CME CREDIT

ELLEN S. ROME, MD, MPH
Head, Section of Adolescent Medicine, Cleveland Clinic; Assistant Professor, Ohio State University School of Medicine; Clinical Instructor, Case Western Reserve University School of Medicine.

Pelvic inflammatory disease: The importance of aggressive treatment in adolescents

ABSTRACT

Pelvic inflammatory disease (PID), an infection of the female genital tract, presents a number of difficult challenges in diagnosis and management. Adolescents in particular require aggressive care of PID to prevent the long-term sequelae of chronic pelvic pain and infertility. This article reviews the etiology, microbiology, diagnosis, and management of PID, with an emphasis on treating adolescents with PID.

KEY POINTS

A recent study found that many clinicians were not following specific CDC recommendations for PID, such as those concerning hospitalization of adolescents.

Clinicians should consider the diagnosis of PID in any adolescent or young woman with abdominal pain, but also when mild or nonspecific symptoms or signs (eg, abnormal bleeding, dyspareunia, or vaginal discharge) are present.

In caring for patients suspected of having PID, especially adolescents, physicians should establish trust by explaining patient confidentiality before taking a sexual history.

Most cases of PID are diagnosed based on clinical criteria, although laparoscopy remains the gold standard for diagnosis.

PELVIC INFLAMMATORY DISEASE (PID) causes more morbidity in young women of reproductive age than all other serious infections combined. Nonetheless, PID and its major sequelae of tubal scarring, chronic pelvic pain, and infertility are preventable if physicians diagnose it early and treat it aggressively.

Unfortunately, many young women, and especially adolescents, delay seeking care and fail to comply with treatment. And, as the Centers for Disease Control and Prevention noted in its 1998 Guidelines for the Treatment of Sexually Transmitted Diseases,[1] many cases of PID go undiagnosed because both patients and physicians fail to recognize the implications of mild, nonspecific symptoms.

This article describes the diagnosis and treatment of PID, with a special emphasis on adolescents, the age group most at risk.

WHO GETS PID?

PID occurs in 1% of women ages 15 to 25 in the United States,[2,3] and of the 1 million women who develop PID annually, approximately 200,000 require hospitalization. Major surgical procedures are required as a consequence of infection in over 100,000 women.[4] The annual cost in this country was over $4.2 billion in 1990 and is expected to exceed $10 billion by the year 2000.[4]

For many reasons, adolescents remain the group at highest risk for sexually transmitted diseases and PID. Westrom[5] found that 15-year-old girls had a risk of 1:8 for PID, whereas 16-year-old girls had a risk of 1:10, and 24-year-old women had a risk of 1:80.

Adolescents display a combination of physiologic (FIGURE 1) and sociologic factors that account for this increased risk.

Physiologic factors

Physiologically, the adolescent may have low levels of protective antibodies in the local immune system due to lack of previous exposure to the various pathogens.[6] Also, estrogenic dominance and cervical ectopy (columnar epithelium on the ectocervix) in postpubertal girls enhance risk. The cervical mucus may be more penetrable in this age group.[7] Adolescents ages 15 to 19 have a higher prevalence of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* than is seen in older age groups.

Menses increases the risk of PID, possibly due to the spread of infection by retrograde flow from the uterus out to the fallopian tubes, shown to occur in 25% of healthy women.

Vaginal douching has also been shown to increase the risk of PID.[8–10] In a study of 131 women ages 18 to 40 after a first episode of PID, as compared with 294 control subjects with no history of PID from the same patient population, women who douched had a relative risk of acquiring PID of 2.1 (95% confidence interval 1.2–3.9). Those who douched once weekly increased their relative risk to 3.9 (95% CI, 1.4–10.9).[8] The relative risk increased further to 7.9 (95% CI, 2.6–24.3) for those women who cited infection as the reason for douching; in this group, douching may be a marker of infection, rather than a causative factor. Possible mechanisms of action for the increased risk of PID include upward spread of a lower genital tract infection by mechanical pressure and creation of a more hospitable environment for infection through altered vaginal pH.

Vaginal douching increases PID risk

Insertion of intrauterine devices. Despite earlier studies implicating specific intrauterine devices (IUDs) as a possible risk factor for nongonococcal, nonchlamydial PID,[11,12] a more recent review argued against the IUD as a significant risk factor.[13] However, insertion of an IUD may introduce infection.[14] Since adolescents are more likely to have multiple partners, even with serial monogamy, the IUD is not an ideal form of contraception due to the risk of infection with insertion.

Use of prophylactic antibiotics. This increased risk may be reduced with prophylactic use of antibiotics at insertion; preliminary data suggest that use of doxycycline 200 mg orally 1 hour prior to IUD insertion and then daily for 2 days after insertion may decrease the risk of PID.[15]

Sociologic factors

Sociologically, adolescent risk behaviors tend to be multifactorial and to occur in clusters. That is, risk breeds risk—and infection. A teen who drinks alcohol or uses drugs is more likely to have unprotected sex, increasing the risk of acquiring a sexually transmitted disease, and teens who engage in one risky behavior are more likely to participate in other risky behaviors. Teens who initiate sexual activity at younger ages are less likely to use condoms and are more likely to have multiple partners, even by serial monogamy, thereby increasing their risk of sexually transmitted diseases and PID.[16,17]

PATHOGENESIS OF PID

PID is polymicrobial in origin. In the United States, *C trachomatis* has been isolated in 25% to 40% of cases, *N gonorrhoeae* in 30% to 50%, and various other anaerobes and facultative aerobes in fallopian tube samples in 25% to 50% of women with acute PID.[18] Anaerobes include *Bacteroides*, *Peptostreptococcus*, and *Peptococcus*; facultative bacteria include *Gardnerella vaginalis*, *Streptococcus*, *Escherichia coli*, and *Haemophilus influenzae*. Cervical recovery of *N gonorrhoeae* has been found in as many as 81% of women with PID.[19] However, the use of culdocentesis and laparoscopy to obtain cultures from the fallopian tubes or the peritoneal cavity, or both, has shown that the presence of pathogenic bacteria in the endocervix does not indicate that such bacteria are associated with salpingitis. When gonococcal salpingitis occurs, symptoms develop within 7 days of menses in up to 65% to 75% of patients.

Bacterial vaginosis

In the past 10 years, bacterial vaginosis has been shown to be associated with PID.[2,20–22] In 9 (29%) of 31 women with laparoscopically confirmed acute PID, bacterial vaginosis

Physiological factors in pelvic inflammatory disease (PID) in adolescents

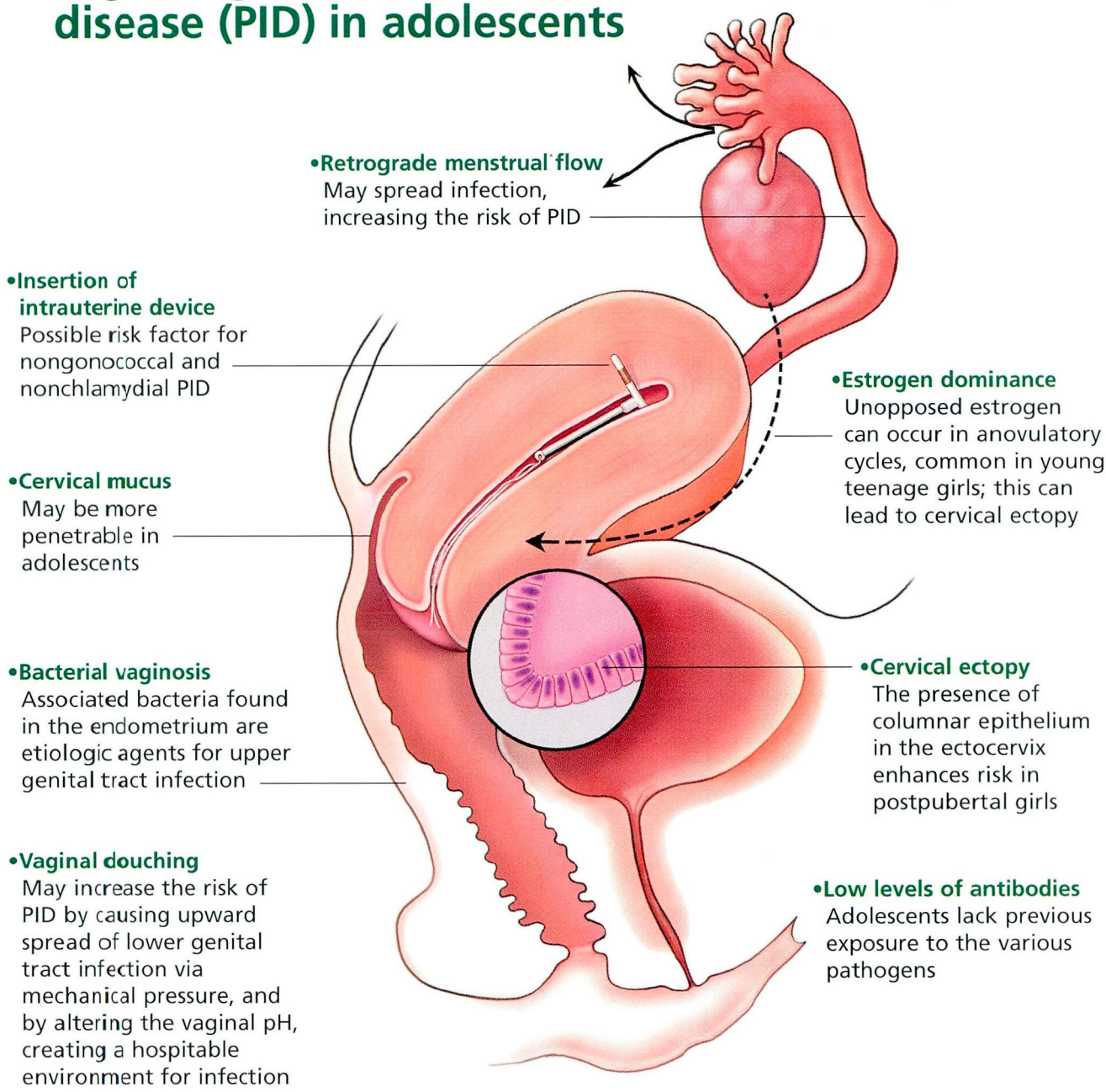

FIGURE 1

with histologic endometritis was detected by endometrial biopsy.[20] Hillier et al[21] confirmed that organisms such as *Prevotella bivia*, *Peptostreptococcus* species, and *Mycoplasma hominis* associated with bacterial vaginosis were among the pathogens associated with histologic endometritis. The researchers concluded that the bacteria associated with bacterial vaginosis, when found in the endometrium, are etiologic agents for upper genital tract infection independent of gonococcal or chlamydial infection.

TABLE 1

Major and minor criteria for the diagnosis of acute pelvic inflammatory disease

All three of the following must be present:

- Lower abdominal pain
- Cervical motion tenderness
- Adnexal tenderness (may be unilateral)

Plus at least one of the following:

- Temperature > 38°C
- White blood cell count > 10,500/mm^3
- Purulent material obtained by culdocentesis
- Pelvic mass on bimanual exam or sonogram
- Sedimentation rate > 15 mm/hour
- Gram-negative intracellular diplococci on Gram's stain
- Monoclonal antibody or other test for *C trachomatis*
- Presence of > 5 white blood cells per oil-immersion field on Gram's stain of endocervical discharge

SOURCE: MODIFIED FROM SWEET RL, REFERENCE 24

TABLE 2

Laboratory evaluation for suspected pelvic inflammatory disease

- Complete blood count with differential
- Beta human chorionic gonadotropin (HCG)
- Test for *C trachomatis* and *N gonorrhoeae*
- Rapid plasma reagin test for syphilis
- Sedimentation rate
- Sonogram (if tubo-ovarian abscess or mass is suspected)

ESTABLISHING TRUST WITH THE PID PATIENT

Adolescents with PID tend to seek medical attention later than adults do,[23] increasing their risk for complications from PID.

When meeting with an adolescent patient for the first time, the physician should clearly outline the confidentiality of care before trying to identify high-risk behaviors via the sexual history. Teens are more likely to seek care, appear at follow-up appointments, and comply with treatment regimens if they feel they can trust the care provider.

DIAGNOSIS OF ACUTE PID

Clinicians should consider the diagnosis of PID in any adolescent girl with abdominal pain. Those clinicians who do not provide gynecologic care to their patients should know when to refer patients for further evaluation. Pregnancy, either normal or ectopic, must also be considered in the differential diagnosis.

Because many cases of PID go unrecognized, clinicians should have a low threshold for suspecting PID, especially in adolescent and young adult women who present with mild or nonspecific symptoms or signs (eg, abnormal bleeding, dyspareunia, vaginal discharge).

The role of laparoscopy

Laparoscopy continues to be the gold standard for diagnosing PID. However, most patients with PID are diagnosed based on their clinical symptoms, as laparoscopy requires technical skill, surgical risk, and added cost, making it impractical for use as a screening procedure.[6,24]

Unfortunately, clinical diagnosis is less precise than laparoscopy: Jacobson and Westrom[25] found that laparoscopy confirmed the clinical diagnosis in only 65% of cases, with 12% having other surgically identified conditions and 23% showing no pelvic pathology at laparoscopy. When laparoscopy is used as the gold standard, the positive predictive value of a clinical diagnosis of PID is 65% to 90%.[26]

Clinical diagnosis

Sweet[24] devised a set of major criteria (lower abdominal pain, cervical motion tenderness, and adnexal tenderness) and eight minor criteria (TABLE 1) for the diagnosis of acute PID. Diagnosis is based on the presence of all three major criteria and at least one minor criterion.

Other clinical clues include the onset of pain 1 week after menses in those with gonococcal PID, new or increased vaginal discharge, a partner with recent urethritis, dysuria in those with concomitant urethral infection, and increased menstrual flow or cramps. Diagnoses to be excluded include ectopic pregnancy, which is a surgical emergency requiring prompt recognition, ruptured

ovarian cyst, endometriosis, appendicitis, and a normal pelvis. Useful laboratory tests can be found in TABLE 2.

At initial presentation, pregnancy should be excluded with a urine beta human chorionic gonadotropin (HCG) test, and a blood workup should include a complete blood count, sedimentation rate, and a rapid plasma reagin test for syphilis. If PID is suspected, endocervical tests for chlamydia and gonorrhea should be performed before initiating antibiotic treatment. Pelvic ultrasound should be performed if a pelvic mass is suspected, or if there is no clinical improvement at 48 hours after initiating antibiotic treatment.

Subacute or "silent" PID can occur with *C trachomatis*, and substantial tubal destruction can still occur despite the absence of symptoms. Hillis et al[27] found that women with chlamydial infection are more likely to delay care than women with gonorrhea, and that a delay in care in women with PID was associated with a threefold increase in risk of infertility and ectopic pregnancy. The burden is on the clinician to diagnose and treat chlamydial infections promptly, so as to prevent subacute PID in the first place. Adolescent patients, in particular, need to be educated on risk reduction and disease prevention. Each teen should be aware that she should have a pelvic examination within 3 to 6 months of any new partner to detect hidden infection.

Gynecologic consult should be obtained when tubo-ovarian abscess is suspected, in all cases of ectopic pregnancy, and when pelvic pain persists despite appropriate use of antibiotics.

Fitz-Hugh–Curtis syndrome. A syndrome of right upper quadrant pain due to perihepatitis is seen in about 5% to 20% of all women with PID and has been called Fitz-Hugh–Curtis syndrome. The syndrome includes:

- Perihepatitis associated with PID
- Pain and tenderness; abnormal liver function tests
- A direct association with *N gonorrhoeae* and *C trachomatis*.

Right upper quadrant pain may radiate to the shoulder or the back. The pain may occur either simultaneously with symptoms of salpingitis or up to 2 weeks later.

TABLE 3

Clinical characteristics useful in identifying tubo-ovarian abscess in adolescents with pelvic inflammatory disease

Last menstrual period > 18 days prior to admission
Previous episode of pelvic inflammatory disease
Palpable adnexal mass
White blood cell count > 10,500/mm^3
Sedimentation rate > 15 mm/hour
Heart rate > 90

TABLE 4

Treatment guidelines for pelvic inflammatory disease

REGIMEN A
Cefoxitin 2 g IV every 6 hours, or
Cefotetan 2 g IV every 12 hours

PLUS

Doxycycline 100 mg orally or IV every 12 hours

REGIMEN B
Clindamycin 900 mg IV every 8 hours

PLUS

Gentamycin 2 mg/kg body weight as a loading dose IV or intramuscularly, then maintenance doses of 1.5 mg/kg every 8 hours

ADDITIONAL PARENTERAL REGIMENS
Ofloxacin 400 mg IV every 12 hours

PLUS

Metronidazole 500 mg IV every 8 hours

Ampicillin/sulbactam 3g IV every 6 hours

PLUS

Doxycycline 100 mg IV or orally every 12 hours

Ciprofloxacin 200 mg IV every 12 hours

PLUS

Doxycycline 100 mg IV or orally every 12 hours

PLUS

Metronidazole 500 mg IV every 8 hours

SOURCE: CENTERS FOR DISEASE CONTROL AND PREVENTION, 1998 SEXUALLY TRANSMITTED DISEASE TREATMENT GUIDELINES FOR PELVIC INFLAMMATORY DISEASE, REFERENCE 1

DIAGNOSIS OF TUBO-OVARIAN ABSCESS: A COMPLICATION OF PID

Another complication of PID is tubo-ovarian abscess, a consequence of purulent material from an infected fallopian tube coming into contact with the adjacent ovary. Tubo-ovarian abscess occurs in 7% to 16% of all cases of acute PID. A ruptured tubo-ovarian abscess is a surgical emergency; and as many as 3% to 15% of all tubo-ovarian abscesses rupture. Women with tubo-ovarian abscesses may be acutely ill at presentation.

In a retrospective study, Slap et al[28] found that the clinical characteristics listed in TABLE 3 correctly identified 78% of women who had tubo-ovarian abscesses and 88% of those who did not. The investigators validated these characteristics in a subsequent series of women, in whom the model correctly identified 83% of those who had tubo-ovarian abscesses and 77% of those who did not.

Ultrasound can be a useful adjunct in the diagnosis of PID with tubo-ovarian abscess; Golden et al[29] found sonographic evidence of tubo-ovarian abscess in 11 (19.3%) of 57 adolescents with PID. Transvaginal ultrasound increases the sensitivity to 85% and the specificity to 100% according to one small study which used endometrial biopsy to confirm the diagnosis.[30] However, sonographic examination may be negative in patients with laparoscopically confirmed PID.[28]

Ultrasound can aid the diagnosis of PID with tubo-ovarian abscess

TREATMENT OF PID

According to the 1993 Sexually Transmitted Diseases Treatment Guidelines from the Centers for Disease Control and Prevention (CDC),[31] all adolescents with PID should be hospitalized because of the high risk of noncompliance and the severity of side effects if untreated.

The 1998 Sexually Transmitted Diseases Treatment Guidelines no longer require hospitalization as long as ongoing antibiotic therapy is ensured. These guidelines emphasize that no current data compare the efficacy of parenteral vs oral therapy or inpatient vs outpatient therapy. The issues of compliance and future risk to fertility remain greater in the adolescent age group; hospitalization should be recommended for any adolescent patient who may be at risk for poor follow-up or noncompliance. No evidence on long-term outcome and sequelae after use of oral regimens in adolescents with PID currently exists, so caution is encouraged.

Use of broad-spectrum antibiotics is recommended to cover possible *C trachomatis*, penicillinase-producing *N gonorrhoeae*, gram-negative enterics, penicillinase-producing anaerobes, and those bacteria associated with bacterial vaginosis.[1,21] The 1998 CDC recommendations are listed in TABLE 4, with efficacy confirmed by a recent meta-analysis of antibiotic regimens.[1]

After the initial 48 hours of inpatient care, the bimanual examination should be repeated. If the teen has increasing or persisting pain, further evaluation may be needed to exclude the diagnosis of tubo-ovarian abscess or other pelvic disease. If the pain is improving but is still significant, the teen may need another 24 hours of intravenous antibiotics. If she has no pain, she may be sent home to finish a 10- to 14-day course of doxycycline.

Follow-up. A follow-up appointment should be arranged prior to discharge to aid in compliance and to minimize the risk of reinfection. Although the 1998 CDC treatment guidelines do not mandate a test of cure, if a culture for *C trachomatis* or *N gonorrhoeae* is positive, repeat culture should be performed to evaluate for reinfection. Since polymerase chain reaction and ligase chain reaction tests for chlamydia and gonorrhea can remain positive for up to 3 weeks after treatment, test for reinfection should be performed 1 month after treatment.

Patient education. The clinician should also use the hospitalization as a time for patient education and for partner notification and treatment, if possible. Clinical pathway guidelines for use on an inpatient ward have been developed and can help ensure that these tasks are achieved.[32]

Further studies are necessary to evaluate whether outpatient treatment with a strong emphasis on patient education and close follow-up can improve compliance and decrease the incidence of negative sequelae in this group.

PREVENTION OF PID IN PATIENTS WITH SEXUALLY TRANSMITTED DISEASES

In 1994, the prevention of chlamydial infection became a national priority because of its significant impact on the reproductive health of women.[33] A recent cost analysis compared the use of azithromycin vs doxycycline to treat chlamydial infection to prevent PID.[34] This analysis found that use of a single dose of azithromycin, compared with the standard, less-expensive 7-day course of doxycycline, would prevent an additional 54,000 cases of PID among an estimated 2 million women who become infected with *Chlamydia* annually.[4,34] Single-dose therapy with azithromycin was also estimated to save approximately $190 million in PID-associated medical costs.[34] Although azithromycin has been shown to be effective in the treatment of asymptomatic and uncomplicated chlamydial cervicitis, its efficacy in the direct treatment of PID in the adolescent remains to be determined.[35,36]

THE IMPORTANCE OF AGGRESSIVE MANAGEMENT OF PID BY PHYSICIANS

A study of 1,165 physicians in California revealed that more than half (553 physicians) had treated a case of PID in the past year. However, 52% of these clinicians were not following the CDC recommendations for PID[37] because they were unaware of specific recommendations, especially concerning hospitalization of adolescents. Pediatricians and physicians with more years since residency training were more likely to follow the CDC 1993 treatment guidelines, while family practitioners were more likely to deviate from the guidelines.

The CDC guidelines were designed to reduce adverse health sequelae and to be cost-effective. Other regimens that include effective antimicrobial coverage against gonococcus and anaerobes can be used but may be more expensive. Use of a clinical pathway guideline in one small study for inpatient care of adolescents with PID preliminarily resulted in decreased length of stay and cost per case.[32]

A single dose of azithromycin prevents PID in women with *Chlamydia*

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ADDRESS: *Ellen S. Rome, MD, Department of Adolescent Medicine, A120, The Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195.*