Published in final edited form as:

Infect Dis Clin North Am. 2013 December ; 27(4): . doi:10.1016/j.idc.2013.08.004.

Pelvic Inflammatory Disease: Current concepts in pathogenesis, diagnosis and treatment

Caroline Mitchell, MD, MPH¹ and Malavika Prabhu, MD¹

¹Department of Obstetrics & Gynecology, University of Washington

Pelvic inflammatory disease (PID) is characterized by infection and inflammation of the upper genital tract in women: the uterus, fallopian tubes and/or ovaries. While a definitive diagnosis of PID can be made by laparoscopic visualization of inflamed, purulent fallopian tubes, PID is generally a clinical diagnosis and thus represents a diagnostic challenge. This condition can cause significant reproductive health sequelae for women; therefore, diagnosis and treatment algorithms advise a high index of suspicion for PID in any reproductive age woman with pelvic or abdominal pain, and err on the side of recommending what likely amounts to overtreatment with antibiotic regimens.

Epidemiology

In the United States in 2000, there were an estimated 1.2 million medical visits for PID, [1] a number that has been decreasing since 1985. [2–4] This decrease is attributed in part to widespread adoption of screening for *Chlamydia trachomatis*, the goal of which is to identify and treat asymptomatic cases of cervicitis before they can progress to PID. [5] Estimated direct medical costs associated with PID and its sequelae (ectopic pregnancy, chronic pelvic pain and tubal infertility) were as high as 1.88 billion USD in 1998, even though the majority of women receive care as outpatients. [6]

Risk factors for PID are the same as those for acquisition of sexually transmitted diseases: multiple sexual partners, young age, smoking, and illicit drug use. [6–9] Douching has been implicated in some studies, and has been observed to double a woman's risk of upper genital tract infection. [8, 10, 11] Oral contraceptive use has been associated with lower rates of clinical PID, though it is not clear whether this is due to fewer infections or fewer symptoms, and thus under diagnosis. [12–14] Bacterial vaginosis (BV) has also been associated with PID, though primarily in cross-sectional studies that were unable to determine causality. [15] In the prospective Gyn Infections Follow-through study (GIFT), women with BV at enrollment did not have higher risk for PID over 4 years of follow-up, though women with *Neisseria gonorrhoeae* and *C. trachomatis* did. [16]

Etiology

In early studies of PID, *N. gonorrhoeae* was the most commonly isolated pathogen, and is still more likely to cause severe symptoms than other pathogens. [13, 17–19] However, as

© 2013 Elsevier Inc. All rights reserved.

Corresponding author: Caroline Mitchell, Harborview Women's Clinic, 325 9th Ave, Box 359865, Seattle, WA 98105, camitch@uw.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

the prevalence of gonorrhea has decreased, its importance as a causal agent for PID has diminished. [20, 21] *Chlamydia trachomatis* remains a significant pathogen associated with PID, detected in up to 60% of women with confirmed salpingitis or endometritis. [22–24] *Mycoplasma genitalium* has been independently associated with PID, though its prevalence is low in most populations that have been studied. [25, 26] The proportion of cases of PID that involve non-gonococcal, non-chlamydial etiology ranges between 9–23% in women with confirmed salpingitis or endometritis, even as diagnostic testing for gonorrhea and chlamydia become more sensitive. [7, 22, 24, 27, 28] In these cases, the microbial community is often diverse and includes anaerobes like *Peptostreptococcus spp.* and *Prevotella spp.* [23, 27] Even in women with gonorrhea or chlamydia, detection of anaerobes in the upper genital tract is frequent and is associated with more severe disease. [16, 22] In a study of Kenyan women with laparoscopically confirmed salpingitis, polymerase chain reaction (PCR) assay of tubal samples for the bacterial 16S rRNA gene identified multiple species, including several associated with BV such as *Atopobium vaginae*, *Leptotrichia spp.*, *Peptostreptococcus spp.*, and *Prevotella spp.* [29]

Pathogenesis

Mathematical modeling based on epidemiologic and microbiologic studies suggests that 8–10% of women with *C. trachomatis* infection will develop PID if not treated, [30] although in studies that followed women with chlamydial endocervical infection without treatment, the rate was even lower. [31, 32] When both the lower and upper genital tract are sampled, there is a clear gradient of infections, with a higher proportion of women testing positive at the vagina and/or cervix, fewer in the endometrium, and less frequently in the fallopian tubes. [23, 24, 27] One component of protection from bacterial ascent is the physical barrier of the cervix and its mucus barrier. Endometrial detection of gonorrhea or chlamydia is more frequent in the proliferative phase of the menstrual cycle [18] when cervical mucus is thinner, [33] and the peristaltic contractions of the uterus move fluid cephalad. [34] There is also likely an immunologic component to the cervical barrier; genetic polymorphisms in toll-like receptor (TLR) genes appear to increase the risk of upper genital tract infection [24] as do certain HLA class II alleles, suggesting that individual differences in immune function may increase the risk of developing PID in the setting of cervical infection.

Tubal damage is best described in the context of chlamydial infection and appears to be related both to an innate immune inflammatory response initiated by the epithelial cells infected by *C. trachomatis*, [35] and to an adaptive T-cell response. [36, 37] Although antibody titers to chlamydial antigens are increased in severe disease, [38, 39] higher titers have not been associated with worse reproductive outcomes. [40] In human studies, evaluation of tubal inflammation is difficult without surgical intervention; thus, many studies use endometritis as a marker for tubal inflammation. Kiviat et al correlated the presence of both neutrophils and plasma cells in endometrial biopsies with visible salpingitis. [41] In a cohort of women with mild-moderate PID who were treated with broad-spectrum antibiotics, the presence of either neutrophils or plasma cells in an endometrial biopsy was not associated with decreased fertility. [42] Plasma cells alone were found in 33% of endometrial samples of low risk women [43] and were not associated with laparoscopic abnormalities, but in women at high risk of sexually transmitted infections, plasma cell endometritis appears to be associated with decreased fertility. [44] The heterogeneity of these findings suggests that there is a range of individual immune response to upper genital tract infection, and that not all women have the same likelihood of reproductive sequelae from PID.

Clinical Evaluation and Differential Diagnosis

Practically, in the clinic or emergency department, when a sexually active woman presents with lower abdominal or pelvic pain, PID must be considered in the differential diagnosis, which also includes appendicitis, ectopic pregnancy, ovarian torsion, intrapelvic bleeding, rupture of an adnexal mass, endometriosis, and gastroenteritis. [45] Key components of the physical exam include:

1. abdominal exam, including palpation of the right upper quadrant,
2. vaginal speculum exam, including inspection of the cervix for friability and mucopurulent cervical discharge,
3. bimanual exam, assessing for cervical motion, uterine, or adnexal tenderness, as well as pelvic masses.
4. Microscopic evaluation of a sample of cervicovaginal discharge to assess for *T. vaginalis*, bacterial vaginosis, and/or leukorrhea.

The clinical presentation of PID is quite variable (Table 1), thus a high index of suspicion is necessary. Symptoms may differ depending on the pathogens responsible. In the PID Evaluation and Clinical Health (PEACH) trial, women with PID associated with *C. trachomatis* or *M. genitalium* took almost one week longer to present to care than women with gonorrhea-associated PID, suggesting milder symptoms. [19] Women with gonococcal infection are more likely to have fever, adnexal tenderness, mucopurulent cervicitis and an elevated peripheral white blood count (WBC). [46]

Sensitivity and Specificity of CDC Diagnostic Criteria

The clinical diagnosis of PID is based on recommendations from the Centers for Disease Control and Prevention (CDC). Minimum diagnostic criteria (see Box 1) have been set with a high sensitivity and low specificity, in order to detect as many cases of clinical disease as possible, thus potentially avoiding the long-term reproductive sequelae and economic costs associated with delayed diagnosis and lack of treatment.

In a cohort of patients with suspected PID who underwent laparoscopy in Lund, Sweden,, PID was considered when a patient presented with lower abdominal pain and at least two of the following: abnormal vaginal discharge, fever, vomiting, menstrual irregularities, urinary symptoms, proctitis symptoms, marked tenderness of the pelvic organs on bimanual, palpable adnexal mass or ESR > 15mm/hr. Only 65% of women suspected to have PID using these criteria actually had salpingitis. [47] A 2003 re-analysis of data from this cohort demonstrated that the combination of fever > 38.3°C, elevated ESR, and adnexal tenderness achieved the highest combination of sensitivity and specificity, 65% and 66%, respectively, for acute salpingitis. [48] In other words, these criteria would have a 35% false negative rate for predicting laparoscopically determined PID.

It is difficult to calculate the exact sensitivity and specificity of the CDC diagnostic criteria, as there are at least two potential “gold standards” for a true positive diagnosis of PID: salpingitis at laparoscopy or endometritis on endometrial biopsy. Since laparoscopy is expensive, invasive and not part of a standard evaluation of PID, many studies use endometritis as a marker of upper genital tract infection and inflammation. Endometritis and salpingitis are correlated; histologic endometritis has a sensitivity of 89–92% and specificity of 63–87% for laparoscopically-diagnosed acute salpingitis, with only 7–22% of patients with clinically suspected PID having salpingitis without endometritis. [28, 41, 49, 50] However, while presence and severity of salpingitis is correlated with risk of ectopic pregnancy and infertility, [21] endometritis is not as consistently associated with these

outcomes. [42] This may be due to the fact that not all women with endometritis have salpingitis (Table 2), thus diluting the association.

Laboratory testing

Because PID is a clinical diagnosis, laboratory data or imaging studies are not usually necessary, but they can be helpful in establishing the diagnosis or in defining its severity. [51] In the PEACH trial, which enrolled women with abdominal pain, pelvic tenderness and evidence of lower genital tract inflammation, an elevated leukocyte count ($> 10,000$ cells/mL) had 41% sensitivity and 76% specificity for the presence of endometritis. [52] The presence of ≥ 1 neutrophil per 1000x field saline wet mount of vaginal discharge had 91% sensitivity and 26.3% specificity for endometritis. [53] In another cohort study, an elevated ESR (> 15 mm/hr) had 70% sensitivity and 52% specificity for endometritis or salpingitis. Elevated WBC had 57% sensitivity and 88% specificity, while presence of increased numbers of vaginal neutrophils (≥ 3 /HPF) had 78% sensitivity and 39% specificity. [54] In a cohort of women at high risk for pelvic infections, absence of vaginal white blood cells had excellent negative predictive value (95%). [53] These data suggest that if an evaluation of a saline microscopy of vaginal fluid reveals no white blood cells (leucorrhea), an alternative diagnosis to PID should be considered.

Imaging studies

Ultrasonography can also be used to aid in diagnosis of PID and direct treatment. A finding of thickened, fluid-filled tubes have an 85% sensitivity and 100% specificity for endometritis among women with clinically diagnosed PID. [55] Timor-Tritsch detailed the various transvaginal sonographic markers of acute tubal inflammatory disease, including dilated tubal shape, abnormal wall structure, increased wall thickness (≥ 5 mm), and presence of pelvic peritoneal fluid (free fluid or inclusion cyst). [56] In a study comparing 30 patients with clinical PID confirmed with laparoscopy and 20 normal women, power Doppler demonstrating tubal hyperemia was 100% sensitive and 80% specific for PID; in addition, altered tubal shape, structure, and wall thickness were seen in an overwhelming majority of patients with pyosalpinx. [57] Magnetic resonance imaging (MRI), with its highly sensitive and specific ability to identify thickened, fluid-filled tubes, pyosalpinx, pelvic free fluid, and tubo-ovarian abscesses, has also been proposed as a diagnostic modality for PID; however, it is very costly and not easily accessible or applicable to women seeking outpatient evaluation for possible PID. [58]

Inpatient vs. Outpatient Management

The therapeutic goal for the treatment of PID is two-fold: short-term microbiologic and clinical cure and long-term prevention of sequelae, namely tubal infertility, ectopic pregnancy, and chronic pelvic pain. Since the 1980s, PID therapy has shifted from the inpatient setting to the outpatient setting, with a 68% decline in hospitalization [4] due in part to several studies showing equivalent short-term outcomes with outpatient versus inpatient therapy for mild-moderate PID. [59, 60] Between 1995 and 2001, 89% of all PID visits occurred in the ambulatory setting. [4] Current criteria for inpatient hospitalization are summarized in Box 2.

The PEACH trial compared inpatient administration of parenteral cefoxitin and doxycycline (parenteral/oral) versus outpatient administration of intramuscular cefoxitin and oral doxycycline and found no short-term (30-day) differences in microbiologic or clinical cure [61] or long term differences in reproductive health outcomes (Table 3). [62] A secondary analysis among participants of the PEACH trial also saw no long-term outcome differences by treatment group among those with clinically confirmed endometritis or upper genital tract

gonorrheal or chlamydial infection. [61, 62] Interestingly, a representative subpopulation from PEACH revealed a 70% mean treatment adherence rate, with only 17% of participants taking doxycycline exactly as prescribed. [63] Similar rates of poor adherence to doxycycline or tetracycline prescribed for outpatient therapy of STI have been seen, particularly in the setting of gastrointestinal side effects. [64, 65] This may explain the relatively high rates of ongoing disease and long-term sequelae in the PEACH cohort.

While many of the original efficacy studies mandated inpatient IV treatment for 48–96 hours before switching to oral therapy, [61, 66] current practice is to treat with IV medications until there is clinical improvement for 24 hours or more. However, since IV doxycycline can cause significant phlebitis, and its oral bioavailability is comparable to parenteral, an earlier switch to oral doxycycline can be made if a patient is tolerating oral medications. [61]

CDC Recommendations for Antimicrobial Therapy

Current recommendations for antimicrobial treatment regimens in PID were published in 2010 (Table 4), and are scheduled for update in 2014. [67] A guiding principle for selection of antimicrobial therapy for PID is that the regimen should cover *N. gonorrhoeae* and *C. trachomatis*, regardless of results of diagnostic testing for these pathogens. Therapy of gonorrhea, and therefore PID, shifted away from fluoroquinolone-based regimens between the 2006 and 2010 iterations of the CDC Treatment Guidelines, given the rapid emergence of fluoroquinolone resistance. [68] In 2012, after reports of increasing prevalence of cefixime-resistant gonorrhea, the guidelines were changed again to drop cefixime as one of the first line outpatient treatment options for cervicitis. [69] With additional cephalosporin resistance to gonorrhea reported as discussed in the article by Barbee and Dombrowski elsewhere in this issue, the potential for development of resistance that could compromise treatment of gonorrhea-associated PID is of great concern.

Alternative Antimicrobial Regimens

Although not part of CDC's recommendations, newer data suggest that parenteral followed by oral azithromycin, either as monotherapy or in combination with doxycycline and metronidazole, produces clinical cure rates of 97–98% at 2 weeks post-treatment and microbiologic cure rates of 90–94% at 6 weeks post-treatment. [70] The azithromycin-based regimens were compared to third-generation cephalosporin-based regimens or parenteral amoxicillin-based regimens and showed no statistically significant difference in clinical or microbiologic cure rates, although the study had a high dropout rate and low proportion of anaerobic bacteria isolated from endocervix and endometrium. [70] Another trial compared intramuscular ceftriaxone plus oral azithromycin versus the standard of oral doxycycline and found higher rates of clinical and histologic cure with azithromycin, although rates of cure in both arms were less than 80%. [71]

While *M. genitalium* is neither tested for or considered when choosing therapy, newer evidence suggests a greater than 4-fold higher risk of treatment failure with a cefoxitin/doxycycline regimen when *M. genitalium* is present, although there were no differences in reproductive sequelae or recurrent PID, as discussed in the article by Manhart elsewhere in this issue. [72] Doxycycline has poor efficacy against *M. genitalium* (cure rates from 17–94%), and while azithromycin is more effective (67–100% cure), moxifloxacin seems to be the most effective treatment. [73] In cases of persistent PID not responsive to standard therapy, testing for and treatment of *M. genitalium* should be considered, and presumptive therapy with moxifloxacin may be warranted.

Anaerobes: To Cover or Not?

There is little clarity on the need for empiric coverage for anaerobic bacteria when PID is diagnosed, in part because there is a lack of clear understanding of the contribution of anaerobes to pathogenesis in PID. Several studies have shown that BV is associated with PID, with BV-associated anaerobic bacteria present in endometritis, but that BV may not actually cause acute PID. [16, 61, 74] However, other data have not shown any long-term reproductive sequelae of histologically-diagnosed anaerobic endometritis, even when treatment with a cephalosporin-based regimen with poor anaerobic coverage was provided. [42] Few studies have specifically examined microbiologic cure rates of antimicrobial treatment regimens targeting anaerobic bacteria. Some BV-associated microbes may form a biofilm on the endometrial surface, which could limit the ability of antibiotics to eliminate colonization. [75] The CDC currently recommends consideration of treatment regimens with anaerobic coverage until data suggest equivalent prevention of reproductive sequelae in treatment regimens lacking anaerobic coverage. [67] Anaerobic coverage should be included in women with a tubo-ovarian abscess and with BV, regardless of the latter's potential etiologic role in the development of acute PID. [67, 76]

Additional treatment considerations

Among patients who qualified for outpatient therapy, re-evaluation of clinical status should occur within 72 hours, or sooner if indicated. If no meaningful clinical response is detected, patients with PID may require inpatient hospitalization, transition to parenteral antibiotics, further diagnostic tests, including additional laboratory studies and imaging to evaluate for possible tubo-ovarian abscess (TOA), and possible surgical intervention.

Empiric treatment for gonorrhea and chlamydia is recommended for all male sexual partners within the past 60 days, or the most recent sexual partner if >60 days ago, regardless of symptoms or the result of gonorrhea and chlamydia testing in the female patient with PID. [67] Women diagnosed with PID should be offered an HIV test at the time of diagnosis. Repeat testing for gonorrhea or chlamydia in 3 to 6 months is recommended if initial testing was positive for either infection. [67]

Tubo-ovarian abscess (TOA)

Although the presenting signs and symptoms of a TOA are not often distinct from those with salpingitis/endometritis, there are often more objective signs of infection and inflammation. A large series of patients with ultrasound- or surgically-confirmed TOA found that 60% had a temperature >37.8°C, 68% had a leukocytosis >10,000 cells/mL, 26% had nausea, and 19% had chronic abdominopelvic pain. [77] In women with PID, palpation of an adnexal mass on physical exam, significant pain limiting proper evaluation of the adnexa, severe illness, or lack of clinical response to antimicrobial therapy should prompt imaging studies. In addition, imaging can be helpful to evaluate for alternative diagnoses such as appendicitis, ovarian torsion or cyst rupture.

Inpatient observation is recommended for at least 24 hours among hemodynamically stable women with a tubo-ovarian abscess, with the aim of observing for early signs of sepsis or potential abscess rupture. Surgical exploration on initial evaluation is indicated in the setting of an acute abdomen and signs of sepsis or hemodynamic instability, particularly if a ruptured TOA is suspected. Antimicrobial therapy should be parenteral to start, and should include clindamycin or metronidazole to cover anaerobes. [67] Antimicrobial therapy alone, with appropriate anaerobic coverage and the ability to penetrate and function in abscess cavities, is effective in 70–84% of women. [77, 78]

In one cohort of women admitted with TOA, 60% of those with an abscess larger than 10cm needed surgical management compared to 20% of those with 4–6cm abscesses. [78] When no clinical improvement is noted within 72 hours of antibiotic initiation, minimally-invasive drainage of the abscess or surgical management can be pursued; however, significant clinical deterioration at any time point usually indicates the need for surgical exploration. [77] A study of empiric transvaginal ultrasound-guided aspiration of TOAs at the time of diagnosis, in concert with antimicrobial therapy, revealed that the procedure is safe, well tolerated, and averted surgical management in 93% of cases. [79]

Special populations: HIV-infected women

The presenting signs and symptoms of PID generally do not differ significantly by HIV infection status, [81, 82] although some studies have demonstrated an increased odds of fever, higher clinical severity scores and higher likelihood of having a tubo-ovarian abscess among HIV-infected women. [83–85] Clinical severity correlated with immunosuppression among HIV-infected women with laparoscopically confirmed PID. [83]

Treatment for PID or TOA has been shown to be as effective in HIV-infected women as in uninfected women. [81, 83, 84, 86] In a prospective study, the 12% clinical failure rate of outpatient therapy was not predicted by HIV serostatus. [81] Duration of hospitalization and antibiotic therapy also did not differ by HIV-serostatus; however, among HIV-infected women, immunosuppressed patients required longer inpatient therapy and antibiotic regimens. [83]

Special populations: Post-menopausal Women

Although rare, post-menopausal women can develop PID, presenting most commonly with lower abdominal pain and postmenopausal bleeding, as well as fever, nausea, and altered bowel habits; they are considerably more likely to have TOAs. [87, 88] Among 20 post-menopausal women with TOAs in one case series, although only 20% of patients were febrile, 45% had elevated white blood cell counts, 55% had a palpable pelvic mass, and 90% had tubo-ovarian abscesses on surgical exploration. [89] In several small case series, pathology of the surgical specimens revealed a concurrent gynecologic malignancy (cervix, endometrium, or ovary) in 40–47% of the patients. [88–90] Based on these data, any post-menopausal woman with PID should be evaluated for the presence of a pelvic cancer.

Special populations: Intrauterine Devices

In the 1970's the Dalkon Shield intrauterine device (IUD) was associated with increased rates of PID, and led to significant concerns about the safety of IUDs in women at risk for sexually transmitted infections (STI). [91] Modern IUDs, including the levonorgestrel IUD (Mirena) and the copper IUD (Paraguard), have not been associated with an increased risk of PID over the long term. [92] There does appear to be a slightly increased rate of PID in the 20 days post insertion: in one study the rate of PID during this time was 9.66/1000 women, while after that it was 1.38/1000 women. [93] A review of studies assessing PID after IUD insertion in the presence of gonococcal or chlamydial cervicitis showed an increased, but overall quite low risk (0–5%). [94] Recent studies suggest that screening for GC/CT at the time of insertion, as opposed to requiring a negative test prior to the procedure, does not significantly increase adverse sequelae. [95] There does not appear to be any difference in risk of PID with hormone-containing compared with copper IUDs. [96] The presence of an intrauterine device (IUD) at time of diagnosis of acute PID does not alter the management, and empiric removal of the IUD is not indicated. [67, 97]

Sequelae

Women with PID have an increased risk of ectopic pregnancy, infertility and chronic pelvic pain due to tubal scarring and damage from inflammation. In the PEACH trial 36% of participants reported chronic pelvic pain; women with 2 or more episodes of PID were at highest risk. [98] In a cohort study of women with laparoscopically confirmed salpingitis in Sweden, followed for a mean of 94 months, the infertility rate was 16%, 67% of which was attributable to tubal factor infertility compared to an infertility rate of 2.7% in women without salpingitis. Of women who became pregnant, 9% of women with salpingitis had an ectopic compared to 1.9% of control women. [21] The risk of infertility increased with severity of salpingitis and number of episodes of PID. Chlamydial cervicitis also increases the risk of ectopic with repeat infections; women with 3 or more episodes had 4.5 times increased odds of PID. [21]

In the PEACH trial, upper genital tract detection of gonorrhea, chlamydia, or endometritis was sufficient to confirm the diagnosis of PID. However, there were no differences in reproductive health outcomes between women with and without endometritis or upper genital tract infection. [42] A more recent study of women with lower genital tract infection but no PID by clinical criteria used a permissive definition of endometritis (1 plasma cell per hpf) and showed a 40% decrease in pregnancy rates among women with endometritis (or subclinical PID). [44] The differences in these analyses may be due to a slightly higher rate of *C. trachomatis* infection in the latter study.

Prevention

As gonorrhea and chlamydia contribute over half to three-quarters of PID, screening for and treating these infections should decrease the incidence and sequelae. Four randomized trials have examined whether this strategy is effective. The earliest was conducted between 1990 and 1992 in Seattle, Washington. Over 1000 women in a managed care organization were randomized to receive an invitation for chlamydia screening, then were followed for a year and compared to approximately 1600 women receiving standard care. Although only 64% of the intervention group were screened, during the 12 month follow-up there were 9 PID cases in the screening group and 33 in the control group (RR 0.44 (0.2, 0.9)). [99] A second study used cluster randomization to randomize students at 17 high schools to receive the offer of chlamydia screening and then followed them for PID over 12 months. At one year the PID incidence was 2.1% in the screening group (of whom 48% were screened) and 4.2% in the control group. [100] Most recently, the Prevention Of Pelvic Infections (POPI) trial in England enrolled sexually active women under age 27 and randomized them to early vs. delayed screening for chlamydia. The early screening group had a chlamydia prevalence of 5.4%, and 15/1191 (1.3%) developed PID over the course of the study. In the delayed group, 5.9% had chlamydia detected on their enrollment swab when it was tested a year later. During that time, 23/1186 (1.9%) in that group developed PID. The relative risk for PID in those with early screening was not significant (0.65 (0.34, 1.22), [32] but the study was underpowered given the low rate of PID.

Summary

PID is associated with significant reproductive morbidity, which appears to be reduced with prompt, proactive treatment of cervicitis and lower genital tract infections. It is a clinical diagnosis, and providers should maintain a high index of suspicion when presented with a reproductive age women complaining of abdominal and pelvic pain. Sexually transmitted infections are commonly associated with PID, but vaginal anaerobes also appear to be involved, and antibiotic coverage for these pathogens should be considered when treating women with severe symptoms or pelvic abscesses.

References

1. Rein DB, Kassler WJ, Irwin KL, Rabiee L. Direct medical cost of pelvic inflammatory disease and its sequelae: Decreasing, but still substantial. *Obstet Gynecol.* 2000; 95(3):397–402. [PubMed: 10711551]
2. Bender N, Herrmann B, Andersen B, Hocking JS, van Bergen J, Morgan J, et al. Chlamydia infection, pelvic inflammatory disease, ectopic pregnancy and infertility: Cross-national study. *Sex Transm Infect.* 2011; 87(7):601–8. [PubMed: 22028428]
3. Paik CK, Waetjen LE, Xing G, Dai J, Sweet RL. Hospitalizations for pelvic inflammatory disease and tuboovarian abscess. *Obstet Gynecol.* 2006; 107(3):611–6. [PubMed: 16507932]
4. Sutton MY, Sternberg M, Zaidi A, St Louis ME, Markowitz LE. Trends in pelvic inflammatory disease hospital discharges and ambulatory visits, united states, 1985–2001. *Sex Transm Dis.* 2005; 32(12):778–84. [PubMed: 16314776]
5. Owusu-Edusei K Jr, Bohm MK, Chesson HW, Kent CK. Chlamydia screening and pelvic inflammatory disease: Insights from exploratory time-series analyses. *Am J Prev Med.* 2010; 38(6): 652–7. [PubMed: 20494242]
6. Bohm MK, Newman L, Satterwhite CL, Tao G, Weinstock HS. Pelvic inflammatory disease among privately insured women, united states, 2001–2005. *Sex Transm Dis.* 2010; 37(3):131–6. [PubMed: 20051931]
7. Ness RB, Soper DE, Holley RL, Peipert J, Randall H, Sweet RL, et al. Hormonal and barrier contraception and risk of upper genital tract disease in the pid evaluation and clinical health (peach) study. *Am J Obstet Gynecol.* 2001; 185(1):121–7. [PubMed: 11483915]
8. Ness RB, Soper DE, Holley RL, Peipert J, Randall H, Sweet RL, et al. Douching and endometritis: Results from the pid evaluation and clinical health (peach) study. *Sex Transm Dis.* 2001; 28(4):240–5. [PubMed: 11318257]
9. Simms I, Stephenson JM, Mallinson H, Peeling RW, Thomas K, Gokhale R, et al. Risk factors associated with pelvic inflammatory disease. *Sex Transm Infect.* 2006; 82(6):452–7. [PubMed: 16901918]
10. Scholes D, Daling JR, Stergachis A, Weiss NS, Wang SP, Grayston JT. Vaginal douching as a risk factor for acute pelvic inflammatory disease. *Obstet Gynecol.* 1993; 81(4):601–6. [PubMed: 8459976]
11. Wolner-Hanssen P, Eschenbach DA, Paavonen J, Stevens CE, Kiviat NB, Critchlow C, et al. Association between vaginal douching and acute pelvic inflammatory disease. *JAMA.* 1990; 263(14):1936–41. [PubMed: 2313870]
12. Kimani J, Maclean IW, Bwayo JJ, MacDonald K, Oyugi J, Maitha GM, et al. Risk factors for chlamydia trachomatis pelvic inflammatory disease among sex workers in nairobi, kenya. *J Infect Dis.* 1996; 173(6):1437–44. [PubMed: 8648217]
13. Ness RB, Keder LM, Soper DE, Amortegui AJ, Gluck J, Wiesenfeld H, et al. Oral contraception and the recognition of endometritis. *Am J Obstet Gynecol.* 1997; 176(3):580–5. [PubMed: 9077610]
14. Wolner-Hanssen P, Svensson L, Mardh PA, Westrom L. Laparoscopic findings and contraceptive use in women with signs and symptoms suggestive of acute salpingitis. *Obstet Gynecol.* 1985; 66(2):233–8. [PubMed: 3160985]
15. Taylor BD, Darville T, Haggerty CL. Does bacterial vaginosis cause pelvic inflammatory disease? *Sex Transm Dis.* 2013; 40(2):117–22. [PubMed: 23324974]
16. Ness RB, Hillier SL, Kip KE, Soper DE, Stamm CA, McGregor JA, et al. Bacterial vaginosis and risk of pelvic inflammatory disease. *Obstet Gynecol.* 2004; 104(4):761–9. [PubMed: 15458899]
17. Eschenbach DA, Buchanan TM, Pollock HM, Forsyth PS, Alexander ER, Lin JS, et al. Polymicrobial etiology of acute pelvic inflammatory disease. *N Engl J Med.* 1975; 293(4):166–71. [PubMed: 806017]
18. Sweet RL. Pelvic inflammatory disease. *Sex Transm Dis.* 1986; 13(3 Suppl):192–8. [PubMed: 3532371]
19. Taylor BD, Ness RB, Darville T, Haggerty CL. Microbial correlates of delayed care for pelvic inflammatory disease. *Sex Transm Dis.* 2011; 38(5):434–8. [PubMed: 21124257]

20. Haggerty CL, Totten PA, Astete SG, Ness RB. *Mycoplasma genitalium* among women with nongonococcal, nonchlamydial pelvic inflammatory disease. *Infect Dis Obstet Gynecol*. 2006; 2006:30184. [PubMed: 17485798]
21. Westrom L, Joesoef R, Reynolds G, Hagdu A, Thompson SE. Pelvic inflammatory disease and fertility. A cohort study of 1,844 women with laparoscopically verified disease and 657 control women with normal laparoscopic results. *Sex Transm Dis*. 1992; 19(4):185–92. [PubMed: 1411832]
22. Heinonen PK, Miettinen A. Laparoscopic study on the microbiology and severity of acute pelvic inflammatory disease. *Eur J Obstet Gynecol Reprod Biol*. 1994; 57(2):85–9. [PubMed: 7859910]
23. Hillier SL, Kiviat NB, Hawes SE, Hasselquist MB, Hanssen PW, Eschenbach DA, et al. Role of bacterial vaginosis-associated microorganisms in endometritis. *Am J Obstet Gynecol*. 1996; 175(2):435–41. [PubMed: 8765265]
24. Taylor-Robinson D, Jensen JS, Svenstrup H, Stacey CM. Difficulties experienced in defining the microbial cause of pelvic inflammatory disease. *Int J STD AIDS*. 2012; 23(1):18–24. [PubMed: 22362682]
25. Bjartling C, Osser S, Persson K. *Mycoplasma genitalium* in cervicitis and pelvic inflammatory disease among women at a gynecologic outpatient service. *Am J Obstet Gynecol*. 2012; 206(6): 476, e1–8. [PubMed: 22483084]
26. Cohen CR, Manhart LE, Bukusi EA, Astete S, Brunham RC, Holmes KK, et al. Association between *mycoplasma genitalium* and acute endometritis. *Lancet*. 2002; 359 (9308):765–6. [PubMed: 11888591]
27. Soper DE, Brockwell NJ, Dalton HP, Johnson D. Observations concerning the microbial etiology of acute salpingitis. *Am J Obstet Gynecol*. 1994; 170(4):1008–14. discussion 14–7. [PubMed: 8166184]
28. Wasserheit JN, Bell TA, Kiviat NB, Wolner-Hanssen P, Zabriskie V, Kirby BD, et al. Microbial causes of proven pelvic inflammatory disease and efficacy of clindamycin and tobramycin. *Ann Intern Med*. 1986; 104(2):187–93. [PubMed: 3004276]
29. Hebb JK, Cohen CR, Astete SG, Bukusi EA, Totten PA. Detection of novel organisms associated with salpingitis, by use of 16s rDNA polymerase chain reaction. *J Infect Dis*. 2004; 190(12):2109–20. [PubMed: 15551209]
30. Herzog SA, Althaus CL, Heijne JC, Oakeshott P, Kerry S, Hay P, et al. Timing of progression from chlamydia trachomatis infection to pelvic inflammatory disease: A mathematical modelling study. *BMC Infect Dis*. 2012; 12:187. [PubMed: 22883325]
31. Morre SA, van den Brule AJ, Rozendaal L, Boeke AJ, Voorhorst FJ, de Blok S, et al. The natural course of asymptomatic chlamydia trachomatis infections: 45% clearance and no development of clinical pid after one-year follow-up. *Int J STD AIDS*. 2002; 13(Suppl 2):12–8. [PubMed: 12537719]
32. Oakeshott P, Kerry S, Aghaizu A, Atherton H, Hay S, Taylor-Robinson D, et al. Randomised controlled trial of screening for chlamydia trachomatis to prevent pelvic inflammatory disease: The popi (prevention of pelvic infection) trial. *BMJ*. 2010; 340:c1642. [PubMed: 20378636]
33. Katz DF. Human cervical mucus: Research update. *Am J Obstet Gynecol*. 1991; 165(6 Pt 2):1984–6. [PubMed: 1755453]
34. Kunz G, Beil D, Deininger H, Wildt L, Leyendecker G. The dynamics of rapid sperm transport through the female genital tract: Evidence from vaginal sonography of uterine peristalsis and hysterosalpingoscintigraphy. *Hum Reprod*. 1996; 11(3):627–32. [PubMed: 8671281]
35. Darville T, Hiltke TJ. Pathogenesis of genital tract disease due to chlamydia trachomatis. *J Infect Dis*. 2010; 201(Suppl 2):S114–25. [PubMed: 20524234]
36. Patton DL, Kuo CC. Histopathology of chlamydia trachomatis salpingitis after primary and repeated reinfections in the monkey subcutaneous pocket model. *J Reprod Fertil*. 1989; 85(2):647–56. [PubMed: 2704001]
37. Van Voorhis WC, Barrett LK, Sweeney YT, Kuo CC, Patton DL. Repeated chlamydia trachomatis infection of macaca nemestrina fallopian tubes produces a th1-like cytokine response associated with fibrosis and scarring. *Infect Immun*. 1997; 65(6):2175–82. [PubMed: 9169748]

38. Peeling RW, Kimani J, Plummer F, Maclean I, Cheang M, Bwayo J, et al. Antibody to chlamydial hsp60 predicts an increased risk for chlamydial pelvic inflammatory disease. *J Infect Dis.* 1997; 175(5):1153–8. [PubMed: 9129079]
39. Toye B, Laferriere C, Claman P, Jessamine P, Peeling R. Association between antibody to the chlamydial heat-shock protein and tubal infertility. *J Infect Dis.* 1993; 168(5):1236–40. [PubMed: 7901289]
40. Ness RB, Soper DE, Richter HE, Randall H, Peipert JF, Nelson DB, et al. Chlamydia antibodies, chlamydia heat shock protein, and adverse sequelae after pelvic inflammatory disease: The pid evaluation and clinical health (peach) study. *Sex Transm Dis.* 2008; 35(2):129–35. [PubMed: 18300379]
41. Kiviat NB, Wolner-Hanssen P, Eschenbach DA, Wasserheit JN, Paavonen JA, Bell TA, et al. Endometrial histopathology in patients with culture-proved upper genital tract infection and laparoscopically diagnosed acute salpingitis. *Am J Surg Pathol.* 1990; 14(2):167–75. [PubMed: 2137304]
42. Haggerty CL, Ness RB, Amortegui A, Hendrix SL, Hillier SL, Holley RL, et al. Endometritis does not predict reproductive morbidity after pelvic inflammatory disease. *Am J Obstet Gynecol.* 2003; 188(1):141–8. [PubMed: 12548208]
43. Achilles SL, Amortegui AJ, Wiesenfeld HC. Endometrial plasma cells: Do they indicate subclinical pelvic inflammatory disease? *Sex Transm Dis.* 2005; 32(3):185–8. [PubMed: 15729157]
44. Wiesenfeld HC, Hillier SL, Meyn LA, Amortegui AJ, Sweet RL. Subclinical pelvic inflammatory disease and infertility. *Obstet Gynecol.* 2012; 120(1):37–43. [PubMed: 22678036]
45. Jacobson L. Differential diagnosis of acute pelvic inflammatory disease. *Am J Obstet Gynecol.* 1980; 138(7 Pt 2):1006–11. [PubMed: 6451174]
46. Short VL, Totten PA, Ness RB, Astete SG, Kelsey SF, Haggerty CL. Clinical presentation of mycoplasma genitalium infection versus neisseria gonorrhoeae infection among women with pelvic inflammatory disease. *Clin Infect Dis.* 2009; 48(1):41–7. [PubMed: 19025498]
47. Jacobson L, Westrom L. Objectivized diagnosis of acute pelvic inflammatory disease. Diagnostic and prognostic value of routine laparoscopy. *Am J Obstet Gynecol.* 1969; 105(7):1088–98. [PubMed: 4242830]
48. Simms I, Eastick K, Mallinson H, Thomas K, Gokhale R, Hay P, et al. Associations between mycoplasma genitalium, chlamydia trachomatis, and pelvic inflammatory disease. *Sex Transm Infect.* 2003; 79(2):154–6. [PubMed: 12690141]
49. Eckert LO, Hawes SE, Wolner-Hanssen PK, Kiviat NB, Wasserheit JN, Paavonen JA, et al. Endometritis: The clinical-pathologic syndrome. *Am J Obstet Gynecol.* 2002; 186(4):690–5. [PubMed: 11967492]
50. Paavonen J, Kiviat N, Brunham RC, Stevens CE, Kuo CC, Stamm WE, et al. Prevalence and manifestations of endometritis among women with cervicitis. *Am J Obstet Gynecol.* 1985; 152(3):280–6. [PubMed: 3923837]
51. Kahn JG, Walker CK, Washington AE, Landers DV, Sweet RL. Diagnosing pelvic inflammatory disease. A comprehensive analysis and considerations for developing a new model. *JAMA.* 1991; 266(18):2594–604. [PubMed: 1834868]
52. Peipert JF, Ness RB, Blume J, Soper DE, Holley R, Randall H, et al. Clinical predictors of endometritis in women with symptoms and signs of pelvic inflammatory disease. *Am J Obstet Gynecol.* 2001; 184(5):856–63. discussion 63–4. [PubMed: 11303192]
53. Yudin MH, Hillier SL, Wiesenfeld HC, Krohn MA, Amortegui AA, Sweet RL. Vaginal polymorphonuclear leukocytes and bacterial vaginosis as markers for histologic endometritis among women without symptoms of pelvic inflammatory disease. *Am J Obstet Gynecol.* 2003; 188(2):318–23. [PubMed: 12592233]
54. Peipert JF, Boardman L, Hogan JW, Sung J, Mayer KH. Laboratory evaluation of acute upper genital tract infection. *Obstet Gynecol.* 1996; 87(5 Pt 1):730–6. [PubMed: 8677076]
55. Cacciatore B, Leminen A, Ingman-Friberg S, Ylostalo P, Paavonen J. Transvaginal sonographic findings in ambulatory patients with suspected pelvic inflammatory disease. *Obstet Gynecol.* 1992; 80(6):912–6. [PubMed: 1448258]

56. Timor-Tritsch IE, Lerner JP, Monteagudo A, Murphy KE, Heller DS. Transvaginal sonographic markers of tubal inflammatory disease. *Ultrasound Obstet Gynecol.* 1998; 12(1):56–66. [PubMed: 9697286]
57. Molander P, Finne P, Sjoberg J, Sellors J, Paavonen J. Observer agreement with laparoscopic diagnosis of pelvic inflammatory disease using photographs. *Obstet Gynecol.* 2003; 101(5 Pt 1): 875–80. [PubMed: 12738143]
58. Tukey TA, Aronen HJ, Karjalainen PT, Molander P, Paavonen T, Paavonen J. Mr imaging in pelvic inflammatory disease: Comparison with laparoscopy and us. *Radiology.* 1999; 210(1):209–16. [PubMed: 9885610]
59. Wolner-Hanssen P, Paavonen J, Kiviat N, Young M, Eschenbach DA, Holmes KK. Outpatient treatment of pelvic inflammatory disease with cefoxitin and doxycycline. *Obstet Gynecol.* 1988; 71(4):595–600. [PubMed: 3353051]
60. Arredondo JL, Diaz V, Gaitan H, Maradiegue E, Oyarzun E, Paz R, et al. Oral clindamycin and ciprofloxacin versus intramuscular ceftriaxone and oral doxycycline in the treatment of mild-to-moderate pelvic inflammatory disease in outpatients. *Clin Infect Dis.* 1997; 24(2):170–8. [PubMed: 9114143]
61. Ness RB, Soper DE, Holley RL, Peipert J, Randall H, Sweet RL, et al. Effectiveness of inpatient and outpatient treatment strategies for women with pelvic inflammatory disease: Results from the pelvic inflammatory disease evaluation and clinical health (peach) randomized trial. *Am J Obstet Gynecol.* 2002; 186(5):929–37. [PubMed: 12015517]
62. Ness RB, Trautmann G, Richter HE, Randall H, Peipert JF, Nelson DB, et al. Effectiveness of treatment strategies of some women with pelvic inflammatory disease: A randomized trial. *Obstet Gynecol.* 2005; 106(3):573–80. [PubMed: 16135590]
63. Dunbar-Jacob J, Sereika SM, Foley SM, Bass DC, Ness RB. Adherence to oral therapies in pelvic inflammatory disease. *J Womens Health (Larchmt).* 2004; 13(3):285–91. [PubMed: 15130257]
64. Augenbraun MH, McCormack WH. Pelvic inflammatory disease: An ongoing epidemic. *Hosp Pract (Minneap).* 1995; 30(9):61–6.
65. Katz BP, Zwickl BW, Caine VA, Jones RB. Compliance with antibiotic therapy for chlamydia trachomatis and neisseria gonorrhoeae. *Sex Transm Dis.* 1992; 19(6):351–4. [PubMed: 1492264]
66. Hemsell DL, Little BB, Faro S, Sweet RL, Ledger WJ, Berkeley AS, et al. Comparison of three regimens recommended by the centers for disease control and prevention for the treatment of women hospitalized with acute pelvic inflammatory disease. *Clin Infect Dis.* 1994; 19(4):720–7. [PubMed: 7803638]
67. Workowski KA, Berman S. Sexually transmitted diseases treatment guidelines, 2010. *MMWR Recomm Rep.* 2010; 59(RR-12):1–110. [PubMed: 21160459]
68. Workowski KA, Berman SM. Sexually transmitted diseases treatment guidelines, 2006. *MMWR Recomm Rep.* 2006; 55(RR-11):1–94. [PubMed: 16888612]
69. Katz AR, Lee MV, Wasserman GM. Sexually transmitted disease (std) update: A review of the cdc 2010 std treatment guidelines and epidemiologic trends of common stds in hawaii'i. *Hawaii J Med Public Health.* 2012; 71(3):68–73. [PubMed: 22454816]
70. Bevan CD, Ridgway GL, Rothermel CD. Efficacy and safety of azithromycin as monotherapy or combined with metronidazole compared with two standard multidrug regimens for the treatment of acute pelvic inflammatory disease. *J Int Med Res.* 2003; 31(1):45–54. [PubMed: 12635534]
71. Savaris RF, Teixeira LM, Torres TG, Edelweiss MI, Moncada J, Schachter J. Comparing ceftriaxone plus azithromycin or doxycycline for pelvic inflammatory disease: A randomized controlled trial. *Obstet Gynecol.* 2007; 110(1):53–60. [PubMed: 17601896]
72. Haggerty CL, Totten PA, Astete SG, Lee S, Hoferka SL, Kelsey SF, et al. Failure of cefoxitin and doxycycline to eradicate endometrial mycoplasma genitalium and the consequence for clinical cure of pelvic inflammatory disease. *Sex Transm Infect.* 2008; 84(5):338–42. [PubMed: 18445635]
73. Manhart LE, Broad JM, Golden MR. Mycoplasma genitalium: Should we treat and how? *Clin Infect Dis.* 2011; 53(Suppl 3):S129–42. [PubMed: 22080266]
74. Haggerty CL, Hillier SL, Bass DC, Ness RB. Bacterial vaginosis and anaerobic bacteria are associated with endometritis. *Clin Infect Dis.* 2004; 39(7):990–5. [PubMed: 15472851]

75. Swidsinski A, Verstraelen H, Loening-Baucke V, Swidsinski S, Mendling W, Halwani Z. Presence of a polymicrobial endometrial biofilm in patients with bacterial vaginosis. *PLoS One*. 2013; 8(1):e53997. [PubMed: 23320114]
76. Walker CK, Workowski KA, Washington AE, Soper D, Sweet RL. Anaerobes in pelvic inflammatory disease: Implications for the centers for disease control and prevention's guidelines for treatment of sexually transmitted diseases. *Clin Infect Dis*. 1999; 28(Suppl 1):S29–36. [PubMed: 10028108]
77. Landers DV, Sweet RL. Tubo-ovarian abscess: Contemporary approach to management. *Rev Infect Dis*. 1983; 5(5):876–84. [PubMed: 6635426]
78. Reed SD, Landers DV, Sweet RL. Antibiotic treatment of tuboovarian abscess: Comparison of broad-spectrum beta-lactam agents versus clindamycin-containing regimens. *Am J Obstet Gynecol*. 1991; 164(6 Pt 1):1556–61. discussion 61–2. [PubMed: 2048603]
79. Gjelland K, Ekerhovd E, Granberg S. Transvaginal ultrasound-guided aspiration for treatment of tubo-ovarian abscess: A study of 302 cases. *Am J Obstet Gynecol*. 2005; 193(4):1323–30. [PubMed: 16202721]
80. Goharkhay N, Verma U, Maggiorotto F. Comparison of ct- or ultrasound-guided drainage with concomitant intravenous antibiotics vs. Intravenous antibiotics alone in the management of tubo-ovarian abscesses. *Ultrasound Obstet Gynecol*. 2007; 29(1):65–9. [PubMed: 17171628]
81. Irwin KL, Moorman AC, O'Sullivan MJ, Sperling R, Koestler ME, Soto I, et al. Influence of human immunodeficiency virus infection on pelvic inflammatory disease. *Obstet Gynecol*. 2000; 95(4):525–34. [PubMed: 10725484]
82. Korn AP, Landers DV, Green JR, Sweet RL. Pelvic inflammatory disease in human immunodeficiency virus-infected women. *Obstet Gynecol*. 1993; 82(5):765–8. [PubMed: 8414323]
83. Cohen CR, Sinei S, Reilly M, Bukusi E, Eschenbach D, Holmes KK, et al. Effect of human immunodeficiency virus type 1 infection upon acute salpingitis: A laparoscopic study. *J Infect Dis*. 1998; 178(5):1352–8. [PubMed: 9780255]
84. Kamenga MC, De Cock KM, St Louis ME, Toure CK, Zakaria S, N'Gbichi JM, et al. The impact of human immunodeficiency virus infection on pelvic inflammatory disease: A case-control study in abidjan, ivory coast. *Am J Obstet Gynecol*. 1995; 172(3):919–25. [PubMed: 7892886]
85. Mugo NR, Kiehlbauch JA, Nguti R, Meier A, Gichuhi JW, Stamm WE, et al. Effect of human immunodeficiency virus-1 infection on treatment outcome of acute salpingitis. *Obstet Gynecol*. 2006; 107(4):807–12. [PubMed: 16582116]
86. Bukusi EA, Cohen CR, Stevens CE, Sinei S, Reilly M, Grieco V, et al. Effects of human immunodeficiency virus 1 infection on microbial origins of pelvic inflammatory disease and on efficacy of ambulatory oral therapy. *Am J Obstet Gynecol*. 1999; 181(6):1374–81. [PubMed: 10601915]
87. Heaton FC, Ledger WJ. Postmenopausal tuboovarian abscess. *Obstet Gynecol*. 1976; 47(1):90–4. [PubMed: 1246403]
88. Protopapas AG, Diakomanolis ES, Milingos SD, Rodolakis AJ, Markaki SN, Vlachos GD, et al. Tubo-ovarian abscesses in postmenopausal women: Gynecological malignancy until proven otherwise? *Eur J Obstet Gynecol Reprod Biol*. 2004; 114(2):203–9. [PubMed: 15140516]
89. Lipscomb GH, Ling FW. Tubo-ovarian abscess in postmenopausal patients. *South Med J*. 1992; 85(7):696–9. [PubMed: 1631680]
90. Hoffman M, Molpus K, Roberts WS, Lyman GH, Cavanagh D. Tuboovarian abscess in postmenopausal women. *J Reprod Med*. 1990; 35(5):525–8. [PubMed: 2352246]
91. Gareen IF, Greenland S, Morgenstern H. Intrauterine devices and pelvic inflammatory disease: Meta-analyses of published studies, 1974–1990. *Epidemiology*. 2000; 11(5):589–97. [PubMed: 10955413]
92. Feldblum PJ, Caraway J, Bahamondes L, El-Shafei M, Quan Ha D, Morales E, et al. Randomized assignment to copper iud or depot-medroxyprogesterone acetate: Feasibility of enrollment, continuation and disease ascertainment. *Contraception*. 2005; 72(3):187–91. [PubMed: 16102553]

93. Farley TM, Rosenberg MJ, Rowe PJ, Chen JH, Meirik O. Intrauterine devices and pelvic inflammatory disease: An international perspective. *Lancet*. 1992; 339 (8796):785–8. [PubMed: 1347812]
94. Mohllajee AP, Curtis KM, Peterson HB. Does insertion and use of an intrauterine device increase the risk of pelvic inflammatory disease among women with sexually transmitted infection? A systematic review. *Contraception*. 2006; 73(2):145–53. [PubMed: 16413845]
95. Sufrin CB, Postlethwaite D, Armstrong MA, Merchant M, Wendt JM, Steinauer JE. Neisseria gonorrhea and chlamydia trachomatis screening at intrauterine device insertion and pelvic inflammatory disease. *Obstet Gynecol*. 2012; 120(6):1314–21. [PubMed: 23168755]
96. Sivin I, Stern J, Diaz J, Diaz MM, Faundes A, el Mahgoub S, et al. Two years of intrauterine contraception with levonorgestrel and with copper: A randomized comparison of the tcu 380ag and levonorgestrel 20 mcg/day devices. *Contraception*. 1987; 35(3):245–55. [PubMed: 3111785]
97. Soderberg G, Lindgren S. Influence of an intrauterine device on the course of an acute salpingitis. *Contraception*. 1981; 24(2):137–43. [PubMed: 7297065]
98. Haggerty CL, Peipert JF, Weitzen S, Hendrix SL, Holley RL, Nelson DB, et al. Predictors of chronic pelvic pain in an urban population of women with symptoms and signs of pelvic inflammatory disease. *Sex Transm Dis*. 2005; 32(5):293–9. [PubMed: 15849530]
99. Scholes D, Stergachis A, Heidrich FE, Andrilla H, Holmes KK, Stamm WE. Prevention of pelvic inflammatory disease by screening for cervical chlamydial infection. *N Engl J Med*. 1996; 334(21):1362–6. [PubMed: 8614421]
100. Ostergaard L, Andersen B, Moller JK, Olesen F. Home sampling versus conventional swab sampling for screening of chlamydia trachomatis in women: A cluster-randomized 1-year follow-up study. *Clin Infect Dis*. 2000; 31(4):951–7. [PubMed: 11049776]
101. Marrazzo JM, Martin DH. Management of women with cervicitis. *Clin Infect Dis*. 2007; 44(Suppl 3):S102–10. [PubMed: 17342663]
102. Paavonen J, Aine R, Teisala K, Heinonen PK, Punnonen R. Comparison of endometrial biopsy and peritoneal fluid cytologic testing with laparoscopy in the diagnosis of acute pelvic inflammatory disease. *Am J Obstet Gynecol*. 1985; 151(5):645–50. [PubMed: 3156502]
103. Walker CK, Landers DV, Ohm-Smith MJ, Robbie MO, Luft J, Schachter J, et al. Comparison of cefotetan plus doxycycline with cefoxitin plus doxycycline in the inpatient treatment of acute salpingitis. *Sex Transm Dis*. 1991; 18(2):119–23. [PubMed: 1862460]
104. Comparative evaluation of clindamycin/gentamicin and cefoxitin/doxycycline for treatment of pelvic inflammatory disease: A multi-center trial. The european study group. *Acta Obstet Gynecol Scand*. 1992; 71(2):129–34. [PubMed: 1316041]
105. McGregor JA, Crombleholme WR, Newton E, Sweet RL, Tuomala R, Gibbs RS. Randomized comparison of ampicillin-sulbactam to cefoxitin and doxycycline or clindamycin and gentamicin in the treatment of pelvic inflammatory disease or endometritis. *Obstet Gynecol*. 1994; 83(6):998–1004. [PubMed: 8190448]
106. Walters MD, Gibbs RS. A randomized comparison of gentamicin-clindamycin and cefoxitin-doxycycline in the treatment of acute pelvic inflammatory disease. *Obstet Gynecol*. 1990; 75(5):867–72. [PubMed: 2183112]
107. Piyadigamage A, Wilson J. Improvement in the clinical cure rate of outpatient management of pelvic inflammatory disease following a change in therapy. *Sex Transm Infect*. 2005; 81(3):233–5. [PubMed: 15923292]

Key Points

- The diagnosis of PID is based on clinical findings and requires a high index of suspicion.
- PID is caused both by common sexually transmitted infections like *N. gonorrhoeae* and *C. trachomatis*, and by anaerobic vaginal microbes.
- Antibiotic coverage for anaerobic bacteria should be considered when treating severe PID
- Early identification and treatment of cervical infections can prevent PID.

Table 1

Prevalence of signs and symptoms in women with confirmed salpingitis or endometritis.

Symptom	Prevalence	Reference
Fever > 38.5	33–34%	[47, 49]
WBC > 10,000 cells/mL	36–70%	[49, 50]
ESR > 15 mm/hour	36–77%	[49, 50]
Mucopurulent cervical discharge	56%	[49]
Leukorrhea (> 10 WBC/hpf on wet mount)	22.1%	[53]
Irregular vaginal bleeding	36–64%	[47, 50]

Table 2

Incidence of endometritis and salpingitis among women with suspected PID and both laparoscopic and endometrial evaluation.

Study	Endometritis Alone	Salpingitis Alone	Endometritis + Salpingitis
Paavonen [102]	3/27 (11.1%)	2/27 (7.4%)	16/27 (59.3%)
Wasserheit [28]	8/33 (24.2%)	1/33 (3.0%)	14/33 (42.4%)
Eckert [49]	26/152 (17.1%)	11/144 (7.6%)	64/144 (44.4%)

Table 3

Summary of short-term and long-term effects of outpatient compared to inpatient therapy for mild-moderate PID in the PEACH trial

	Outpatient	Inpatient	P value
Short term (30 days)			
Gonorrhea positive	3.9%	2.4%	0.44
Chlamydia positive	2.7%	3.6%	0.52
Persistent tenderness	20.6%	18.4%	0.50
Endometritis	45.9%	37.6%	0.09
Long term outcomes (mean 35 months)			
Pregnancy	59.4%	55.6%	NS
Ectopic	1.2%	0.2%	NS
Infertility	16.7%	20.6%	NS
Chronic pelvic pain	40.7%	44.6%	NS
Recurrent PID	18.4%	24.3%	NS

Adapted from Ness et al 2002 [61], and Ness et al 2005 [62]

NS = Not statistically significant

Table 4

Reported efficacy of CDC-recommended treatment regimens for inpatient and outpatient management of PID

TnQTable5	% Response to treatment	References
Inpatient		
Cefotetan 2g IV q12h AND Doxycycline 100mg PO/IV q12h [§] followed by Doxycycline 100mg PO BID for a total of 14 days	89–94%	[66, 103]
Cefoxitin 2g IV q6h AND Doxycycline 100mg PO/IV q12h [§] followed by Doxycycline 100mg PO BID for a total of 14 days	84–95%	[61, 103–106]
Clindamycin 900mg IV q8h AND Gentamicin 2mg/kg IV/IM load then 1.5 mg/kg maintenance OR 3–5mg/kg daily dosing Followed by Doxycycline 100mg PO BID OR Clindamycin 450mg PO QID [¶] , total 14 day course	84–90%	[66, 104, 106]
Ampicillin/Sulbactam 3g IV q6h AND Doxycycline 100mg PO/IV q12h [§] Followed by Doxycycline 100mg PO BID, total 14 day course	85–94%	[71, 105]
Outpatient**		
Ceftriaxone 250mg IM once AND Doxycycline 100mg PO BID, total 14 days;	72–95%	[60, 70, 107]
Cefoxitin 2mg IM once, with Probenecid 1g PO once AND Doxycycline 100mg PO BID, total 14 days;	90%	[61]
Other parenteral third-generation cephalosporin (cefotaxime, ceftizoxime) AND Doxycycline 100mg PO BID, total 14 days	-	

[§]Equivalent oral and IV bioavailability for doxycycline. IV doxycycline causes burning, therefore elect for oral doxycycline if able to be tolerated

[°]Must add clindamycin 450mg PO QID or metronidazole 500mg PO q6h in the setting of tubo-ovarian abscess, for a total 14 day course

[¶]Continue clindamycin in the setting of tubo-ovarian abscess

* Higher end of range is a regimen including metronidazole

** for all three regimens, consider adding metronidazole 500mg PO BID for 7 days

Box 1

CDC Criteria for PID Diagnosis (adapted from Workowski et al [67])

Minimum Criteria (at least one needed for diagnosis)	Additional Criteria (support a diagnosis of PID)	Definitive Criteria (confirm the diagnosis of PID)
<ul style="list-style-type: none"> • Cervical motion tenderness • Uterine tenderness • Adnexal tenderness 	<ul style="list-style-type: none"> • Oral temperature >101°F, or 38.3°C • Abnormal vaginal or cervical discharge • White blood cells on saline wet mount (>10 polymorphonuclear leukocytes per high-power field [101]) • Elevated erythrocyte sedimentation rate (> 15 mm/??) • Elevated C-reactive protein, • Elevated white blood cell count > 10,000 cells/mL • Laboratory evidence of <i>Neisseria gonorrhoea</i> or <i>Chlamydia trachomatis</i> infection 	<ul style="list-style-type: none"> • Histopathologic evidence of endometritis • Imaging showing thickened, fluid-filled tubes, with or without pelvic free fluid or tubo-ovarian complex, • Doppler studies suggesting pelvic infection, • Intra-abdominal findings consistent with PID on laparoscopy

Box 2

Criteria for Inpatient Management of PID

- Surgical emergencies cannot be ruled out
- Pregnancy
- Lack of clinical response to oral antimicrobial PID therapy after 72 hours
- Inability to tolerate or comply with outpatient management
- Severe illness, high fever, nausea, vomiting
- Presence of tubo-ovarian abscess