Pelvic Inflammatory Disease: Diagnosis And Management

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Background: **Acute pelvic inflammatory disease (PID) is a major gynecologic health problem in the United States, afflicting more than 1 million women each year and generating annual direct and indirect costs estimated at $4.2 billion. Family physicians can play an important role in the prevention, as well as diagnosis and treatment, of PID.**

Methods: **A MEDLINE search for articles published from 1985 to the present was made using the key words "pelvic inflammatory disease," "endometritis," "salpingitis," "tubo-ovarian abscess," "adnexitis," "pelvic abscess," "parametritis," and "oophoritis." The bibliographies of these articles and the author's personal files were also sources of information.**

Results and Conclusions: **A number of risk factors have been linked to PID, including young age, age at first intercourse, multiple sex partners, the presence of bacterial vaginosis, vaginal douching, the use of an intrauterine contraceptive device, and a history of a sexually transmitted disease. The diagnosis of PID represents a major clinical challenge that requires a careful history and physical examination coupled with selective and knowledgeable use of the diagnostic tests and procedures currently available. Broad-spectrum antibiotics, which represent the cornerstone of therapy, must adequately cover the polymicrobial spectrum of pathogens implicated in this infection, which includes *Neisseria gonorrhoeae, Chlamydia trachomatis,* and specific cervicovaginal anaerobic and aerobic bacteria. The numerous sequelae associated with PID, which include infertility, ectopic pregnancy, and chronic pelvic pain syndromes, underscore the need for effective measures for preventing pelvic inflammatory disease. (J Am Board Fam Pract 1994; 7:110-23.)**

Acute pelvic inflammatory disease (PID) is an ascending infection of the female genital tract involving the uterus, fallopian tubes, and adjacent pelvic structures. It is the most frequent serious infection encountered by United States women[1] and is responsible for more than 250,000 hospital admissions and 2.5 million outpatient visits each year. Direct and indirect costs of PID were estimated at greater than $4.2 billion in 1990.[2]

In light of the medical and socioeconomic consequences associated with this disorder, it is imperative that the primary care physician be proficient in its recognition and treatment. This report reviews the clinical aspects of acute PID with a special focus on its epidemiology, diagnosis, and management.

Methods

A MEDLINE search for articles published from 1985 to the present was made using the key words "pelvic inflammatory disease," "endometritis," "salpingitis," "tubo-ovarian abscess," "adnexitis," "pelvic abscess," "parametritis," and "oophoritis." The bibliographies of these articles and the author's personal files were also sources of information.

Incidence

Acute PID is not a reportable disease, and thus precise incidence rates are unavailable. The incidence appears to be increasing, however, as evidenced by estimates of 850,000 cases per year[3] in the mid-1970s rising to more than 1.4 million cases annually by the late-1980s.[2] From a survey conducted in 1988, Aral, et al.[4] found that nearly 11 percent of United States women of reproductive age report having had PID in the past.

Epidemiology

A number of epidemiologic risk factors are associated with PID. Awareness of these factors is of value not only in assessing a patient's risk for having PID but also when counseling female patients regarding contraceptive methods and sexual practices.

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Age

Young women are at greatest risk for acute PID, and nearly 70 percent of cases occur in women younger than 25 years. Scandinavian studies have determined the risk of PID developing in sexually active adolescent girls to be 1 in 8 compared with 1 in 80 in women older than 24 years of age.[5]

Age at First Intercourse

A sexual debut before the age of 16 years was reported by Lidegaard and Helm[6] to be associated with a twofold increased risk of PID compared with women whose age at first intercourse was 18 years or older. Similarly, Aral, et al.[4] found that white women who were sexually active before the age of 15 years were three times more likely to have been treated for PID than those who initiated intercourse after 19 years of age.

Number of Sex Partners

The risk of acute PID is increased two- to threefold for those women who have multiple sex partners.[4,7]

History of PID

Four to 23 percent of patients who have had one episode of PID have a subsequent episode.[8]

History of a Sexually Transmitted Disease

A self-reported history of gonococcal, chlamydial, or herpesvirus infection was reported by Aral and associates[4] to increase a woman's likelihood of PID by 2.5-fold.

Method of Contraception

It is well established that the use of contraceptives influences the risk of development of PID. The presence of an intrauterine contraceptive device (IUD) is associated with a 1.5- to 2.6-fold increased risk of developing acute PID.[1,9] Barrier methods of contraception afford protection against PID, and the Women's Health Study found a 40 percent reduction of risk in users of diaphragms or condoms.[9] The use of combined oral contraceptives has generally been shown to have a protective effect, reducing the risk of PID by up to 50 to 80 percent.[9,10] Although concerns have been expressed regarding the possible enhancement of *Chlamydia trachomatis* infections among oral contraceptive users,[11] a study by Wolner-Hanssen, et al.[12] suggested that oral contraceptives were capable of inhibiting the spread of inflammation into the upper genital tract in patients with chlamydial infections of the cervix.

Vaginal Douching

In a multivariate analysis that controlled for a number of potentially confounding variables (including age, age at first intercourse, history of *Chlamydia trachomatis* or *Neisseria gonorrhoeae* infection or PID, current birth control method, and presence of bacterial vaginosis), Wolner-Hanssen and associates[13] reported that women who douched three or more times a month were 3.4-fold more likely to have acute PID than women who douched less than once a month. This finding was corroborated by Scholes, et al.[14] in a case-control study, which found that women who douched once or more a week had a 3.9-fold increase in risk. Possible mechanisms for this increased risk include flushing of cervicovaginal bacteria into the uterus by the act of douching, as well as a douching-induced alteration of the vaginal environment to one less protective against vaginal pathogens.[13,14]

Bacterial Vaginosis

A positive Gram stain for bacterial vaginosis was found by Eschenbach, et al.[15] to be significantly associated with the clinical diagnosis of acute PID. Corroboration of this finding was provided by Paavonen, et al.[16] who reported a strong association between bacterial vaginosis and patients with histopathologic evidence of PID.

Other

Nonwhite groups are generally regarded as being at increased risk for PID, as are women of a low socioeconomic class. An increased risk has also been observed in women never married, divorced, or separated.[17,18] Marchbanks, et al.[19] recently reported a twofold increased risk of PID among current and former cigarette smokers.

Microbiology

Studies relying on advanced microbiological techniques and upper genital tract cultures have clearly established the polymicrobial causation of acute PID.[16,17,20-23] Moreover, these studies have also demonstrated the lack of concordance between findings on cervical cultures and findings on the microbiologic investigation of upper geni-

tal tract infections. Organisms most frequently implicated in PID, individually as well as sometimes in combination, include *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, endogenous cervicovaginal bacteria, and the genital mycoplasmas.

Neisseria gonorrhoeae

N. gonorrhoeae is a strictly aerobic, gram-negative diplococcus that has long been recognized as an important pathogen in acute PID. Although the number of cases reported to the Centers for Disease Control (CDC) in 1991 was 700,000, an additional one to two cases are thought to occur for every reported case.[24] Ten to 17 percent of women with untreated gonococcal infections of the cervix develop PID, with 66 to 77 percent of these women becoming symptomatic during or within 7 days of the onset of menses.[25] *N. gonorrhoeae* has been isolated from the lower genital tract in 27 to 80 percent of cases of acute PID and from the upper genital tract in 13 to 33 percent of cases.[16]

Chlamydia trachomatis

C. trachomatis is an obligate, intracellular pathogen that currently ranks as the most common sexually transmitted disease in the United States with more than 3 million cases each year.[26] Similar to gonococcal PID, chlamydial PID begins as a cervical infection with an ascending infection developing in 10 to 30 percent of untreated patients.[25] *C. trachomatis* has been implicated on the basis of lower genital tract specimens in 5 to 51 percent of cases of acute PID[17] and on the basis of upper genital tract specimens in 0 to 33 percent of cases.[17,27]

Endogenous Cervicovaginal Bacteria

A variety of anaerobic and facultative aerobic bacteria have been implicated in the causation of acute PID. These organisms, which are derived from the endogenous cervicovaginal flora, have been isolated from the upper genital tract in 38 to 84 percent of patients with PID.[20,21,23,28] Anaerobic bacteria are the major cause of tubo-ovarian abscesses and have been isolated in 63 to 100 percent of cases. Conversely, chlamydia has never been isolated from a tubo-ovarian abscess, and gonorrhea is isolated in less than 4 percent of cases.[29]

Anaerobic bacteria regarded as pathogens in PID include *Peptococcus* species, *Peptostreptococcus* species, *Bacteroides bivius*, *Bacteroides disiens*, and *Bacteroides fragilis*. Facultative aerobes are isolated less frequently than anaerobes and include gram-negative bacilli (including *Escherichia coli*), group B streptococcus, *Gardnerella vaginalis*, and *Haemophilus influenzae*.[20,21,23,25]

Genital Mycoplasmas

Mycoplasma hominis and *Ureaplasma urealyticum* are the two genital mycoplasmas linked to PID. Although commonly recovered from the lower genital tract of patients with PID, they have been infrequently isolated from the upper genital tract.[17,23] Whether they represent true pathogens or are simply commensal organisms (whose presence is simply a marker of the sexual activity of the patient) remains an area of controversy that awaits further elucidation.

Pathogenesis

N. gonorrhoeae and *C. trachomatis* have traditionally been regarded as primary pathogens — sexually transmitted agents deemed capable of initiating infection in a normal upper genital tract. Cervicovaginal bacteria have generally been cast in the role of secondary pathogens — opportunistic organisms capable of infecting only an upper genital tract that has previously been immunologically compromised. Causes of such a compromised state would include (1) an antecedent infection caused by a primary pathogen (which subsequently can be replaced by secondary invaders), (2) instrumentation of the uterus (e.g., cervical dilatation, IUD insertion, endometrial biopsy, hysterosalpingography, abortion procedure), or (3) the overgrowth of endogenous anaerobic and aerobic organisms at the cervical-vaginal interface as seen in patients with bacterial vaginosis.[8,15,17]

In the early 1980s, Sweet and co-workers[21] presented data documenting the presence of cervicovaginal bacteria in the upper genital tract during the early phases of PID, thereby lending indirect support to the hypothesis that these organisms might also be capable of independently initiating infection. In this laparoscopic study, anaerobic bacteria were found in the upper genital tract in 55 percent of patients experiencing their first episode of PID and were isolated from the fallopian tubes in 37 percent of patients within 24 hours of symptom onset. Moreover, in 19 percent of

patients, anaerobes represented the sole isolates. Although it could be argued that the isolated cervicovaginal bacteria represented secondary invaders in patients who had had a previous (albeit unrecognized) subclinical infection attributable to gonorrhea or chlamydia, such data clearly demonstrated the polymicrobial nature of PID even in the early stages of clinical disease.

In an effort to explain the ascension of cervicovaginal bacteria, as well as gonorrhea and chlamydia, into the upper genital tract, a number of theories have been proposed.[30] The vector theory suggests that pathogens present in the lower genital tract are transported in a piggyback fashion by organisms possessing greater powers of locomotion. Both *Trichomonas vaginalis* and spermatozoa have been shown in vitro to be capable of transporting potential pathogens that adhere to their surfaces and have been nominated as possible vectors. Arguing against *T. vaginalis* acting as a vector for gonorrhea, however, is a study by Street, et al.[31] that demonstrated a reduced viability of the latter organism when incubated with *T. vaginalis*. The "in-suck" theory hypothesizes that pressure gradients between the lower and upper genital tracts are generated as the result of uterine contractions occurring during coitus or menstruation and that such gradients might facilitate the ascent of organisms into the upper tract.[30] The existence of such a gradient was established by Fox and associates[32] who recorded a fall in intrauterine pressure to a -25 cm H_2O following female orgasm. Furthermore, it has been shown by Egli and Newton[33] that uterine contractions induced by oxytocin administration can transport inert carbon particles placed in the vaginal cavity up into the fallopian tubes.

Clinical Findings

Acute PID causes a broad spectrum of illness ranging from mild and subclinical illness to severe symptoms with obvious signs of peritonitis. Lower abdominal pain is the most common symptom cited by patients with acute PID but can be absent in 6 percent of patients (Table 1).[34-37] The pain is less than 14 days in duration in 83 percent and typically is aggravated by coitus, movement, and the Valsalva maneuver.[38] Other symptoms include an abnormal vaginal discharge in 38 to 73 percent, vaginal bleeding in 16 to 50 percent, gastrointestinal upset in 10 to 56 percent, and urinary symptoms in approximately 20 percent.

Adnexal and cervical motion tenderness are the physical findings most frequently elicited in patients with acute PID (Table 1),[34-37] with the adnexal tenderness being unilateral in 8 to 20 percent.[37,38] Rebound tenderness can be elicited in 61 to 76 percent of patients, and the presence of an adnexal mass was reported in 16 to 49 percent. Fever is a variable finding present in 24 to 60 percent of patients.

Although considerable overlap exists, the clinical appearance of the patient can offer clues to the responsible pathogen(s). For example, gonococcal PID is classically associated with an acute, abrupt illness, with a greater occurrence of fever and a shorter duration of symptoms prior to the seeking of medical attention compared with patients with nongonococcal PID. Conversely, chlamydial PID tends to be more subtle and has a lesser degree of fever and milder clinical signs and symptoms.[39] Nongonococcal-nonchlamydial PID is more likely in the patient with a tubo-ovarian abscess, as well as the patient who has recently undergone a procedure requiring uterine instrumentation.[17,23]

Laboratory Evaluation

Blood Studies

Blood studies traditionally ordered to evaluate suspected acute PID lack both sensitivity and specificity. Leukocytosis is associated with numerous inflammatory conditions other than PID and can be absent in 33 to 50 percent of cases.[38,40] Both the erythrocyte sedimentation rate (ESR) and the serum C-reactive protein (CRP) determination are also nonspecific indicators of inflammation. Although classically elevated in patients with PID, they can be normal (ESR less than 15 mm/h and CRP less than 20 mg/L) in 25 percent[36] and 26 percent[41] of cases, respectively.

Cervical Gram Stain

The cervical Gram stain is a potentially useful though oftentimes overlooked test for investigating the patient with suspected acute PID. The finding of 10 or more white cells per oil immersion field is diagnostic for mucopurulent cervicitis[42] and is believed to corroborate the diagnosis of PID.[40,43] In addition, in the setting of acute pelvic pain, the finding of gram-negative intracellular diplococci identified within three or more neutrophils on Gram stain has a reported 68 percent sensitivity and a 98 percent specificity for gonococcal cervicitis[38,44] and is similarly supportive of the diagnosis of PID.

Table 1. Historical Aspects of Acute Pelvic Inflammatory Disease: Percentage of Symptoms and Signs Encountered.

Symptoms and signs	Morcos, et al.[34] (n = 134)	Wolner-Hanssen, et al.[35] (n = 76)	Jacobson & Westrom[36] (n = 623)	Bongard, et al.[37] (n = 45)
Abdominal pain	100	100	94	—
Vaginal discharge	73	68	55	38
Vaginal bleeding	16	50	36	31
Nausea or vomiting	28	31	10	56
Urinary symptoms	22	21	19	—
History of PID or STD	25	—	21	44
Adnexal tenderness	90	100	92	78
Unilateral	—	—	—	20
Cervical motion tenderness	80	—	—	82
Abdominal rebound-guarding	61	—	—	76
Adnexal mass	19	24	49	16
Fever	30	24	41	60

Examination of the Male Partner

If available, the male sex partner of the patient should be examined for the presence of a urethritis, because such a finding is thought to corroborate the clinical diagnosis of acute PID.[38] Because more than one-half of men with gonococcal urethritis[45] and one-third of men with chlamydial urethritis[46] can be asymptomatic, a urethral Gram stain and cultures for gonorrhea and chlamydia (or an appropriate nonculture test) should be obtained even in the absence of symptoms. In a study by Wasserheit, et al.,[47] examination of the male partner would have provided confirmatory evidence for the diagnosis of PID in more than 50 percent of cases.

Pregnancy Testing

Excluding ectopic pregnancy is a critical diagnostic step when examining the patient with suspected PID. In light of the inadequacy of the clinical history and physical examination in differentiating these two entities,[36,48] modern management mandates that a sensitive pregnancy test be routinely obtained. Urine monoclonal antibody, enzyme-linked immunosorbent pregnancy tests become positive at human chorionic gonadotropin levels (hCG) as low as 50 mIU/mL in the urine and detect 90 to 96 percent of ectopic pregnancies.[49,50] Qualitative serum pregnancy tests, which include serum monoclonal antibody tests and qualitative radioimmunoassays, become positive at serum hCG levels as low as 25 mIU/mL and can detect 96 percent of patients with extrauterine pregnancies.[51] Even more sensitive are the quantitative serum pregnancy tests, which can detect hCG levels as low as 5 mIU/mL. These tests have a reported 98.8 to 100 percent sensitivity for ectopic pregnancy, and a negative result virtually excludes this diagnosis.[52]

Cervical Studies to Detect N. gonorrhoeae *and* C. trachomatis

Laboratory confirmation of an endocervical infection with gonorrhea or chlamydia is regarded as supporting evidence for the diagnosis of acute PID. Cultures for gonorrhea and chlamydia remain the reference standard for diagnosis despite a reported sensitivity of 85 to 95 percent[53] and 80 to 95 percent,[54] respectively. Nonculture methods have been developed and are now available. In addition to being less technically demanding, these methods offer several other advantages over culture including a more rapid turnaround, a wider clinical availability, as well as less rigorous specimen transport and storage requirements because organism viability is not required.[43,53,54]

Nonculture tests for the laboratory detection of *N. gonorrhoeae* include the enzyme immunoassay and the DNA probe test. Studies evaluating the performance of the enzyme immunoassay in female populations with gonorrhea have reported sensitivities ranging from 74 to 100 percent and specificities of 86 to 100 percent.[55] A DNA probe test that binds with gonococcal ribosomal RNA is now commercially available and in two recent studies demonstrated a sensitivity of 86 percent and a specificity of 99 to 100 percent in women with a high disease prevalence.[53,56]

Nonculture systems for detecting chlamydia include the direct smear immunofluorescent antibody test, the enzyme immunoassay, and a DNA probe test. The direct smear immunofluorescent antibody test and the enzyme immunoassay are both antigen detection tests; the former uses fluorescein-tagged, species-specific monoclonal antibodies to *C. trachomatis* to identify elementary bodies in infected secretions, whereas the latter is designed for immunochemical detection of solubilized chlamydial antigens. When studied in female populations with chlamydial infections, the direct smear immunofluorescent antibody and the enzyme immunoassay tests have sensitivities ranging from 61 to 99 percent and 60 to 98 percent, respectively, and specificities of 89 to 99 percent and 86 to 98 percent, respectively.[43] The clinical use of a commercially available DNA probe for *C. trachomatis* was recently studied by Iwen, et al.,[54] and a sensitivity of 93 percent and a specificity of 98 percent were reported.

Culdocentesis

Culdocentesis is a rapid and relatively simple diagnostic aid that detects and samples fluid present in the cul-de-sac. Purulent fluid found on culdocentesis corroborates the diagnosis of acute PID[57] but can also be seen in other causes of peritonitis, such as acute appendicitis or a ruptured diverticular abscess. In a series of 204 patients with acute PID (with moderate to severe adnexal tenderness and involuntary guarding on examination), culdocentesis was productive of purulent fluid in 82 percent of cases.[20] Aerobic, anaerobic, and gonococcal cultures should be obtained on the fluid aspirated. Because involved pathogens are likely to be present on both Gram stain and culture, a Gram stain of the fluid can help differentiate such pathogens from the 30 percent of isolates likely to represent vaginal contaminants of the specimen.[58] Contraindications to culdocentesis include a mass in the cul-de-sac (absolute) and a markedly retroflexed uterus (relative).[59]

Pelvic Ultrasonography

Pelvic sonography plays primarily an adjunct role in the diagnosis of acute PID. Sonographic findings consistent with PID include distention and dilation of the fallopian tubes; enlargement of the ovaries, tubes, and ligaments; fluid in the cul-de-sac; and the appearance of a complex, multiloculated mass with cystic and solid elements incorporating the uterus. Even with the improved image resolution offered by endovaginal sonography, careful clinical correlation is required because the sonographic findings associated with PID lack specificity and can be seen in other intrapelvic disorders.[60,61] In addition to being of value in examining the patient in whom pain, obesity, or uncooperativeness precludes an adequate pelvic examination, a pelvic ultrasound scan is also a highly accurate method for detecting pelvic abscesses (93 percent sensitivity and 99 percent specificity) and can be used to monitor their response to medical therapy.[62]

Endometrial Biopsy

Transcervical endometrial biopsy is an office procedure that has been proposed as a possible alternative to laparoscopy in the diagnosis of acute PID. The histopathologic diagnosis of endometritis is based on the finding of plasma cells in the endometrial stroma, with the severity proportionate to the degree of stromal infiltration.[16,63] In a study assessing the diagnostic value of endometrial biopsy in 27 patients with suspected PID (18 of whom were subsequently determined to have acute salpingitis on laparoscopy), Paavonen, et al.[63] reported a sensitivity of 89 percent, a specificity of 67 percent, and a positive predictive value of 84 percent. A major drawback of this technique is that its results might not be available for several days.

Diagnostic Laparoscopy

Diagnostic laparoscopy is a procedure that enables the clinician to visualize the fallopian tubes and other pelvic structures. Laparoscopic criteria required for the diagnosis of PID include abnormal erythema and edema of the fallopian tubes and spontaneous or expressible tubal inflammatory exudate.[16,36] Although regarded by many investigators as the reference standard for the diagnosis of PID, questions regarding the diagnostic accuracy of laparoscopy were recently raised by Sellors, et al.[64] In their study they compared PID diagnosed visually by laparoscopy with PID diagnosed histopathologically from a fimbrial minibiopsy specimen obtained at laparoscopy, and only 50 percent of patients with histopathologically diagnosed PID had tubal erythema and edema on laparoscopic examination, and less than 40 percent had a spontaneous or expressible exudate.

Although some authorities have advocated that laparoscopy be routinely performed in all patients in whom acute PID is suspected, the risk-benefit ratio and cost effectiveness of such an approach remain uncertain. Although generally regarded as a safe procedure when performed by an experienced laparoscopist, it is not without risk. There are an estimated five deaths for every 100,000 laparoscopies performed and five major morbid events for every 1000 performed, including blood vessel injury, penetration of a hollow viscus, bleeding, and gas embolism.[65] Nevertheless, diagnostic laparoscopy should be strongly considered for patients with suspected PID unresponsive to medical therapy, as well as patients for whom the diagnosis remains unclear despite a comprehensive evaluation and for whom the need exists to exclude a surgical emergency, such as ectopic pregnancy or acute appendicitis.

Establishing the Diagnosis

The clinical differentiation of acute PID from other causes of acute pelvic pain is a notoriously difficult task. Jacobson and Westrom[36] examined by laparoscope 814 women thought clinically to have acute PID, but they confirmed the diagnosis in only 65 percent. In 23 percent of patients a normal pelvis was found, and in 12 percent another pathologic disorder was found (e.g., acute appendicitis, ectopic pregnancy, endometriosis, and complications of ovarian cysts). Similar experiences were reported by Morcos, et al.[34] and Allen and Schoon[48] who were able to confirm their prelaparoscopic diagnoses of PID in only 76 and 61 percent of patients, respectively.

In light of the unreliability of the clinical diagnosis of PID, many authorities have argued that a diagnosis of PID cannot be confidently or reliably made unless specific criteria derived from laparoscopic studies are fulfilled.[66] Such criteria generally require lower abdominal, cervical motion and adnexal tenderness, plus at least one of the following:

1. Temperature exceeding 38°C
2. Leukocytosis exceeding 10,500 per cubic mm
3. Purulent material aspirated on culdocentesis
4. Inflammatory mass on pelvic ultrasonography
5. Erythrocyte sedimentation rate exceeding 15 mm/h
6. Culture or nonculture evidence of gonococcal or chlamydial infection of the endocervix
7. A finding of mucopurulent cervicitis on the basis of finding more than 5 to 10 white cells per oil immersion field on Gram stain of the endocervical discharge

Recognizing that insistence on stringent diagnostic criteria would result in an unacceptable number of cases of mild PID going undiagnosed and untreated, the CDC published diagnostic guidelines in 1991 that call for a lowering of the clinical threshold for making a presumptive diagnosis of PID in patients with mild disease.[57] Provided competing diagnoses can be adequately excluded, the CDC recommends that a provisional diagnosis of PID be made and a therapeutic trial of antibiotics initiated in patients who simply have lower abdominal, adnexal, and cervical motion tenderness on examination.

Regardless of how the diagnosis of PID is made, the importance of close clinical follow-up cannot be overstated. Patients treated for PID require periodic evaluations, and, if no clinical improvement is seen in 2 to 3 days, other possible diagnoses (i.e., appendicitis, endometriosis, ruptured ovarian cyst, or adnexal torsion) warrant serious reconsideration.[57] Diagnostic laparoscopy (or possibly endometrial biopsy) should be strongly considered for such patients, as well as the patient whose clinical symptoms are severe enough to require that a definitive diagnosis be made rapidly.

Management

After making the diagnosis of PID, the physician must next decide whether to hospitalize the patient. Despite hospitalization being standard practice in many European countries, only 15 to 30 percent of patients with acute PID are hospitalized in the United States.[23,66] The superiority of hospitalization and inpatient treatment to ambulatory management has never been proved,[67] and studies are urgently needed comparing the efficacy of these two options with respect to both short-term and long-term outcomes. The CDC favors hospitalization in the following situations:[57]

1. The diagnosis is uncertain, or a surgical emergency, such as ectopic pregnancy or acute appendicitis, cannot be excluded
2. A pelvic abscess is suspected
3. The patient is pregnant
4. The patient is an adolescent

5. Severe illness precludes outpatient management
6. The patient is unable to follow or tolerate an outpatient regimen
7. The patient fails to respond to outpatient therapy
8. Clinical follow-up within 72 hours of starting antibiotic treatment cannot be arranged

Antibiotic Therapy

Antibiotics remain the cornerstone of treatment for acute PID. Although the efficacy of current antibiotic therapy in preventing PID sequelae remains unclear, a number of studies attest to antibiotics providing high rates of clinical cure.[67] In addition, in a recent study reported by Hillis, et al.,[68] starting treatment early (within 3 days of the onset of symptoms) in patients with PID was associated with a threefold reduced risk of subsequent infertility or ectopic pregnancy.

When prescribing an antibiotic regimen, it is important that physicians recognize the polymicrobial nature of PID and that they prescribe adequate coverage. CDC treatment guidelines published in 1993 provide recommendations for inpatient and outpatient treatment (Tables 2 and 3).[69]

Inpatient regimen A (cefoxitin or cefotetan plus doxycycline) (Table 2) offers excellent activity against gonorrhea and chlamydia and good activity against gram-negative bacilli and anaerobic bacteria (including *Bacteroides fragilis*), although the emergence of cefoxitin-resistant anaerobes has been described.[70] Inpatient regimen B (clindamycin plus gentamicin) provides optimal activity against anaerobes and gram-negative organisms and is particularly favored in patients who have suspected tubo-ovarian and pelvic abscesses. The efficacy of these two regimens was recently confirmed in a study by Landers, et al.,[40] which also supported the adequacy of high-dose clindamycin in the treatment of *C. trachomatis*.

The inclusion of the combination of ofloxacin plus either clindamycin or metronidazole as an outpatient antibiotic option represents the major change seen in the 1993 CDC guidelines pertaining to the management of PID (Table 3). Ofloxacin provides excellent coverage against gonorrhea and gram-negative enteric bacilli. Although a lack of efficacy against chlamydia has been reported for ciprofloxacin,[71] ofloxacin has been highly active against chlamydia,[67,72] and both Soper, et al.[73] and Wendel, et al.[74] found ofloxacin to be efficacious as a single agent in patients with uncomplicated PID. Concerns about the lack of activity by ofloxacin against anaerobic bacteria (a limitation shared by all quinolone antibiotics), however, are responsible for the recommendation that it be used in combination with either clindamycin or metronidazole. The other option, which calls for an intramuscular injection of a cephalosporin followed by oral doxycycline, is active against chlamydia and gonorrhea but provides less than optimal coverage against anaerobes and gram-negative enteric bacilli.

A number of antibiotic regimens other than those currently recommended by the CDC have also been proposed and studied.[23,67] When considering alternative regimens, physicians should be aware of the spectrum of antimicrobial activity provided and recognize that the wide distribution of antimicrobial-resistant *N. gonorrhoeae* has pre-

Table 2. 1993 Centers for Disease Control Guidelines* for the Inpatient Treatment for Acute Pelvic Inflammatory Disease.

Regimen A	Cefoxitin 2 g intravenously every 6 h or cefotetan 2 g intravenously every 12 h plus doxycycline 100 mg orally or intravenously every 12 hours. Continue for at least 48 h after clinical improvement and follow with doxycycline 100 mg orally twice a day for a total of 14 d
Regimen B	Clindamycin 900 mg intravenously every 8 h plus a gentamicin loading dose intravenously or intramuscularly of 2 mg/kg followed by a maintenance dose of 1.5 mg/kg every 8 h. Continue for at least 48 h after clinical improvement and follow with either doxycycline 100 mg orally twice a day or clindamycin 450 mg orally 4 times a day to complete 14 d of total therapy

*Source: Centers for Disease Control.[69]

Table 3. 1993 Centers for Disease Control Recommendations* for Ambulatory Management of Acute Pelvic Inflammatory Disease.

Regimen A	Cefoxitin 2g intramuscularly plus probenecid (1 g) or ceftriaxone 250 mg intramuscularly (or an equivalent third-generation cephalosporin, such as ceftixoxime or cefotaxime) followed by doxycycline 100 mg orally twice a day for 14 d. For patients unable to tolerate doxycycline, erythromycin 500 mg orally four times a day can be substituted
Regimen B	Ofloxacin 400 mg orally twice a day for 14 d plus clindamycin 450 mg orally four times a day for 14 d or ofloxacin 400 mg orally twice a day plus metronidazole 500 mg orally twice a day for 14 d

*Source: Centers for Disease Control.[69]

cluded the use of tetracycline and penicillin as first-line therapy.[75]

Monotherapy with a second- or third-generation cephalosporin provides good coverage against gonorrhea and gram-negative rods. Although these agents (particularly cefoxitin and cefotetan) also possess activity against anaerobes, more effective antianaerobic agents are available including metronidazole, chloramphenicol, clindamycin, and β-lactam–β-lactamase inhibitor combinations.[76] Furthermore, all cephalosporins are ineffective against chlamydia, a weakness underscored in a study by Sweet, et al.[28] that isolated chlamydia in post-treatment upper genital tract cultures in 12 of 13 patients with chlamydial PID despite apparently adequate clinical cure following monotherapy with a β-lactam antibiotic. Inadequate activity against chlamydia is also the major shortcoming for regimens calling for metronidazole in combination with an aminoglycoside as well as monotherapy with a β-lactam–β-lactamase inhibitor combinations (i.e., ampicillin-sulbactam, ticarcillin-clavulanate, amoxicillin-clavulanate).[67]

Combination therapy with doxycycline and metronidazole provides excellent activity against chlamydia and anaerobes but unreliable coverage against gonorrhea and gram-negative bacilli.[77] Doxycycline combined with either a third-generation cephalosporin or aztreonam provides excellent coverage against gonorrhea, chlamydia, and gram-negative aerobic rods but less than optimal coverage against anaerobic bacteria.[76] An outpatient combination antibiotic regimen offering fairly comprehensive antimicrobial coverage is amoxicillin-clavulanate plus doxycycline.[78] A major drawback of this regimen, however, is a reported 20 percent discontinuation rate because of associated nausea and diarrhea.

Additional Measures

General supportive measures, such as bed rest, sexual abstinence until cure is achieved, hydration, and the provision of antipyretics and analgesia, are recommended in the management of acute PID. Placing the patient in a semi-Fowler position has been suggested in the past for comfort and to facilitate drainage.[23] If the patient has an intrauterine device, removal of the device is generally recommended following the institution of antibiotic therapy.[23,25]

Surgical Therapy

Surgical interventions have a limited role in the management of acute PID. Possible indications for surgery include (1) absence of clinical response despite optimal antibiotic coverage for 48 to 72 hours, (2) a pelvic mass that enlarges or persists despite therapy, (3) intraperitoneal bleeding caused by erosion of a major vessel, (4) suspected rupture or leakage of a tubo-ovarian abscess, and (5) a pointing abscess that can be drained extraperitoneally.[62]

Available surgical procedures include diagnostic laparoscopy or laparotomy, laparoscopic drainage and lysis of adhesions, computed tomography-guided drainage of abscesses, posterior colpotomy, and the surgical excision of involved structures (e.g., unilateral adnexectomy, total abdominal hysterectomy-bilateral salpingo-oophorectomy). Current surgical practice calls for conservative management whenever possible, limiting extirpation to those structures that have to be resected.[62,79]

Sequelae

In addition to its immediate impact, acute PID is responsible for a number of sequelae as well. The development of a tubo-ovarian abscess is a well-recognized complication seen in 3 to 16 percent of patients hospitalized with PID.[79] Recurrent PID is another important complication and is reported in 4 to 23 percent of cases.[8] PID is also a common cause of chronic pelvic pain, and 17 to 18 percent of patients develop chronic pain syndromes that include dyspareunia and painful adhesions.[5]

Pelvic inflammatory disease can also have a dramatic impact on the reproductive potential of the woman afflicted. Acute PID is a major cause of infertility, rendering more than 11 percent of those afflicted infertile. The risk of infertility resulting from tubal occlusion rises with each succeeding episode, for an incidence of 8 percent after the first episode, 20 percent following the second episode, and 40 percent following the third.[80] Other factors associated with a greater likelihood of infertility following an episode of PID include an age older than 25 years at the time of diagnosis and severe inflammatory changes found at laparoscopy. Conversely, the risk of tubal factor infertility arising from PID appears to be reduced in patients who are taking oral contra-

ceptives, as well as those who have nonchlamydial PID.[17,68]

Pelvic inflammatory disease has also been a major contributing factor to the dramatic increase in ectopic pregnancies seen in the United States during the past two decades, numbering more than 88,000 cases in 1989.[81] A history or pathologic evidence of PID has been found in 20 to 56 percent of cases of ectopic pregnancy. It has been estimated that an episode of PID increases the risk of having an ectopic gestation by 2.0- to 7.5-fold.[82]

Prevention

In light of the enormous medical and socioeconomic costs associated with PID, it is evident that effective measures directed toward its prevention are needed. The importance of these measures is further underscored by the uncertainty surrounding the efficacy of current therapy in preventing the sequelae of PID,[23,67,83] as well as the growing appreciation of the existence of subclinical or so-called silent PID.[17] Although research is still required to determine the magnitude of this condition, as well as to develop criteria for its clinical diagnosis, evidence for its occurrence can be derived from studies that report the absence of a history of PID in more than half of patients with tubal factor infertility despite having tubal scarring and peritubal adhesions indistinguishable from that seen in patients with a history of PID and despite serologic evidence of past chlamydial and gonococcal infection.[84-86] Preventive efforts include measures directed at minimizing the risk for recurrent disease, as well as epidemiologic measures designed to prevent the transmission of sexually transmitted diseases (STDs).

Treatment and Follow-up

Clinicians need to impress upon patients the necessity of completing the full course of therapy and the importance of close clinical follow-up. Reevaluation of the patient 48 to 72 hours after initiating treatment, as well as following completion of therapy, is crucial to determine the adequacy of therapy.[23] Patients with PID also require examination for other STDs (including syphilis, trichomoniasis, and human papillomavirus) and, at a minimum, should be provided counseling regarding the need for HIV testing and safer sexual practices.

Treatment of Sex Partners

All sex partners of women with PID should be examined for gonococcal and chlamydial infections, as well as other STDs. The importance of contact tracing is underscored by estimates that male partners of women with PID have infection rates ranging up to 53 percent for chlamydial infections and 41 percent for gonorrhea.[57] CDC guidelines call for epidemiologic treatment (i.e., presumptive treatment at the time of initial examination before culture results are available) of gonorrhea and chlamydia for all sex partners of patients with PID.[69]

Sexual Counseling

The advisability of abstinence and the practice of safe sex should be routinely discussed with all patients at risk for contracting a sexually transmitted disease. Suggested areas of discussion include delaying the age at first intercourse, limiting the number of sex partners, and avoiding sexual relations with potential partners at risk for having an STD.[83] In addition, sexually active patients should be strongly encouraged to use condoms as a measure to reduce the risk of transmission of STDs.

Contraceptive Counseling

Barrier methods of contraception, such as mechanical barriers or locally applied spermicidal agents, are thought to reduce the risk of developing PID and are favored for women at risk for exposure to STDs.[83,87,88] Although further study is required,[83] recent investigations suggest that combined oral contraceptives can also confer protection against PID.[10,89] Conversely, the use of the intrauterine contraceptive device increases the risk of PID[9,89] and thus should be discouraged in women at risk for PID.

Recognition and Management of Cervicitis

Because it is generally believed that most cases of PID begin as a cervical infection,[17,90] early recognition and treatment of cervicitis represent important areas of prevention. Although universal screening for gonorrhea and chlamydia has been proposed as a potentially effective public health measure, selective screening (determined on the basis of disease prevalence, as well as the availability, costs, and accuracy of the screening test) is considered to be a more realistic, cost-effective

alternative. In a cost-effective analysis by Phillips, et al.,[91] routine screening with gonorrhea cultures was deemed justifiable when the prevalence of infection exceeded 1.5 to 2.1 percent. A similar analysis for chlamydial cervicitis justified screening with the rapid antigen test when the disease prevalence exceeded 7 percent and screening with culture in groups in whom the prevalence exceeded 14 percent.[92] High-risk groups of women in whom routine screening has been recommended have included prostitutes; illicit drug users; and female patients examined in jails, venereal disease clinics, and emergency departments.[83] Screening studies should also be considered in sexually active women who are adolescents, who have abnormal friability of the endocervix when swabbed during examination, who report multiple sex partners or a new partner within the previous 2 months, who report recent contact with a person with an STD, or who have a partner who might have had other partners during the preceding 3 months.[83,91-94]

Prophylactic Antibiotics

In an effort to reduce the incidence of iatrogenic PID, the use of prophylactic antibiotics before procedures requiring uterine instrumentation has been proposed. A role for prophylactic antibiotics before IUD insertion is supported by studies that suggest that the greatest risk of PID associated with IUD use occurs shortly following insertion.[9] In a study by Sinei and associates,[95] the routine administration of oral doxycycline at the time of IUD insertion reduced the likelihood of PID by 31 percent. On the basis of a literature review by Grimes, et al.,[96] antibiotic prophylaxis given before curettage abortion reduced associated infectious morbidity by one-half. Finally, recognizing the growing body of evidence implicating bacterial vaginosis in the pathogenesis of PID, Thomason, et al.[97] have recently advocated prophylactic treatment of bacterial vaginosis in asymptomatic women scheduled to undergo ambulatory invasive procedures, such as endometrial biopsy, IUD insertion, hysteroscopy, and hysterosalpingography.

Conclusion

Acute pelvic inflammatory disease is a major public health problem in the United States, afflicting more than 1 million women in the United States each year and generating an estimated $4.2 billion in direct and indirect costs in 1990. A number of important risk factors for PID have been identified, including young age, multiple sex partners, use of an intrauterine contraceptive device, vaginal douching, bacterial vaginosis, and a history of a sexually transmitted disease. Acute PID has been clearly established as a polymicrobial infection with *N. gonorrhoeae*, *C. trachomatis*, and endogenous cervicovaginal aerobic and anaerobic bacteria playing important pathogenic roles. Although diagnostic laparoscopy represents the reference standard for the diagnosis of PID, economic and logistical considerations often dictate that a presumptive clinical diagnosis of PID be made. The unreliability of a clinical diagnosis of PID mandates that, in addition to a careful history and physical examination, adjunctive diagnostic tests and procedures be selectively and knowledgeably used to help corroborate the diagnosis, as well as to help exclude competing diagnoses. Broad-spectrum antibiotic therapy remains the cornerstone of therapy for acute PID, with surgical management generally reserved for patients who fail to respond to medical therapy. The numerous sequelae of PID, which include infertility, chronic pelvic pain, and ectopic pregnancy, serve to underscore the importance of preventive measures.

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