sexually experienced women 18 to 44 years of age were interviewed regarding a lifetime diagnosis of PID. This graph shows the correlation of age of sexual debut and lifetime prevalence of PID.

Source: Kreisel K, Torrone E, Bernstein K, Hong J, Gorwitz R. Prevalence of Pelvic Inflammatory Disease in Sexually Experienced Women of Reproductive Age - United States, 2013-2014. MMWR Morb Mortal Wkly Rep. 2017;66:80-3.

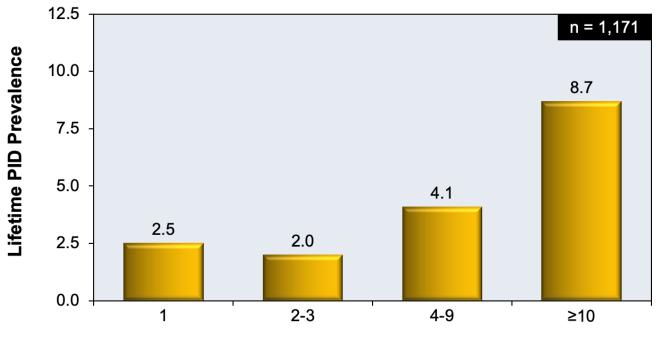


Age at Sexual Debut in Years

Figure 5 Prevalence of Self-Reported Lifetime PID and Number of Sexual Partners

In the National Health and Nutrition Examination Survey (NHANES) 2013-2014, a total of 1,171 sexually experienced women 18 to 44 years of age were interviewed regarding a lifetime diagnosis of PID. This graph shows the correlation of number of male lifetime vaginal sex partners and lifetime prevalence of PID.

Source: Kreisel K, Torrone E, Bernstein K, Hong J, Gorwitz R. Prevalence of Pelvic Inflammatory Disease in Sexually Experienced Women of Reproductive Age - United States, 2013-2014. MMWR Morb Mortal Wkly Rep. 2017;66:80-3.



Number of Male Lifetime Vaginal Sex Partners

Figure 6 Pathologic Changes in the Epithelial Surface of the Fallopian Tube after Pelvic Inflammatory Disease

Scanning electron micrographs show normal human fallopian tube epithelia (Panel A) and the epithelial surface after pelvic inflammatory disease (Panel B). Pelvic inflammatory disease causes a selective loss of ciliated epithelial cells, which interferes with intratubal ovum transport, resulting in infertility or ectopic pregnancy. Original images Dorothy L. Patton, University of Washington, Seattle.

Source: Brunham RC, Gottlieb SL, Paavonen J. Pelvic inflammatory disease. N Engl J Med. 2015;372:2039-48. Reproduced with permission. Massachusetts Medical Society. ©2015.

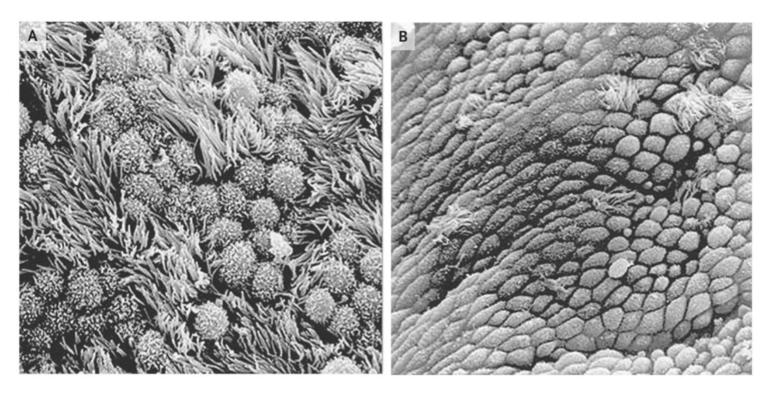


Figure 7 Pelvic Inflammatory Disease and Reproductive Damage

Pelvic inflammatory disease in women caused by *C. trachomatis* (sites of infection shown) can result in tubal factor infertility, ectopic pregnancy, and chronic pelvic pain.

Source: Brunham RC. Immunology. A Chlamydia vaccine on the horizon. Science. 2015;348:1322-3. Illustration by C. Bickel/Science. Reproduced with permission from AAAS. This image may not be reproduced without permission from AAAS publisher.

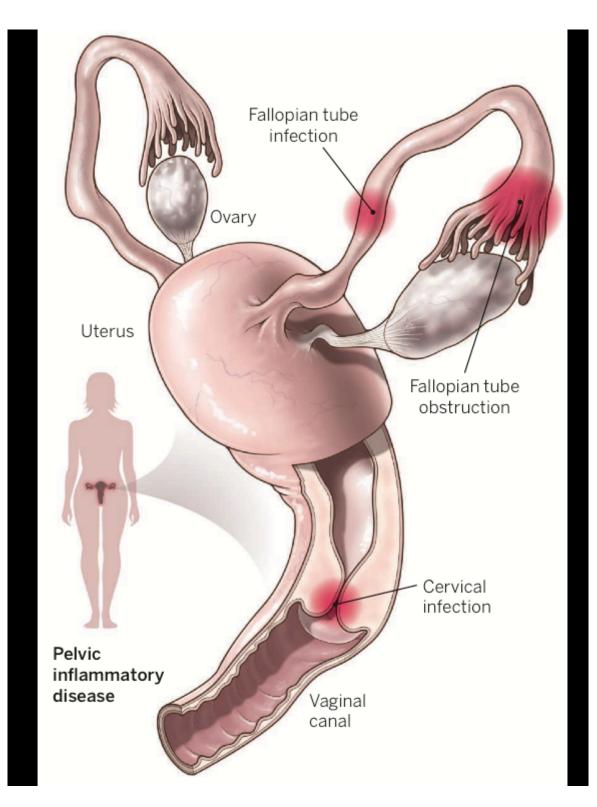
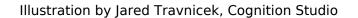


Figure 8 Acute Salpingitis with Pelvic Inflammatory Disease

With acute PID women may develop salpingitis and marked fallopian tube swelling. This may be accompanied by fallopian adhesions, tube obstruction, and the development of a tubo-ovarian abscess.



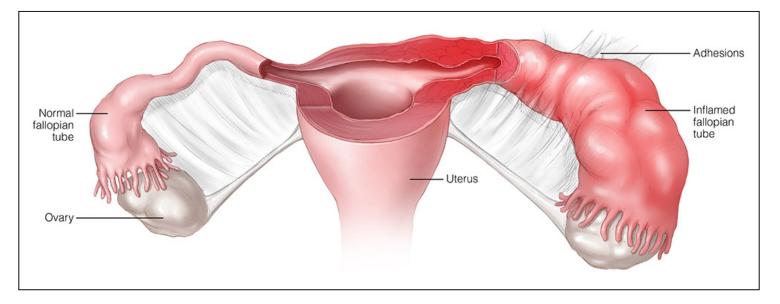


Table 1.

Clinical Classification of Pelvic Inflammatory Disease and Likely Microbial Causes

with permission.
Cervical pathogens (Neisseria gonorrhoeae, Chlamydia trachomatis, and Mycoplasma genitalium)
Bacterial vaginosis pathogens (<i>Peptostreptococcus</i> species, <i>Bacteroides</i> species, <i>Atopobium</i> species, <i>Leptotrichia</i> species, <i>M. hominis, Ureaplasma</i> <i>urealyticum,</i> and <i>Clostridia</i> species)
Respiratory pathogens (<i>Haemophilus influenzae,</i> <i>Streptococcus pneumoniae,</i> group A streptococci, and <i>Staphylococcus aureus</i>)
Enteric pathogens (<i>Escherichia coli, Bacteroides fragilis,</i> group B streptococci, and <i>Campylobacter</i> species)
C. trachomatis and N. gonorrhoeae
Mycobacterium tuberculosis and Actinomyces species

• Brunham RC, Gottlieb SL, Paavonen J. Pelvic inflammatory disease. N Engl J Med. 2015;372:2039-48. [PubMed Abstract]

Table 2. 2021 STI Treatment Guidelines: Pelvic Inflammatory Disease (PID)Parenteral Regimens

Clinical experience should guide decisions regarding transition to oral therapy, which usually can be initiated within 24–48 hours of clinical improvement. The oral regimen should be based on the initial parenteral regimen, as outlined below. In women with tubo-ovarian abscesses, at least 24 hours of inpatient observation is recommended.

Ceftriaxone	+	Doxycycline	+	Metronidazole	
1 g IV every 24 hours	•	100 mg orally or IV eve 12 hours*	ery	500 mg orally or IV every 12 hours^	
	ed ins	tead of IV for wome	en witho	out severe illness or tub	al metronidazole is well absorbed o-ovarian abscess when possible oned to oral therapy with
	twice				mplete 14 days of antimicrobial
therapy.		daily plus metronic			
doxycycline 100 mg therapy. Recommended Reg Cefotetan 2 g IV every 12 hours		daily plus metronic ns Do	dazole 5 xycycli	500 mg twice daily to co	

therapy.

Recommended Regimens			
Cefoxitin	⊥ Do	xycycline	
2 g IV every 6 hours	T 100	mg orally or IV every 12 hours	

Because of the pain associated with intravenous infusion, doxycycline should be administered orally when possible. Oral and IV administration of doxycycline provide similar bioavailability.

Note: Within 24 to 48 hours of clinical improvement, therapy can be transitioned to oral therapy with doxycycline 100 mg twice daily plus metronidazole 500 mg twice daily to complete 14 days of antimicrobial therapy.

Alternative Regimens Ampicillin-Sulbactam

+ Doxycycline

3 g IV every 6 hours

100 mg orally or IV every 12 hours*

*Because of the pain associated with intravenous infusion, doxycycline should be administered orally when possible. Oral and IV administration of doxycycline provide similar bioavailability.

Note: Within 24 to 48 hours of clinical improvement, therapy can be transitioned to oral therapy with doxycycline 100 mg twice daily plus metronidazole 500 mg twice daily to complete 14 days of antimicrobial therapy.

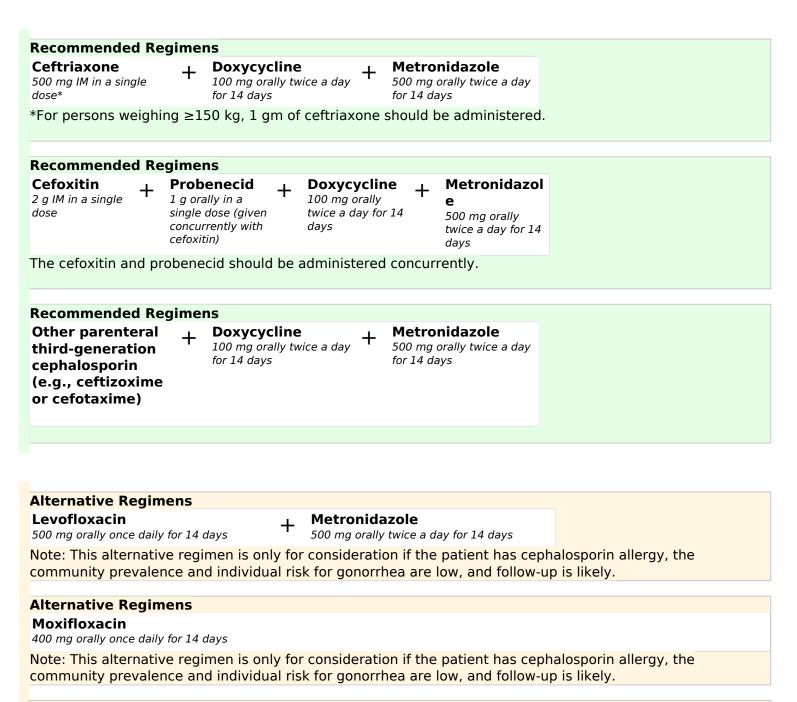
Alternative Regimens		
Clindamycin 900 mg IV every 8 hours	+	Gentamicin loading dose IV or IM (2 mg/kg body weight), followed by a maintenance dose (1.5 mg/kg body weight) every 8 hours; single daily dosing (3-5 mg/kg body weight) can be substituted

Note: Within 24 to 48 hours of clinical improvement, therapy can be transitioned to oral therapy with clindamycin 450 mg four times a day or doxycycline 100 mg twice daily to complete 14 days of antimicrobial therapy.Note: if tubo-ovarian abscess is present, the regimen used when transitioning to oral therapy should consist of doxycycline plus either clindamycin 450 mg four times a day or metronidazole 500 mg twice daily to complete 14 days of antimicrobial therapy.

Source: Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. Pelvic inflammatory disease (PID). MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [2021 STI Treatment Guidelines]

Table 3. 2021 STI Treatment Guidelines: Pelvic Inflammatory Disease (PID)Intramuscular or Oral Regimens

For women with mild-to-moderate acute PID, intramuscular (IM) or oral therapy can be considered because the clinical outcomes among women treated with these regimens are similar to those treated with IV therapy. Women who do not respond to IM/oral therapy within 72 hours should be reevaluated to confirm the diagnosis and should be administered intravenous therapy.



Alternative Regimens

Azithromycin 500 mg IV daily for 1–2 doses, followed by 250 mg orally daily for a total of 7 days

Metronidazole

500 mg orally twice a day for 12-14 days

Note: This alternative regimen is only for consideration if the patient has cephalosporin allergy, the community prevalence and individual risk for gonorrhea are low, and follow-up is likely.

Alternative Regimens

Azithromycin

500 mg IV daily for 1-2 doses, followed by 250 mg orally daily for a total of 7 days

+

Note: This alternative regimen is only for consideration if the patient has cephalosporin allergy, the community prevalence and individual risk for gonorrhea are low, and follow-up is likely.

Source: Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. Pelvic inflammatory disease (PID). MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [2021 STI Treatment Guidelines]

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