

The Challenge of Pelvic Inflammatory Disease

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Pelvic inflammatory disease (PID) is an infection of the upper genital tract in women that can include endometritis, parametritis, salpingitis, oophoritis, tubo-ovarian abscess, and peritonitis. The spectrum of disease ranges from subclinical, asymptomatic infection to severe, life-threatening illness; sequelae include chronic pelvic pain, ectopic pregnancy, and infertility. PID is diagnosed clinically, with laboratory and imaging studies reserved for patients who have an uncertain diagnosis, are severely ill, or do not respond to initial therapy. The Centers for Disease Control and Prevention diagnostic criteria include uterine, adnexal, or cervical motion tenderness with no other obvious cause in women at risk of PID. Empiric treatment should be initiated promptly and must cover *Chlamydia trachomatis* and *Neisseria gonorrhoeae*; the possibility of fluoroquinolone-resistant *N. gonorrhoeae* also should be considered. Hospitalization for initial parenteral therapy is necessary for patients with tubo-ovarian abscess and for those who are pregnant, severely ill, unable to follow a prescribed treatment plan, or unable to tolerate oral antibiotics. Patients also should be hospitalized if a surgical emergency cannot be excluded or if no clinical improvement occurs after three days. Routine screening for asymptomatic chlamydial infection can help prevent PID and its sequelae. (*Am Fam Physician* 2006;73:859-64. Copyright © 2006 American Academy of Family Physicians.)

► **Patient information:**
A handout on pelvic inflammatory disease is available online at <http://www.familydoctor.org/213.xml>.

Pelvic inflammatory disease (PID) is a polymicrobial infection that originates from upward spread of infecting organisms through the cervix and into the uterus, fallopian tubes, or peritoneal cavity. It affects up to 1.5 million women in the United States and costs an estimated \$1.06 billion each year.¹ The etiologic agent often is never identified, but common causal agents are *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and aerobic and anaerobic vaginal flora (including organisms involved in bacterial vaginosis).

Symptoms of PID include lower abdominal pain, dyspareunia, fever, back pain, and vomiting, as well as symptoms of lower genital tract infection such as abnormal vaginal discharge or bleeding, itching, and odor. In some women, symptoms are mild or even absent. The strong association of the disease with sexually transmitted infection and the potential for serious sequelae such as infertility and ectopic pregnancy contribute to the significant psychological distress that often accompanies a diagnosis of PID.

Clinical Diagnosis

Diagnosing PID is challenging because the infection may be localized in one or more of a

variety of locations; the symptoms can range from absent to subtle to severe; results of microbiologic assessment often are not readily available; and more accurate diagnostic modalities are invasive, costly, or not easily accessible. Risk factors for PID include the presence of a sexually transmitted infection, a previous episode of PID, sexual intercourse at an early age, high number of sexual partners, and alcohol use.² In addition, several risk factors have been identified for urban adolescents: older sex partners (who may be more sexually experienced and thus more likely to have and spread sexually transmitted infections) and previous involvement in child protective services or attempted suicide (which may indicate a history of abuse or rape).²

With the availability of urine tests for gonorrhea and chlamydia, physicians in some settings (e.g., where pelvic examination is difficult to perform) may be examining, diagnosing, and treating women with lower genital tract symptoms without speculum or bimanual examinations. Evidence suggests, however, that bimanual and speculum examinations with testing for chlamydia and gonorrhea should be performed for all women who have lower abdominal pain or dyspareunia in addition to symptoms of

SORT: KEY RECOMMENDATIONS FOR PRACTICE

<i>Clinical recommendation</i>	<i>Evidence rating</i>	<i>References</i>
Physicians should suspect PID and have a low threshold to treat in women who are at risk of PID and have uterine, adnexal, or cervical motion tenderness on bimanual examination with no other apparent cause.	C	4
Women with mild to moderate PID may receive outpatient medical treatment without increased risk of long-term sequelae.	B	15, 16
Fluoroquinolones should not be used in women with PID who have been to an area where fluoroquinolone-resistant <i>Neisseria gonorrhoeae</i> is endemic, who have had a partner who has been to an endemic area, or who have had a male partner who has sex with men.	C	13
Screening for and treating asymptomatic lower genital tract chlamydial infection is recommended to reduce the incidence of PID.	A	15, 18

PID = pelvic inflammatory disease.

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, see page 755 or <http://www.aafp.org/afpsort.xml>.

lower genital tract infection.³ In one small study,³ all patients with a clinical diagnosis of PID reported lower abdominal pain or pain with sexual intercourse in addition to symptoms of lower genital tract infection. The authors suggest that women who have symptoms of lower genital tract infection but who deny lower abdominal pain and dyspareunia are unlikely to have PID and may be evaluated by urine and vaginal swab

testing instead of speculum and bimanual examination.³

The Centers for Disease Control and Prevention (CDC) guidelines on sexually transmitted diseases,⁴ which were updated in 2002, recommend that physicians have a low threshold for the diagnosis of PID and initiate empiric treatment in women who are at risk of PID and have uterine, adnexal, or cervical motion tenderness on bimanual examination with no other apparent cause.⁴ The complete CDC diagnostic criteria for PID are listed in *Table 1*.⁴ The change in CDC criteria is supported by an analysis of data from the Pelvic Inflammatory Disease Evaluation and Clinical Health (PEACH) study⁵ that suggests the 1998 CDC criteria would miss more than 15 percent of true cases of upper genital tract infection. Analysis of the PEACH data⁵ also showed that the presence of adnexal tenderness on bimanual examination had a sensitivity of 95.5 percent for histologic endometritis. The authors recommend that physicians consider empiric treatment for all women who are at risk of PID and have adnexal tenderness with no other obvious cause.⁵

Diagnostic Testing

When the diagnosis of PID is questionable, or when the illness is severe or not responding to therapy, further investigation may be needed. Although not routinely recommended, several laboratory tests, imaging studies, and invasive procedures, with vary-

TABLE 1
CDC Diagnostic Criteria for PID

PID should be suspected and treatment initiated if:

Patient is at risk of PID

and

Patient has uterine, adnexal, or cervical motion tenderness with no other apparent cause

Findings that support the diagnosis

- Cervical or vaginal mucopurulent (green or yellow) discharge
- Elevated erythrocyte sedimentation rate or C-reactive protein
- Laboratory confirmation of gonorrheal or chlamydial infection
- Oral temperature of 101°F (38.3°C) or greater
- White blood cells on vaginal secretion saline wet mount

Most specific criteria for the diagnosis

- Endometritis on endometrial biopsy
- Laparoscopic abnormalities consistent with PID
- Thickened, fluid-filled tubes apparent on transvaginal ultrasound or magnetic resonance imaging

CDC = Centers for Disease Control and Prevention; PID = pelvic inflammatory disease. Information from reference 4.

ing costs and availability, have been evaluated for this purpose.

The absence of vaginal polymorphonuclear leukocytes on the vaginal secretion saline wet mount excluded histologic endometritis more than 90 percent of the time in one study,⁶ with a negative predictive value of 94.5 percent. In a study⁷ of serum white blood cell counts, wet mount polymorphonuclear leukocytes, and erythrocyte sedimentation rates in women with a clinical diagnosis of acute PID or other signs of upper genital tract infection, no single laboratory test had good sensitivity and specificity. However, normal results on all three tests effectively excluded upper genital tract infection.⁷ Often, though, serum blood cell count and erythrocyte sedimentation rate test results are not available rapidly, and if PID is suspected, then treatment should be initiated.⁴

Imaging studies that have been investigated in the evaluation of PID include transvaginal ultrasound,^{8,9} computed tomography,¹⁰ and magnetic resonance imaging (MRI).¹¹ The classic findings of acute PID on transvaginal ultrasound are tubal wall thickness greater than 5 mm, incomplete septae within the tube, fluid in the cul-de-sac, and the cogwheel sign (a cogwheel appearance on the cross-section tubal view).⁸ Transvaginal ultrasound often is helpful in diagnosing tubo-ovarian abscess, which may complicate PID. The addition of color Doppler flow (or “power Doppler”) to the standard black-and-white transvaginal ultrasound has been used to assess vascularity and pulsatility indices. In one small study,⁹ the power Doppler identified all laparoscopically confirmed cases of acute PID in the study group, and thus was found to be 100 percent sensitive for this diagnosis.

Signs of PID apparent on computed tomography of the pelvis are subtle changes in appearance of the pelvic floor fascial planes, thickened uterosacral ligaments, inflammatory changes of the tubes or ovaries, and abnormal fluid collection. If the disease progresses, reactive inflammation of surrounding pelvic and abdominal organs may be observed.¹⁰ On MRI, the diagnosis of PID is indicated by the presence of a tubo-ovarian abscess, a pyosalpinx, a fluid-filled fallopian

tube, or polycystic-like ovaries with free pelvic fluid.¹¹ MRI proved superior to transvaginal ultrasound in diagnosing PID, with a sensitivity of 95 percent and a specificity of 89 percent¹¹; however, MRI is more expensive.

Invasive examination sometimes is needed to confirm the diagnosis of PID or to eliminate other considerations. Endometritis can be diagnosed readily from histologic examination of endometrial biopsy specimens obtained with a suction cannula. Laparoscopy also has been used in diagnosing PID and has been considered the preferred method for this diagnosis. The procedure allows direct visualization of the ovaries, uterus, fallopian tubes, and other abdominal structures; however, it does carry the inherent risks of surgery and anesthesia as well as having other limitations (i.e., high cost, need for facilities, and personnel requirements). Furthermore, despite being considered the preferred method for diagnosing PID, laparoscopy has never been validated as such. One study¹² showed laparoscopic diagnosis of PID to be accurate in only 78 percent of cases, with a sensitivity of 27 percent and a specificity of 92 percent.

The CDC considers the most specific diagnostic criteria for acute PID to be histologic endometritis on endometrial biopsy specimen; thickened, fluid-filled tubes on transvaginal ultrasound or MRI; and abnormal laparoscopic findings.⁴ There is no clear delineation of when these more extensive investigations should be used.

Treatment

Physicians should have a high index of suspicion for PID and should initiate therapy in all women who are at risk of PID and have uterine, adnexal, or cervical motion tenderness on bimanual examination with no other apparent cause.⁴ The antibiotic must cover *N. gonorrhoeae* and *C. trachomatis*, and possibly also anaerobes, gram-negative facultative bacteria, and Streptococcus species. The 2002 CDC guidelines for antibiotic treatment of PID are listed in *Table 2*.⁴

Antibiotic therapy should be initiated in all women at risk of pelvic inflammatory disease who have uterine, adnexal, or cervical motion tenderness with no other apparent cause.

Screening women who are at risk of sexually transmitted lower genital tract infections can reduce the incidence of pelvic inflammatory disease.

Fluoroquinolone-resistant *N. gonorrhoeae* has become an important consideration in directing empiric therapy. The increase in resistant *N. gonorrhoeae* has been limited to particular geographic areas and populations. China, Japan, Korea, the Philippines, Singapore, and Vietnam have the highest rates (46 to 92.5 percent); but England, Wales, and Australia all have rates higher than 5 percent,¹³ and high rates also are found in California and certain other areas within the United States (local resistance rates can be found by checking with a local public health official). Increased rates of fluoroquinolone-resistant *N. gonorrhoeae* also have been found in men who

have sex with men. Consequently, fluoroquinolones are not recommended for treatment of gonorrhea in this population or for cases acquired in the endemic areas noted above¹³; thus, fluoroquinolones should not be used to treat PID in a woman who has been in an endemic area, has had a partner from an endemic area, or has had a male partner who also has sex with men.

Generally accepted indications for inpatient management of PID are listed in Table 3.⁴ Hospitalization also may be necessary for patients who are unlikely to adhere to the treatment plan and to follow up as requested. If none of these conditions is present, then the patient may be managed initially as an outpatient. However, outpatients should be reevaluated within three

TABLE 2
CDC Recommendations for Antibiotic Treatment of PID

Parenteral regimen*

Cefotetan (Cefotan) 2 g IV every 12 hours or cefoxitin (Mefoxin) 2 g IV every six hours[†]; plus doxycycline (Vibramycin) 100 mg orally or IV every 12 hours[‡]

Alternatives:

Clindamycin (Cleocin) 900 mg IV every eight hours[§]; plus gentamicin loading dose IV or IM (2 mg per kg) followed by a maintenance dose (1.5 mg per kg) every eight hours (single daily dosing may be substituted)

Ofloxacin (Floxin) 400 mg IV every 12 hours or levofloxacin (Levaquin) 500 mg IV once daily; with or without metronidazole (Flagyl) 500 mg IV every eight hours

Ampicillin/sulbactam (Unasyn) 3 g IV every six hours; plus doxycycline 100 mg orally or IV every 12 hours

Oral regimen

Ofloxacin 400 mg orally twice daily for 14 days or levofloxacin 500 mg orally once daily for 14 days^{||}; with or without metronidazole 500 mg orally twice daily for 14 days

Alternative:

Ceftriaxone (Rocephin) 250 mg IM in a single dose or cefoxitin 2 g IM in a single dose with concurrent probenecid (Benemid) 1 g orally in single dose or other parenteral third-generation cephalosporin; plus doxycycline 100 mg orally twice daily for 14 days with or without metronidazole 500 mg orally twice daily for 14 days

CDC = Centers for Disease Control and Prevention; PID = pelvic inflammatory disease; IV = intravenous; IM = intramuscular.

*—Parenteral therapy generally can be discontinued 24 hours after clinical improvement.

†—Cefotetan and cefoxitin have greater anaerobic activity than other third-generation cephalosporins.

‡—Doxycycline should be given orally whenever possible because of pain with infusion. Doxycycline 100 mg orally twice daily should be continued to complete 14 days of therapy. If tubo-ovarian abscess is present, the addition of clindamycin or metronidazole for continued therapy should be considered.

§—Continued oral therapy may consist of clindamycin 450 mg four times daily or doxycycline 100 mg twice daily.

||—Consider possibility of fluoroquinolone-resistant *Neisseria gonorrhoeae*.

Information from reference 4.

days, and if there is no improvement, then inpatient parenteral therapy should be instituted.⁴ The CDC does not consider the nulligravid state to be an indication for hospital admission, but the International Infectious Disease Society for Obstetrics and Gynecology-USA disagrees: it recommends that all nulligravid adolescents be admitted to the hospital for therapy and education.¹⁴

The PEACH study was designed to investigate whether inpatient treatment of PID

was superior to outpatient treatment in preventing long-term sequelae (*Table 4*¹⁵ lists treatment regimens used).^{15,16} The findings showed no statistical differences in frequency of PID recurrence, chronic pelvic pain, infertility, or ectopic pregnancy between participants treated as inpatients and those treated as outpatients.¹⁵ Thus, outpatient medical treatment for women with a clinical diagnosis of mild to moderate PID does not appear to lead to increased long-term sequelae.¹⁵

TABLE 3

Criteria for Inpatient Treatment of PID

Failure to improve after three days of outpatient therapy
 Inability to follow or tolerate oral antibiotics
 Pregnancy
 Severe illness (i.e., high fever, vomiting)
 Surgical emergency cannot be excluded
 Tubo-ovarian abscess

PID = pelvic inflammatory disease.

Information from reference 4.

TABLE 4

Treatment Regimens in the PEACH Study

Inpatient (minimum 48 hours admission)

Cefoxitin (Mefoxin) 2 g parenterally every six hours; *plus* doxycycline (Vibramycin) 100 mg parenterally, then 100 mg orally or parentally twice daily* *followed by* doxycycline 100 mg orally twice daily as outpatient for 14 days total therapy.

Outpatient

Cefoxitin 2 g IM; *plus* probenecid (Benemid) 1 g orally *plus* doxycycline 100 mg orally twice daily for 14 days

PEACH = Pelvic Inflammatory Disease Evaluation and Clinical Health; IM = intramuscular; IV = intravenous.

*—Doxycycline initially was administered by IV twice daily for the entire inpatient stay, but because of the high incidence of phlebitis with IV administration, this was changed to an initial IV dose followed by supervised oral administration.

Information from reference 15.

Prevention

One of the major efforts in the prevention of PID has been in screening for and treating asymptomatic lower genital tract chlamydial infections. In a large randomized controlled trial¹⁷ conducted in 1996, the incidence of PID decreased from 18 per 10,000 woman-months to eight per 10,000 woman-months when women 18 to 34 years of age who were at risk of PID were screened for lower genital tract chlamydial infection.

The U.S. Preventive Services Task Force (USPSTF)¹⁸ and the CDC⁴ consider there to be good evidence that screening for lower genital tract chlamydial infection decreases the incidence of PID and the prevalence of community chlamydial infection. They recommend screening all sexually active women younger than 25 years for chlamydial infection.^{4,18} The USPSTF also recommends screening all sexually active women for gonorrhea if they are at increased risk of infection.¹⁹

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