Pelvic Inflammatory Disease

Epidemiology

Background

Pelvic inflammatory disease (PID) is a clinical syndrome comprising a spectrum of infectious and inflammatory diseases of the upper female genital tract. The diagnosis of pelvic inflammatory disease (PID) can include any combination of endometritis, salpingitis, tubo-ovarian abscess, or pelvic peritonitis.\[1\] Each of these disease processes is characterized by ascending spread of organisms from the vagina or cervix to the structures of the upper female genital tract. Although PID is most notable for the associated risk of severe, long-term sequelae, the infections may be asymptomatic ("silent") or overt with mild to severe symptoms. The clinical syndrome of acute (and subacute) PID—usually defined as symptoms for fewer than 30 days—can be due to a variety of pathogens, often including, but not limited to, \textit{Neisseria gonorrhoeae} and \textit{Chlamydia trachomatis}.\[2\] In contrast, chronic pelvic inflammatory disease (symptoms for greater than 30 days) is a separate disorder usually related to infection by \textit{Mycobacterium tuberculosis} or \textit{Actinomyces} species (\textbf{Table 1}).\[2\] This module will focus on acute and subacute PID.

Incidence

There is no single diagnostic test for PID and in the United States PID is not a nationally notifiable disease; thus, it can be difficult to accurately estimate the incidence of PID. Review of a national admission database in 2001 estimated more than 750,000 cases of PID occurred in the United States.\[3\] More recent data from the National Health and Nutrition Examination Survey (NHANES) 2013–2014 estimated a prevalence of self-reported lifetime PID of 4.4% among sexually experienced women 18-44 years of age, which corresponds with an estimate of 2.5 million women aged 18-44 years ever having PID in their lifetime.\[4\] Available data point to an overall trend of decline in the incidence of PID in the United States. A review of national insurance claims found a 25.5% decline in cases from 2001 to 2005 (317.0 to 236.0 per 100,000 enrollees).\[5\] The number of initial visits to office-based physicians for PID declined by 71% between 2005 and 2014—from 176,000 visits in 2005 to 51,000 visits in 2014 (\textbf{Figure 1}).\[6\] Data from 1995 through 2013 likewise show a consistent decrease in the lifetime prevalence of treatment for PID and these decreases occurred across multiple racial/ethnic groups (\textbf{Figure 2}).\[6,7\]

The trend of decreasing PID is primarily attributed to an increase in effective screening and treatment of chlamydial and gonococcal infections in adolescents and young women.\[8,9\] Although total rates of infection with \textit{C. trachomatis} have increased in some populations, the rates of PID have consistently fallen. This highlights the effectiveness of treating lower tract chlamydial infections for prevention of progression to upper tract disease. Of note, several studies suggest a decrease in the proportion of cases attributable to
chlamydial infection. As pathogens other than *C. trachomatis* and *N. gonorrhoeae* are becoming more prominent as a cause of PID, the importance of addressing risk behaviors and monitoring for infections caused by these other organisms may become more important.[10]

**Cost**

Despite a decline in the incidence of PID, the cost of treatment remains significant. An analysis performed in 2008 estimated an average direct medical cost of $3,202 per case of PID.[11] In 2000, investigators from the CDC reported their findings estimating direct medical expenditures for PID and three major sequelae (chronic pelvic pain, ectopic pregnancy, and infertility); the estimated overall cost in 1998 for PID was $1.88 billion, including $1.06 billion for inpatient and outpatient direct treatment of PID, $166 million for chronic pelvic pain, $295 million for ectopic pregnancy, and $360 million for infertility associated with PID.[12] These costs have likely decreased somewhat as the incidence of PID has fallen since 2005.

**Risk Factors**

Epidemiologic studies have revealed numerous risk factors associated with pelvic inflammatory disease and many of these risk factors overlap with those known to be associated with acquisition of infections that cause PID. Multiple partners, age younger than 20 years, and current or prior infection with gonorrhea or chlamydia have consistently been demonstrated as significant risk factors.[13] Other possible risk factors include history of PID, male partners with gonorrhea or chlamydia, current douching, insertion of IUD, bacterial vaginosis, and oral contraceptive use.[7,14] The following provides more detail on the major risk factors:

- **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.[13,15] The increased risk of PID in younger women correlates with the high rates of chlamydia and gonorrhea infection 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 sexual debut is also a risk factor for PID. In the NHANES 2013-2014, the lifetime PID prevalence in sexually experienced women aged 18-44 years was higher in those with a younger sexual debut (Figure 3).[4]

- **Number of Sexual Partners:** Several studies have shown a correlation with greater number of sexual 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 4).[4]

- **History of PID:** A prior history of PID increases the risk for developing PID.[16] The damage that occurs to the fallopian tube mucosa during an episode of PID makes women more susceptible to recurrent infection. Having a history of a gonorrheal or chlamydial infection increases the likelihood of recurrent disease, which, in turn, increases the risk for PID. A woman’s risk also increases if her male partner has gonorrhea or chlamydia.

- **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.[7,14] 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.[17] The relationship of bacterial vaginosis (BV) to PID is similarly unclear. Although the anaerobic bacteria associated with BV have 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.[17]

- **Intrauterine Device (IUD):** The insertion of an intrauterine device (IUD) has been shown to increase the risk of PID approximately six-fold within the first 21 days of placement, but after 21 days, the risk returns to baseline.[18] In addition, the CDC describes mucopurulent cervicitis or current *N. gonorrhoeae* and/or *C. trachomatis* infection as “unacceptable health risk” and thus a contraindication
to IUD insertion.[19] Notably, recent studies have revealed that the rates of PID among new IUD users were 1% or below for both those who tested positive for *N. gonorrhoeae* and/or *C. trachomatis* and those who tested negative.[20,21] The authors of these recent studies suggest that women without clinical evidence of active infection can have intrauterine system placement and sexually transmitted infection screening, if indicated, on the same day. This remains an active area of investigation.

- **Oral Contraceptive Use:** Oral contraceptive (OC) use may increase the risk of cervical chlamydial infection due to cervical ectopy associated with OC use. OC use also causes thickening of the cervical mucous, which may be protective against lower genital tract organisms ascending into the upper genital tract. Overall, many providers conclude that since the absolute risk of pelvic infection is small (1.6 cases per 1,000 woman-years in a meta-analysis) the benefits of these birth-control measures likely outweigh the risks.[18]
Microbiology and Pathogenesis

Organisms Associated with PID

Most cases of PID are polymicrobial.[15,22] The most common pathogens identified in women with PID are *N. gonorrhoeae* or *C. trachomatis* (or both); in addition, *N. gonorrhoeae* coinfection increases the risk for ascending, as well as incident chlamydial infection.[23,24,25] Recent studies, however, suggest the proportion of PID cases attributable to these pathogens is decreasing due to widespread screening and treatment of *N. gonorrhoeae* and *C. trachomatis.[26] Other microbes associated with PID include aerobic gram-negative rods (e.g. *E. coli*), anaerobes (*Bacteroides* species, *Prevotella* species, *Peptostreptococcus* species), and gram-positive organisms (*Streptococcus* species). Among women with bacterial vaginosis who develop PID, anaerobic organisms are often identified, but the role of bacterial vaginosis in causing PID remains unclear.[17,27,28] *Mycoplasma genitalium* and *Ureaplasma urealyticum* have also been isolated from the endometrium and fallopian tubes of women with PID. Newer studies suggest that *M. genitalium* may play a role in the pathogenesis of PID and may be associated with milder symptoms than infection with *C. trachomatis* or *N. gonorrhoeae.[29,30,31,32]

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, because inter-individual differences in the development of symptoms and complications are not fully explained by bacterial factors. For example, single nucleotide polymorphisms (SNPs) in Toll-like receptor 1 and 4 genes (innate inflammatory receptor genes) are associated with *C. trachomatis* infection, upper genital tract infection with *C. trachomatis* and/or *N. gonorrhoeae*, and reduced pregnancy rates among African American women with PID.[33] A trend was also identified for TLR2 haplotype I (-16934T/+2477G) to protect against the development of symptoms and tubal pathology after chlamydia infection among Dutch Caucasian women with complaints of subfertility.[34]

Pathogenesis of Reproductive Damage

With acute PID, the ascending organisms trigger an inflammatory response that involves the endometrium, fallopian tubes, or the pelvic peritoneum. The normal fallopian tube tissue has millions of tiny hair-like cilia that beat in waves that assist in the transportation of 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 5). [2] The damage and scarring caused by PID may lead to the described sequelae of infertility, ectopic pregnancy, and chronic pelvic pain (Figure 6).[2,35,36] This can occur even in women who do not report a history of PID symptoms.
Clinical Manifestations

Women with PID present with a wide array of clinical manifestations that range from virtually asymptomatic to severe and debilitating symptoms. Women with acute PID may experience subtle, nonspecific symptoms such as dyspareunia, dysuria, or gastrointestinal symptoms, which they may not attribute to pelvic infection.[37] This leads to a failure to seek care for many patients. When mild to moderate symptoms of PID do occur, women may describe lower abdominal or pelvic pain, cramping, or dysuria. They may also exhibit signs such as intermittent or post-coital vaginal bleeding, vaginal discharge, or fever. Systemic signs, such as fever, chills, nausea, and vomiting are often absent in mild to moderate cases. On physical examination, there may be no external evidence of infection, but uterine tenderness, cervical motion pain, or adnexal tenderness is most often present. In severe PID, women appear very ill with fever, chills, purulent vaginal discharge, nausea, vomiting, and elevated white blood cell count (WBC). Other laboratory indicators, such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), may also be elevated. As seen with mild and moderate disease, uterine tenderness, cervical motion pain, with or without adnexal tenderness are expected. Available data suggest that some women develop subclinical upper genital tract infection that can nevertheless result in long-term sequelae, including infertility;[38, 39] the development of “silent PID” poses a major diagnostic and treatment challenge.[1]

Acute 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 (Figure 7).[37, 40] Although uncommon, the adhesion formation can involve the liver capsule and cause a perihepatitis referred to as the Fitz-Hugh Curtis Syndrome.[41] The development of a tubo-ovarian abscess can occur as a subacute complication of acute PID and some women will have a tubo-ovarian abscess at the time they present with acute PID.[42, 43]

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. One recent retrospective cohort study of women admitted with PID or tubo-ovarian abscess (TOA) found that, in follow-up, 25.5% of women met the criteria of infertility, 16.0% had recurrent PID, and 13.8% reported chronic pelvic pain.[44] Several studies have demonstrated that multiple episodes or more severe cases dramatically increase women’s risk for infertility as well as for ectopic pregnancy.[45] Appropriate therapy has been shown to significantly decrease the rate of long-term sequelae.[46] The risk of ectopic pregnancy is increased 6- to 10-fold after PID. Tubal infertility occurs in 8% of women after one episode of PID, in 20% of women after two episodes, and in 50% of women after three episodes. If a tubo-ovarian abscess is present, the outcome is largely dependent upon whether there is intra-abdominal rupture and what degree of surgical intervention was required. If intra-abdominal rupture is suspected, and patients 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%.[40]
Diagnosis

Due to the difficulty of diagnosis and the potential for damage to the reproductive health of women, health care providers should maintain a low threshold for the diagnosis of PID. [47] 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. [48] Given the importance of prompt diagnosis and treatment, diagnosis is often made based on less precise clinical findings. [1, 49] Laparoscopy can help to help confirm a clinical diagnosis of PID and obtaining samples for culture during laparoscopy can also provide a microbiologic diagnosis. In many clinical settings, however, laparoscopy may not be available and overall laparoscopy is infrequently done in women with suspected acute PID. Prior studies suggest the sensitivity of a clinical diagnosis for symptomatic PID is the range of 65% to 90%. [50, 51, 52, 53] The positive predictive value of a clinical diagnosis (compared to laparoscopy) varies based on the epidemiologic characteristics of the population. Clinical diagnosis has significantly greater positive predictive value among sexually active young women, women at STD clinics, and women in communities with high prevalence of gonorrhea or chlamydia.

STD Guidelines Diagnostic Criteria

The 2015 STD Treatment Guidelines recommend presumptive PID treatment for sexually active young women and other women at risk for STDs if they are experiencing pelvic or lower abdominal pain, if no cause for the illness other than PID can be identified, and if one or more minimum clinical criteria are met. The CDC guidelines recommend including additional criteria that can be used to enhance the specificity of the minimum clinical criteria in support of a diagnosis of PID; the most specific criteria can establish a firm diagnosis, but are not available in many settings (Table 2). [1]
Treatment

General PID Considerations

As noted above, clinicians need a low threshold for treating sexually active women with pelvic or lower abdominal pain and suspected PID. Treatment regimens must provide empiric, broad-spectrum coverage of likely pathogens (\textit{N. gonorrhoeae}, \textit{C. trachomatis}, anaerobes, gram-negative facultative bacteria, and streptococci). Like other invasive bacterial infections such as meningitis and pneumonia, speed of antibiotic administration has been associated with improved outcomes and prevention of progression and long-term sequelae. In a case-control study nested within a Scandinavian cohort, delayed care (treatment 3 or more days after onset of abdominal pain) was associated with a 3-fold increase in infertility or ectopic pregnancy among 443 women with 1 known episode of PID.\textsuperscript{[54]} Several parenteral and oral antimicrobial regimens have been effective in achieving clinical and microbiologic cure in clinical trials.\textsuperscript{[55,56,57,58,59,60,61,62,63,64]} There are sufficient data to support treatment of patients with either oral regimens or parenteral antimicrobials, both of which are recommended by the CDC for the treatment of PID.

Hospital Admission Criteria with Acute PID

The decision of whether to admit for inpatient monitoring can be challenging. The CDC recommends this decision be made based on provider judgment with certain criteria strongly indicating a need for inpatient monitoring and care. The STD guidelines list the following suggested criteria for hospitalization of women with PID.

- Inability to exclude surgical emergencies (e.g. appendicitis, ectopic pregnancy)
- Tubo-ovarian abscess
- Pregnancy
- Severe illness, nausea and vomiting, or high fever
- Nonresponse to oral therapy—defined as failure to respond clinically to outpatient antimicrobial therapy within 48 to 72 hours, or the inability to tolerate an outpatient oral regimen
- Current immunodeficiency (HIV infection with low CD4 cell count, immunosuppressive therapy)

There is no evidence to suggest that adolescents have improved outcomes from hospitalization for treatment of PID, and clinical response rates to outpatient care are similar between younger and older women; the decision to hospitalize adolescents should thus be based on the same criteria used for older women.\textsuperscript{[1]} However, determination of whether adolescents can comply with outpatient management should depend on developmental stage and availability of support systems (such as parent/guardian involvement), and those youth receiving outpatient treatment for PID warrant close monitoring to ensure medication adherence.

Parenteral Treatment

There are several randomized trials demonstrating the efficacy of parenteral regimens for treatment of acute PID.\textsuperscript{[1,57,64,65,66]} Three regimens are recommended as initial parenteral therapy for PID, with subsequent transition to oral therapy based on clinical improvement (usually around 24 to 48 hours of parenteral therapy) (\textbf{Table 3}).\textsuperscript{[1]} Doxycycline may be given via oral route due to pain with IV infusion. For initial parenteral therapy, third-generation cephalosporins (e.g. cefixime, cefotaxime, and ceftriaxone) are less active than cefotetan or cefoxitin against anaerobic bacteria and thus are less preferable. Ampicillin-sulbactam plus doxycycline is considered an alternative initial parenteral regimen; this combination is effective against \textit{C. trachomatis}, \textit{N. gonorrhoeae}, and anaerobes. Short-term studies with ampicillin-sulbactam plus doxycycline have shown similar clinical cure rates as seen with recommended regimens.\textsuperscript{[60]} Limited data support the use of other parenteral regimens.
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 these regimens are similar to those treated with intravenous therapy (Table 4).[47,61,65] All of the oral regimen components should be continued for a total of 14 days. Patients on oral therapy should be followed up within 72 hours, at which time they should show substantial clinical improvement. If no improvement occurs by 72 hours, the patient should be re-evaluated to confirm the diagnosis and should be switched to parenteral therapy, either in an outpatient or inpatient setting.[1] The addition of metronidazole should be considered, as anaerobic organisms are suspected in many cases. Metronidazole will also treat BV, which frequently is associated with PID.

Alternative Intramuscular/Oral Regimens

Azithromycin has shown short-term clinical effectiveness when used as monotherapy (500 mg IV daily for 1 to 2 doses, followed by 250 mg orally daily for 12-14 days) or in combination with metronidazole.[67] Similar efficacy has been reported with ceftriaxone (250 mg IM as a single dose) given with either azithromycin 1 g weekly for 2 weeks or doxycycline twice daily for 14 days.[61] Due to increasing rates of resistance in N. gonorrhoeae, the CDC no longer recommends regimens including a quinolone for routine treatment of PID. In cases of documented cephalosporin allergy, use of levofloxacin 500 mg orally once daily, ofloxacin 400 mg twice daily, or moxifloxacin 400 mg orally once daily with metronidazole for 14 days (500 mg orally twice daily) can be considered.[1,55,58,59,68] If a fluoroquinolone-containing regimen is used, diagnostic tests for gonorrhea must be obtained before instituting therapy. If the culture for gonorrhea is positive, treatment should be based on results of antimicrobial susceptibility testing. If the isolate is determined to be quinolone-resistant N. gonorrhoeae or if antimicrobial susceptibility cannot be assessed (e.g. if only nucleic acid amplification [NAAT] testing is available), consultation with an infectious diseases specialist is recommended.

Management of PID in Women with HIV Infection

The general antimicrobial therapy management of PID in women with HIV infection is the same as in women who are not infected with HIV. Some women with HIV infection 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, and a higher rate of required surgical intervention.[69,70,71,72,73]

Management of Suspected Tubo-Ovarian Abscess

Patients suspected of having a tubo-ovarian abscess should be admitted to the hospital for more intensive management. Patients should promptly receive intravenous antimicrobials to cover gram-negative and gram-positive organisms with consideration of additional coverage for anaerobic organisms. Imaging is helpful to confirm the presence of abscess and to allow tracking for improvement on therapy. The CDC does not recommend a specific regimen for treatment of tubo-ovarian abscess. Combinations of ampicillin, clindamycin, and gentamicin have been used with success in the past.[74] The CDC recommends a minimum of 24 hours of inpatient observation for women with suspected tubo-ovarian abscess. Those that fail to defervesce or improve symptomatically, or have persistent abscess on interval imaging should be evaluated for possible surgical intervention. 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.[75]

Follow-Up

Patients should be reexamined within 72 hours after initiation of therapy and should demonstrate substantial clinical improvement, typically manifested as resolution of fever, reduction in rebound or direct abdominal tenderness, and diminution in uterine, adnexal, and cervical motion tenderness. Patients 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 who have been diagnosed with chlamydia or gonorrhea is recommended 3-6 months after treatment, regardless of whether their sex partners were treated. All women diagnosed with acute PID should be offered HIV testing. There are no specific recommendations for follow-up regarding possible long-term sequelae after treatment for PID or tubo-ovarian abscess. It is thus imperative that patients receive adequate counseling and education at the time of initial diagnosis and treatment.
Patient Counseling and Education

Patient counseling and education should cover the nature of the disease, transmission issues, and risk reduction. Each of these topics is addressed in the sections below.

Nature of the Disease

- Pelvic inflammatory disease may be asymptomatic or symptomatic. Women should be counselled that recurrences may not be symptomatic or may present with different symptoms.
- A prior history of PID increases the risk for future episodes of PID.
- The potential complications of PID include ectopic pregnancy, chronic pelvic pain, and infertility.

Transmission Issues

- Pelvic inflammatory disease can be caused by a number of bacteria, but are most often caused by \textit{N. gonorrhoeae} or \textit{C. trachomatis}.
- \textit{N. gonorrhoeae} or \textit{C. trachomatis} are efficiently transmitted from males to females via vaginal intercourse.
- Patients and their sex partners should abstain from intercourse until at least 7 days after completing therapy and until they and their sex partners no longer have symptoms.

Risk Reduction Performed by the Clinician

- Assess the patient’s behavior change potential.
- Develop individualized risk-reduction plans with the patient for lasting results.
- Discuss prevention strategies such as abstinence, monogamy with an uninfected partner, use of condoms, and limiting the number of sex partners. Latex condoms, when used consistently and correctly, can reduce the risk of transmission of \textit{N. gonorrhoeae} or \textit{C. trachomatis}, and other sexually transmitted pathogens.

Partner Management

All male sex partners who have had contact with a woman with PID during the 60 days preceding onset of the PID symptoms should be examined, tested, and presumptively treated for gonorrhea and chlamydia. If a patient’s last sexual intercourse was more than 60 days before onset of symptoms or diagnosis, the patient’s most recent sex partner should be treated. Expedited partner therapy may be utilized as detailed in the chlamydia module. 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 \textit{C. trachomatis} or \textit{N. gonorrhoeae} are often asymptomatic.
- Sex partners of women with PID should be treated empirically with regimens effective against both \textit{C. trachomatis} and \textit{N. gonorrhoeae}, regardless of the apparent etiology of PID or pathogens isolated from the infected woman.

Reporting Requirements

Although there is no specific reporting requirement for pelvic inflammatory disease, laws and regulations in all states require that clinicians, laboratories, or both report persons with gonorrhea or chlamydia to public health authorities.
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, including endometritis, salpingitis, tubo-ovarian abscess, perihepatitis, or pelvic peritonitis.
- The trend of decreasing PID is primarily attributed to an increase in effective screening and treatment of chlamydial and gonococcal infections in adolescents and young women.
- Multiple partners, age younger than 20 years, and current or prior infection with gonorrhea or chlamydia have consistently been demonstrated to be significant risk factors.
- Most cases of PID are polymicrobial, most commonly caused by *N. gonorrhoeae* or *C. trachomatis* (or both). Other microbes associated with PID include aerobic gram-negative rods (*e.g.* *E. coli*), anaerobes (*Bacteroides* species, *Prevotella* species, and *Peptostreptococcus* species), gram-positive organisms (*Streptococcus* spp), *M. genitalium*, and *U. urealyticum*.
- Sequelae of PID, including ectopic pregnancy, infertility, or chronic pelvic pain may occur after a single episode of symptomatic PID.
- No single physical examination finding, image, or laboratory test can reliably make a definitive diagnosis; the CDC diagnostic criteria should be utilized in making decisions of whether to initiate presumptive treatment for PID.
- The CDC STD guidelines recommend presumptive PID treatment for sexually active young women and other women at risk for STDs if they are experiencing pelvic or lower abdominal pain, if no cause for the illness other than PID can be identified, and if one or more minimum clinical criteria are met.
- Treatment regimens (oral or parenteral) must provide empiric, broad-spectrum coverage of likely pathogens (*N. gonorrhoeae, C. trachomatis*, anaerobes, gram-negative facultative bacteria, and streptococci).
- Patients should be re-examined within 72 hours after initiation of therapy and should demonstrate substantial clinical improvement.
Citations

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Figures

Figure 1 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 2005-2014


<table>
<thead>
<tr>
<th>Year</th>
<th>Visits (in thousands)</th>
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<td>2013</td>
<td>50</td>
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<tr>
<td>2014</td>
<td>40</td>
</tr>
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</table>

NOTE: The relative standard errors for these estimates are 16%-23%.
Figure 2 Pelvic Inflammatory Disease: Trends in Lifetime Prevalence


In NHANES 2013-2014, 1,171 sexually experienced women 18-44 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.

Figure 4 Prevalence of Self-Reported Lifetime PID and Number of Sexual Partners

In NHANES 2013-2014, 1,171 sexually experienced women 18-44 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.

Figure 5 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.

Figure 6 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.

Figure 7 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.

Illustration by Jared Travnicek, Cognition Studio
## Clinical Classification of Pelvic Inflammatory Disease and Likely Microbial Causes

<table>
<thead>
<tr>
<th>Clinical Syndrome</th>
<th>Causes</th>
</tr>
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<tbody>
<tr>
<td>Acute pelvic inflammatory disease (≤30 days' duration)</td>
<td>Cervical pathogens (<em>Neisseria gonorrhoeae</em>, <em>Chlamydia trachomatis</em>, and <em>Mycoplasma genitalium</em>)</td>
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<td>Respiratory pathogens (<em>Haemophilus influenzae</em>, <em>Streptococcus pneumoniae</em>, group A streptococci, and <em>Staphylococcus aureus</em>)</td>
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<td></td>
<td>Enteric pathogens (<em>Escherichia coli</em>, <em>Bacteroides fragilis</em>, group B streptococci, and <em>Campylobacter</em> species)</td>
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<td>Subclinical pelvic inflammatory disease</td>
<td><em>C. trachomatis</em> and <em>N. gonorrhoeae</em></td>
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<td>Chronic pelvic inflammatory disease (&gt;30 days' duration)</td>
<td><em>Mycobacterium tuberculosis</em> and <em>Actinomyces</em> species</td>
</tr>
</tbody>
</table>

Table 2.

**Diagnosis of PID and Criteria for Initiating Presumptive Treatment**

**Criteria for Initiating Presumptive Treatment for PID** — Presumptive treatment for PID in sexually active young women and other women at risk for STDs if they are experiencing pelvic or lower abdominal pain, if no cause for the illness other than PID can be identified, and if one or more of the following minimum clinical criteria are present on pelvic examination:

- Cervical motion tenderness
  
- Uterine tenderness
  
- Adnexal tenderness

**Additional Criteria** - one or more of the following additional criteria can be used to enhance the specificity of the minimum clinical criteria and support a diagnosis of PID:

- Oral temperature >101°F (>38.3°C);
- Abnormal cervical mucopurulent discharge or cervical friability;
- Presence of abundant numbers of WBC 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*

**Most Specific Criteria for the Diagnosis of PID** - a diagnostic evaluation that includes one or more of the following more extensive procedures might be warranted in some cases:

- Endometrial biopsy with histopathologic evidence of endometritis;**
  
  or

- Transvaginal sonography or magnetic resonance imaging techniques showing thickened, fluid-filled tubes with or without free pelvic fluid or tuboovarian complex, or Doppler studies suggesting pelvic infection (e.g. tubal hyperemia);
  
  or

- Laparoscopic findings consistent with PID

* Most women with PID have either mucopurulent cervical discharge or evidence of WBCs on a saline wet prep of vaginal secretions. If no WBCs are found on the wet prep, the diagnosis of PID is unlikely.

** Endometrial biopsy is warranted in women undergoing laparoscopy who do not have visual evidence of salpingitis, because endometritis is the only sign of PID for some women.

Source:

Table 3. 2015 STD 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. In women with tubo-ovarian abscesses, at least 24 hours of inpatient observation is recommended.

<table>
<thead>
<tr>
<th>Recommended Parenteral Regimens</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cefotetan</strong> 2 g IV every 12 hours</td>
<td><strong>Doxycycline</strong> 100 mg orally or IV every 12 hours</td>
</tr>
</tbody>
</table>

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: Oral therapy with doxycycline 100 mg twice daily can be used 24-48 hours after clinical improvement to complete the 14 days of therapy. When tubo-ovarian abscess is present, clindamycin (450 mg orally four times daily) or metronidazole (500 mg twice daily) should be used to complete at least 14 days of therapy with doxycycline to provide more effective anaerobic coverage than doxycycline alone.

<table>
<thead>
<tr>
<th>Recommended Parenteral Regimens</th>
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</tr>
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<tbody>
<tr>
<td><strong>Cefoxitin</strong> 2 g IV every 6 hours</td>
<td><strong>Doxycycline</strong> 100 mg orally or IV every 12 hours</td>
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</table>

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: Oral therapy with doxycycline 100 mg twice daily can be used 24-48 hours after clinical improvement to complete the 14 days of therapy. When tubo-ovarian abscess is present, clindamycin (450 mg orally four times daily) or metronidazole (500 mg twice daily) should be used to complete at least 14 days of therapy with doxycycline to provide more effective anaerobic coverage than doxycycline alone.

<table>
<thead>
<tr>
<th>Recommended Parenteral Regimens</th>
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</thead>
<tbody>
<tr>
<td><strong>Clindamycin</strong> 900 mg IV every 8 hours</td>
<td><strong>Gentamicin</strong> loading dose IV or IM (2 mg/kg), followed by a maintenance dose (1.5 mg/kg) every 8 hours. Single daily dosing (3-5 mg/kg) can be substituted.</td>
</tr>
</tbody>
</table>

Note: Oral therapy with clindamycin (450 mg orally four times daily) or doxycycline (100 mg twice daily) can be used to complete the 14 days of therapy. When tubo-ovarian abscess is present, clindamycin (450 mg orally four times daily) or metronidazole (500 mg twice daily) should be used to complete at least 14 days of therapy with doxycycline to provide more effective anaerobic coverage than doxycycline alone.

<table>
<thead>
<tr>
<th>Alternative for Parenteral Regimens</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ampicillin-Sulbactam</strong> 3 g IV every 6 hours</td>
<td><strong>Doxycycline</strong> 100 mg orally or IV every 12 hours</td>
</tr>
</tbody>
</table>

Because of the pain associated with intravenous infusion, doxycycline should be administered orally when possible. Oral and IV administration of doxycycline provide similar bioavailability.
Table 4. 2015 STD Treatment Guidelines: Pelvic Inflammatory Disease (PID)

Intramuscular/Oral Treatment

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.

<table>
<thead>
<tr>
<th>Recommended Intramuscular/Oral Regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ceftriaxone</strong> 250 mg IM in a single dose</td>
</tr>
</tbody>
</table>

Ceftriaxone, a third-generation cephalosporin, is limited in the coverage of anaerobes. Therefore, until it is known that extended anaerobic coverage is not important for treatment of acute PID, the addition of metronidazole to treatment regimens with third-generation cephalosporins should be considered.

<table>
<thead>
<tr>
<th>Recommended Intramuscular/Oral Regimens</th>
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<tbody>
<tr>
<td><strong>Cefoxitin</strong> 2 g IM in a single dose</td>
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</table>

The cefoxitin and probenecid should be administered concurrently.

<table>
<thead>
<tr>
<th>Recommended Intramuscular/Oral Regimens</th>
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<tbody>
<tr>
<td><strong>Other parenteral third-generation cephalosporin (e.g. ceftizoxime or cefotaxime)</strong></td>
</tr>
</tbody>
</table>

The recommended third-generation cephalosporins are limited in the coverage of anaerobes. Therefore, until it is known that extended anaerobic coverage is not important for treatment of acute PID, the addition of metronidazole to treatment regimens with third-generation cephalosporins should be considered.
