PELVIC INFLAMMATORY

The Most Serious and Costly Bacterial Sexually

BOB CARUTHERS, CST, PHD
INTRODUCTION

Pelvic inflammatory disease (PID) is a global term that refers to a broad spectrum of disorders of the upper female genital tract. These disorders include any combination of the following: endometritis, salpingitis, tubo-ovarian abscess, or pelvic peritonitis. PID is associated with the ascension of pathogens from the lower to the upper reproductive tract. The most common organisms associated with the disease are *N. gonorrhoeae* and *C. trachomatis*; however, the microorganisms of the vaginal flora (*anaerobes, G. vaginalis, H. influenzae, enteric Gram-negative rods, and Streptococcus agalactiae*) can cause PID. Pelvic inflammatory disease may be acute, subacute or chronic in presentation and may contribute to the formation of adhesions, infertility and ectopic pregnancy.

This disease and its sequelae create diagnostic and treatment issues for the pediatrician, family practitioner, obstetrician, gynecologist and general surgeon. Surgical intervention may be required for diagnostic and/or treatment purposes.

EPIDEMIOLOGY

Approximately 10 percent of all females of reproductive age report a history of PID, and 1 percent of young and sexually active females present with yearly infection. Simms and Rogers, reporting for the Communicable Disease Surveillance Centre of the United Kingdom, found PID diagnosed in general practice in 1.7 percent of women between the ages of 16 and 46. The disease develops in 10 to 40 percent of females who have been inadequately treated for chlamydial or gonococcal cervicitis. Paavonen and Eggert-Kruse recognize *C. trachomatis* infections as the most prevalent bacterial sexually transmitted disease (STD) in the world. Approximately 20 percent of women with lower genital-tract chlamydial infections develop PID. In contradiction to traditional thinking, Abbuhl, Muskin and Shofer demonstrated the presence of PID in 11.7 percent of 209 patients who had previously had bilateral tubal ligation. Lawson and Blythe found the adolescent population to have a significantly higher rate of the disease than any other age group.

The sequelae to PID are also common. In 1997, Hillis and colleagues used a retrospective study to demonstrate increased rates for PID and infertility in women with two or more chlamydial infections. Paavonen and Eggert-Kruse found infertility and adverse pregnancy outcomes at 3 percent and 2 percent respectively following chlamydial infection.
1993, Hillis’ group found that women with PID who delayed in seeking care for the condition were three times as likely to experience infertility or ectopic pregnancy, and the strongest correlation was with chlamydial infections. Lepine et al looked at a large population of women who had been diagnosed with acute PID. Twelve years after the indicated diagnosis, live births had been achieved by 90 percent of those diagnosed with mild cases, 82 percent with moderate cases, and 57 percent with severe cases of PID. Three factors are therefore implicated in increased incidence of infertility and decreased incidence of live birth:

- Delay in initial treatment
- Severity of PID at time of diagnosis
- Chlamydia related infection.

PID is not only common; it is expensive. Direct treatment of PID cost an estimated $5.5 billion in 1994. This figure does not include the indirect costs related to treatment of sequelae.

**PATHOGENESIS**

The most common causes of PID by an individual pathogen are C. trachomatis, N. gonorrhoeae, and genital mycoplasmas (Mycoplasma hominis, Ureaplasma urealyticum, and Mycoplasma genitalium). Agents, such as C. trachomatis and N. gonorrhoeae, are transferred during sexual intercourse and their infective mechanisms are well known. A cluster of infected persons is typical within core groups of sexually active individuals. Today, N. gonorrhoeae infections are disproportionately concentrated in inner city and minority populations.

Chlamydial infections, on the other hand, are distributed relatively equally across most racial, ethnic and economic groups. M. hominis, U. urealyticum, and M. genitalium are known causes of nongonococcal urethritis. Some debate remains concerning the issue of whether these organisms can cause PID as...
a singular agent. Current information suggests that these agents should be covered during antibiotic treatment in spite of clear consensus of the causative power.1

The endogenous lower reproductive tract microorganisms plus gastrointestinal microflora (E. coli) and anaerobic bacteria associated with vaginosis are the most commonly isolated microorganisms following laparoscopy or drainage of pelvic abscesses.

Spread of chlamydial and gonococcal cervical infections to the endometrium and fallopian tubes is facilitated by normal uterine and tubal motility. Other normal factors, such as viscous cervical mucin, may protect against spread as does the use of barrier contraceptives and safe sex practices.

The mechanism of gonococcal and chlamydial infection is relatively well understood. Both have molecules that selectively adhere to genitourinary and other mucosal epithelial cell receptors. Both are intracellular pathogens that create an intense inflammatory response with production of film-like fibrous adhesions. This immunologic response itself adversely affects ovum implantation and trophoblast development.

Gram-negative bacteria (N. gonorrhoeae, E. coli, and species of Bacteroides and Prevotella) can cause tubal damage without direct invasion of the tube itself. They release cell wall lipopolysaccharides and endotoxins resulting in desolation of tubal microcilia and subsequent dysfunction in the tubal transport mechanism.

As indicated above, adolescent females are especially vulnerable to PID. This vulnerability results from sexual activity and the following factors:

- inadequate acquired mucosal immunity to STDs
- advanced endocervical epithelium on the cervical face
- increased prevalence of infection in consort group
- psychological reluctance to seek diagnostic and treatment services
- decreased economic resources.

### TABLE 1. CLINICAL DIAGNOSTIC CRITERIA FOR PID

<table>
<thead>
<tr>
<th>Necessary Findings</th>
<th>Confirmatory Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical examination (requires all to be present)</td>
<td>Clinical or laboratory (one must be present)</td>
</tr>
<tr>
<td>• Abdominal tenderness</td>
<td>• Fever of 38.3°C (101°F) or higher</td>
</tr>
<tr>
<td>• Cervical motion tenderness</td>
<td>• Purulent cervical discharge</td>
</tr>
<tr>
<td>• Adnexal tenderness (unilateral or bilateral)</td>
<td>• Leukocytosis</td>
</tr>
<tr>
<td></td>
<td>• Elevated erythrocyte sedimentation rate</td>
</tr>
<tr>
<td></td>
<td>• Elevated C-reactive protein</td>
</tr>
<tr>
<td></td>
<td>• Documented gonococcal or chlamydial infection of the cervix</td>
</tr>
</tbody>
</table>
The relationship between STD pathogens and PID is summarized in Figure 1.

**DIAGNOSTIC CONSIDERATIONS**
Women present with a broad spectrum of signs and symptoms. To date, no single finding from the patient's history, physical examination, or laboratory results will identify acute PID and rule out other possible diagnoses. Some cases are asymptomatic, but the most common signs and symptoms found in women whose diagnosis was confirmed laparoscopically are:
- tenderness in the lower abdomen (both with and without rebound)
- tenderness to palpation and motion of the uterus and adnexa
- purulent cervical discharge.
Diagnostic criteria are found in Table 1.

With any sign or symptom of pregnancy, a human chorionic gonadotropin (hCG) test should be performed promptly. A pelvic ultrasound may be helpful in demonstrating enlarged fallopian tubes or fluid in the cul-de-sac. Culdocentesis may be performed under local anesthesia if a ruptured ectopic pregnancy is considered possible and ultrasound and hCG testing are inconclusive. Genetic, antigen testing and/or culture should be performed to detect gonococcal and chlamydial infections. (Positive findings in these cases require testing and treatment of consorts.) Laparoscopy is diagnostic 90 percent or more of the time but is expensive, and its use should be reserved for cases in which other possible disease entities can not be ruled out by any other means.

The Center for Disease Control (1998) considers the definitive criteria for PID to be:
- histopathologic evidence of endometritis following endometrial biopsy
- transvaginal sonography (or other diagnostic imaging technique) demonstrating fallopian tubes that are thickened and fluid-filled, with or without free pelvic fluid
- laparoscopic demonstration of abnormalities consistent with PID.

As previously mentioned, these procedures should be restricted to select cases.

### TABLE 2. CDC RECOMMENDED ANTIMICROBIAL REGIMENS FOR TREATMENT OF PID

<table>
<thead>
<tr>
<th>TYPE</th>
<th>REGIMEN</th>
<th>MEDICATION(S)</th>
<th>DOSAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parenteral</td>
<td>A</td>
<td>Cefotan or Cefoxitin combined with Doxycycline</td>
<td>2g IV every 12 hours 2 g IV every 6 hours 100 mg IV or orally every 12 hours</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>Clindamycin combined with Gentamicin</td>
<td>900 mg every 8 hours Loading dose 2mg/kg body weight with maintenance does of 1.5 mg/kg every 8 hours (single daily dose may be used)</td>
</tr>
<tr>
<td>others</td>
<td>little current research support</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral</td>
<td>A</td>
<td>Ofloxacin combined with Metronidazole</td>
<td>400 mg twice a day for 14 days 500 mg twice a day for 14 days</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>Ceftriaxone or Cefoxitin or other third-generation cephalosporin combined with Doxycycline</td>
<td>250 mg IM times 1 2 g IM plus Probenecid 1 g orally concurrently times 1 100 mg orally twice a day for 14 days</td>
</tr>
<tr>
<td></td>
<td>other</td>
<td>research information limited</td>
<td></td>
</tr>
</tbody>
</table>
TREATMENT

Treatment for PID has three basic components: broad-spectrum antimicrobial coverage, management of sexual partners and/or lifestyle, and follow-up monitoring. Typically, treatment may be accomplished without hospitalization. The CDC has established the following criteria for hospitalization:

- unable to rule out other surgically emergent conditions
- pregnancy
- lack of clinical response to oral antimicrobial therapy
- inability to follow or tolerate outpatient oral antimicrobial regimen
- severe illness, nausea and vomiting, or high fever
- presence of tubo-ovarian abscess
- immunodeficient patient (HIV infection with low CD4 count, current immunosuppressive therapy, other immunosuppressive disease).

Treatment should be initiated as soon as PID is established as a presumptive diagnosis. All regimens should provide broad-spectrum coverage of the likely pathogens including N. gonorrhoeae, C. trachomatis, anaerobes, gram-negative bacteria, and Streptococci. Regimens recommended by the CDC are presented in Table 2. A brief description of the primary medications used in these regimens is found in Table 3. In cases in which the patient is pregnant, the risk of maternal morbidity, fetal wastage, and pre-term delivery mandates hospitalization and parenteral antibiotics.

Two other items are especially important to the treatment regimen: (1) follow-up and (2) management of sex partners. Follow-up routines vary somewhat based on severity, treatment regimen, and response to treatment. Lack of improvement in 72 hours generally suggests further diagnostic tests or surgical intervention or both. Patients who respond well may be best served with re-screening for C. trachomatis and/or N. gonorrhoeae four to six weeks following treatment.

Sex partners should be examined and treated if sexual contact has occurred with the patient in the 60 days preceding the onset of symptoms. Treatment for infection is important to decrease the incidence of recurrence in the patient and to eliminate the infection in the partner. It should be noted that male sex partners are often asymptomatic in cases of C. trachomatis or N. gonorrhoeae.

<table>
<thead>
<tr>
<th>MEDICATION</th>
<th>CHEMICAL FORMULA</th>
<th>ACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampicillin/Sulbactam</td>
<td>Ampicillin with a β-lactamase inhibitor</td>
<td>increased effectiveness over ampicillin against organisms which would ordinarily not be susceptible</td>
</tr>
<tr>
<td>Cefotetan Disodium</td>
<td>C17-H15-N7-Na-208-S4</td>
<td>broad spectrum cephalosporin antibiotic</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>C17-H18-FN3-O3*HCl-H20 synthetic fluoroquinolone broad spectrum</td>
<td>antibacterial with activity against a wide range of Gram-negative and Gram-positive organisms</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>7(S)-Chloro-7-deoxylincomycin</td>
<td>antibacterial and antibiotic</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>α-6-Deoxy-5-hydroxytetracycline</td>
<td>antibiotic</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>A broad spectrum antibiotic complex obtained from Micromonospora purpurea and M. echinospora</td>
<td>inhibits the growth of both Gram-positive and Gram-negative bacteria</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>2-Methyl-5-nitroimidazole-1-ethanol</td>
<td>orally effective trichomonicide used in the treatment of infections caused by Trichomonas vaginalis and Entamoeba histolytica</td>
</tr>
</tbody>
</table>
TUBO-OVARIAN ABSCESS

Tubo-ovarian abscess is potentially lethal and is found in 10 percent of the women hospitalized for PID (Figure 2). Approximately half of these occur in instances of the first episode.1 PID is not necessarily the primary cause of tubo-ovarian abscess. Varela et al reviewed tubo-ovarian abscess cases in their facility and found that 30 percent of the patients had recently undergone some form of uterine instrumentation. A history of PID was reported in 15 percent of the cases.10 Rupture of the abscess results in a spread of peritonitis. Identification of more immediate and severe complications such as tubo-ovarian abscess is mandatory. Treatment ranges from oral antibiotics to emergency laparotomy.

Differentiating tubo-ovarian abscess from PID clinically can be difficult. Slap et al studied adolescents with PID with and without tubo-ovarian abscess. Six variables shown in Table 4 proved important. They concluded that tubo-ovarian abscess patients present with fewer signs of acute illness and they tend to develop symptoms later in the menstrual cycle.11

Argument continues concerning the best mode of treatment, ranging from antibiotics only to immediate laparotomy. Risk demonstrates the positive role of laparoscopic intervention.12 A combined antibiotic and surgical approach is clearly warranted in many cases, and cases showing clinical deterioration should be explored surgically.1 In most of these cases, total abdominal hysterectomy with bilateral salpingo-oophorectomy is recommended along with complete removal of all sources of infection. This may be modified on the basis of individual circumstance. An algorithm for the management of tubo-ovarian abscess is found in Figure 3.

SUMMARY

PID with its attendant sequelae presents a common and severe threat to women’s health. Early diagnosis and comprehensive treatment are necessary to good outcomes. Identification of more immediate and severe complications such as tubo-ovarian abscess is mandatory. Treatment and follow-up may extend to sex partners also.

REFERENCES


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**TABLE 4. TUBO-OVARIAN ABSCESS VERSUS UNCOMPPLICATED PID.**

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>TUBO-OVARIAN ABSCESS</th>
<th>PID ONLY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Last menstrual period &gt; 18 days</td>
<td>60%</td>
<td>17%</td>
</tr>
<tr>
<td>Previous PID</td>
<td>53%</td>
<td>22%</td>
</tr>
<tr>
<td>Palpable adnexal mass</td>
<td>13%</td>
<td>3%</td>
</tr>
<tr>
<td>WBC &gt; 10,500 microliters</td>
<td>33%</td>
<td>64%</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate</td>
<td>33%</td>
<td>64%</td>
</tr>
<tr>
<td>Heart rate &gt; 90 per minute</td>
<td>40%</td>
<td>78%</td>
</tr>
</tbody>
</table>

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CE EXAM

1. Which is not considered a disorder of PID?
   a. tubo-ovarian abscess
   b. endometritis
   c. pelvic peritonitis
   d. ectopic pregnancy

2. PID contributes to ________.
   a. infertility
   b. adhesions
   c. ectopic pregnancy
   d. all of the above

3. ________ is recognized as the most prevalent bacterial STD in the world.
   a. C. trachomatis
   b. N. gonorrhoeae
   c. G. vaginalis
   d. H. influenzae

4. Which age group has a significantly higher rate of PID than the others?
   a. adolescent girls
   b. adolescent boys
   c. mature women
   d. elderly women

5. Which factor is not related to an increase of infertility:
   a. Chlamydia-related infection
   b. severity of PID
   c. ethnicity of patient
   d. delay in treatment

6. Which diagnostic test should be performed if pregnancy is suspected.
   a. ultrasound
   b. gonadotropin test
   c. laparoscopy
   d. antigen test

7. Which is not recommended by the CDC as an antimicrobial treatment of PID:
   a. Cefotan and Doxycycline
   b. Cefoxitin and Ofloxacin
   c. Clindamycin and Gentamicin
   d. Ofloxacin and Metronidazole

8. Which of the following is a broad-spectrum synthetic fluoroquinolone used in PID treatments.
   a. Cefotetan Disodium
   b. Metronidazole
   c. Doxycycline
   d. Ciprofloxacin

9. Further diagnostic tests or surgical intervention may be required if the patient does not improve within ________.
   a. 14 days
   b. 60 days
   c. 72 hours
   d. 48 hours

10. Tubo-ovarian abscess is differentiated from uncomplicated PID by ________.
    a. history of PID
    b. tender inflammatory adnexa mass
    c. adnexal torsion
    d. adnexal infection