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Pelvic Inflammatory Disease in the Postmenopausal Woman

S.L. Jackson* and D.E. Soper
Department of Obstetrics and Gynecology, Medical University of South Carolina, Charleston, SC

ABSTRACT

Objective: Review available literature on pelvic inflammatory disease in postmenopausal women.
Design: MEDLINE literature review from 1966 to 1999.
Results: Pelvic inflammatory disease is uncommon in postmenopausal women. It is polymicrobial, often is concurrent with tuboovarian abscess formation, and is often associated with other diagnoses.
Conclusion: Postmenopausal women with pelvic inflammatory disease are best treated with inpatient parenteral antimicrobials and appropriate imaging studies. Failure to respond to antibiotics should yield a low threshold for surgery, and consideration of alternative diagnoses should be entertained. Infect. Dis. Obstet. Gynecol. 7:248–252, 1999. © 1999 Wiley-Liss, Inc.

KEY WORDS
menopause; tuboovarian abscess; diverticulitis

Pelvic inflammatory disease (PID) is a common and serious complication of sexually transmitted diseases in young women but is rarely diagnosed in the postmenopausal woman. The epidemiology of PID, as well as the changes that occur in the genital tract of postmenopausal women, explain this discrepancy. The exact incidence of PID in postmenopausal women is unknown; however, in one series, fewer than 2% of women with tuboovarian abscess formation were postmenopausal.[1] Despite the rarity with which PID occurs in the postmenopausal woman, consideration and early recognition of the diagnosis along with appropriate therapy can decrease the morbidity and mortality associated with what is usually a serious infection.

PATHOPHYSIOLOGY

Pelvic inflammatory disease is an infection of the upper genital tract most commonly seen in young women. Typically, the risk factors associated with PID are young age, low socioeconomic status, substance abuse, lack of barrier contraception, use of an intrauterine device (IUD), and vaginal douching.[2] The pathophysiology involves the ascending spread of pathogens initially found within the endocervix, with the most common etiologic agents being the sexually transmitted microorganisms *Neisseria gonorrhoeae* and *Chlamydia trachomatis.* These bacteria are identified in 60–75% of premenopausal women with PID.[3] Other responsible microorganisms include respiratory pathogens, such as *Haemophilus influenzae*[4,5] and *Streptococcus pyogenes,*[5] and bacterial vaginosis-associated microorganisms (*Prevotella, Peptostreptococcus*).[3,6]

Cervical factors play a role in the development of PID. The columnar epithelium of the endocervix is commonly found everted in women of reproductive age, and this is accentuated with use of oral contraceptive pills. Both *N. gonorrhoeae* and *C. trachomatis* attach preferentially to these columnar endocervical cells. With menopause, the cervical transformation zone is anatomically located within

*Correspondence to: Susan L. Jackson, MD, Department of Obstetrics and Gynecology, Medical University of South Carolina, 96 Jonathan Lucas Street, Suite 634, PO Box 250619, Charleston, SC 29425. E-mail: jacksosu@musc.edu

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the endocervical canal and is smaller than in premenopausal women, decreasing the area of attachment available to *C. trachomatis* and *N. gonorrhoeae.* These changes most likely lower the susceptibility of the postmenopausal woman to infection. The endocervix also acts as a functional barrier to ascending infection. This barrier can be attenuated by the changing rheologic properties of the cervical mucus as noted during ovulation or breached by the occurrence of retrograde menstruation. Physiologically, the cervical mucus of the menopausal woman is more tenacious and serves as a mechanical barrier to ascending infections. Lack of menstruation in menopausal women decreases the risk of infection of the upper genital tract.

The direct extension of infectious processes from adjacent intraabdominal viscera is more likely to be associated with PID in older women. Disorders such as diverticulitis, Crohn disease, colonic cancers, and appendicitis have been associated with a direct spread of infection to the ovaries, oviducts, and uterus and manifest as a unilateral or bilateral tuboovarian abscess.[1,7,8] Fistula formation from an abscess cavity to the genital tract has also been described.[9,10]

RISK FACTORS

Older women are less likely to have risk factors known to be associated with exposure to sexually transmitted microorganisms. Behavioral, physiologic, and anatomic alterations that occur with advancing age offer barriers to the usual means of developing PID.

Sexual activity is a prerequisite for the development of PID in younger women, and high coital frequency has been associated with acquiring the disease.[11] The precise mechanism determining the spread of microorganisms from the lower genital tract to the upper genital tract is poorly understood; however, this suggests a role of spermatozoa as a vehicle for transporting the microorganisms to the upper genital tract. Most older women have fewer sexual partners and less frequent coital activity,[12] making them less likely to develop PID.

A risk factor associated with the development of PID in the postmenopausal woman is uterine instrumentation. Such procedures may introduce microorganisms into the endometrial cavity, which can lead to an infection of the upper genital tract. One series reported that 45% of women with postmenopausal PID had previous uterine instrumentation, the majority within 2 weeks of the diagnosis.[13] Both a fractionated dilation and curettage[11] and office sampling with an aspirating pipette can be associated with the development of PID. Aggressive sampling may lead to uterine perforation, which allows the direct inoculation of microorganisms into the peritoneal cavity.

Structural abnormalities of the genital tract, such as cervical stenosis, uterine anatomic abnormalities, and tubal disease, are also associated with an increased risk of developing PID.[6] A history of cervical conization, cryotherapy, or loop electrosurgical excision procedure can be associated with the development of cervical stenosis. This, in addition to other lesions, such as visible cervical malignancies, submucous myomas, and endometrial polyps, can block the efflux of blood or other fluids from the uterine cavity. A collection of fluid within the uterine cavity, such as blood (hematometra) or clear fluid (hydrometra), can become contaminated with microorganisms, causing a pyometra. This infected fluid may then reflux into the fallopian tubes and subsequently into the peritoneal cavity.

A prior history of PID with subsequent tubal scarring or hydrosalpinx formation results in fallopian tubes that are more susceptible to nonsexually transmitted aerobic pathogens, such as *H. influenzae,* group B streptococcus, and *Escherichia coli.*[5] Chronic or recurring PID, however, appears to be an uncommon cause of pelvic organ infection in the older population.[14]

The vaginal flora of postmenopausal women is more likely to be populated with aerobic gram-negative bacteria, especially *E. coli,* particularly if they do not take estrogen replacement therapy.[15] If these potentially pathogenic bacteria gain entry into the upper genital tract and a concomitant abnormality fails to allow the secretions of the upper genital tract to be drained, an environment conducive to suppurative infection can occur. Degeneration of uterine myomas has been associated with bacterial superinfection and infection of the genital tract.[6]

Finally, a "forgotten" IUD may be associated with a more serious genital tract infection. Landers et al. revealed that up to one third of women with tuboovarian abscess currently or were past users of IUDs.[16] In some cases, infections may be due to *Actinomyces israelii,* a gram-positive anaerobic organ-

ism. This infection occurs almost exclusively in women who have an IUD in situ.[17] Characteristically, these patients have pelvic abscess formation and may exhibit evidence of fistula development. On pelvic exam, palpable indurated masses may be present, suggesting a possible genital tract malignancy.

MICROBIOLOGY

The postmenopausal woman diagnosed with PID is less likely to harbor a sexually transmitted organism than the premenopausal woman. In most reported cases,[1,7,18,19] the organisms most frequently encountered were *E. coli* (76%) and *Klebsiella* (43%). These microorganisms were also identified in combination in 50–67% of bacteriologic cultures obtained from the infected tissues.[1,7,18] Other bacteria isolated include *Pseudomonas* (14%), *Staphylococcus aureus* (<5%), *Staphylococcus albus* (<5%), and *enterococcus* spp.[1,7,18–20] Anaerobic organisms, such as *Bacteroides fragilis*, were recovered in several cases.[8,13,19] Other aerobic pathogens, such as *H. influenzae* and group B streptococcus, may cause an ascending infection, and concomitant genital tract pathology is likely to be detected.

CLINICAL MANIFESTATIONS

The most common presenting symptoms for postmenopausal women with PID are vaginal spotting or bleeding, abdominal pain, fever, nausea, and change in bowel habits.[1,7,8,13,18] Isolated postmenopausal bleeding is a warning of a potentially serious problem and should prompt an investigation into its source. Physical examination should begin with evaluation of vaginal secretions for the presence of inflammation in the lower genital tract. A wet mount of vaginal secretions should reveal a predominance of inflammatory cells. Mucopurulent endocervicitis may be present, with a green or yellow discharge arising from the endocervix. The cervix may also be erythematous and friable (i.e., bleeds easily when touched with a cotton swab).

Tests for *N. gonorrhoeae* and *C. trachomatis* endocervical infection should be obtained, and a bimanual examination should be performed to assess the presence or absence of cervical motion tenderness, uterine tenderness, and adnexal tenderness. Bimanual examination is likely to reveal the presence of a pelvic mass, pelvic tenderness, and, occasionally, physical signs of peritoneal irritation. Additional laboratory values that may aid in the diagnosis include a complete blood count (specifically to identify a leukocytosis) and C-reactive protein. A Papanicolaou smear of the ecto- and endocervix should be obtained if not recently performed. Endometrial biopsy should be considered and, if obtained, sent for pathologic and microbiologic evaluation. Computed tomography (CT) or pelvic ultrasonography should be performed in most postmenopausal women with PID, because the majority will have evidence of a tuboovarian abscess.[1,7,18–20]

In premenopausal patients, pelvic organ tenderness and either leukorrhea or mucopurulent endocervicitis must be present to make the clinical diagnosis of PID. Because contiguous spread of infection from diseased adjacent organs is a common mechanism of PID in older women, leukorrhea and mucopurulent endocervicitis may not be present on examination in these cases.

A review of the literature reveals that the majority of postmenopausal women with PID have an associated tuboovarian abscess.[1,7,8,13,18,19] The diagnosis of this abscess is rarely made preoperatively without appropriate imaging studies, and many women develop morbid complications including colocutaneous fistulas, wound infections, sepsis, renal failure, pulmonary embolism, and death. Associated findings at surgery include leiomyomas, presence of an IUD, squamous cell carcinoma of the cervix, adenocarcinoma of the endocervix, endometrial polyps, hyperplasia, adenocarcinoma, and epithelial ovarian carcinoma. Extragenital findings are primarily bowel related, with diverticulitis, appendicitis, inflammatory bowel disease, diverticulosis, perforations of the gastrointestinal tract, and colorectal carcinoma among those reported.[1,7,14,18–20] Several series reported that greater than 40% of postmenopausal women with PID had an associated malignancy.[13,14]

DIFFERENTIAL DIAGNOSES

The most important differential diagnosis to consider in postmenopausal women with PID is acute diverticulitis with or without associated pelvic abscess. Diverticulitis is the most common nonneoplastic gastrointestinal disorder associated with the diagnosis of postmenopausal PID.[21] Women with diverticulitis will commonly present with a predominance of bowel symptoms, as opposed to the

patient with PID. In addition, women with diverticulitis do not experience concurrent vaginal bleeding. Diverticular disease affects 5–10% of the population over 45 years old, and nearly 80% of those over 85; however, only 20% become symptomatic. The sigmoid and descending colon are the most common sites of involvement. Computed tomography is considered the diagnostic modality of choice for the evaluation of suspected diverticulitis and allows for the exclusion of other intraabdominal and pelvic pathology, including abscess formation.[22]

Appendicitis is an additional consideration in the differential diagnosis of the postmenopausal woman with PID, although it more commonly occurs in the younger population. Diagnostic modalities useful in the evaluation of appendicitis include ultrasonography and CT. Transabdominal ultrasound examination of the right lower quadrant may reveal a noncompressible tubular structure with thickened muscular walls. Sensitivity and specificity of ultrasound in the diagnosis of appendicitis is reported as 76% and 91%, respectively, with a positive predictive value of 95%. Computed tomography evaluation of acute appendicitis reveals a positive predictive value of 96%, with a sensitivity of 96% and specificity of 89%. Computed tomography has also been shown to be more accurate in the diagnosis of associated periappendiceal abscess, as compared with ultrasound.[23]

Laparoscopy has remained the gold standard for the diagnosis of PID, because it provides direct visualization of the pelvis, as well as other intraabdominal organs, to confirm the diagnosis and grade the extent of disease. Liberal use of laparoscopy should be considered in older women with uncertain diagnoses following appropriate imaging studies, because they are more likely to have other intraabdominal pathology associated with the diagnosis of PID.

TREATMENT

Most postmenopausal women with PID will have systemic signs of a severe infection and therefore should be hospitalized. In situ IUDs should be removed after parenteral antibiotics are instituted. Several antimicrobial regimens can be recommended for the treatment of PID in this age group. Any regimen should possess excellent activity against the common microorganisms associated with postmenopausal PID, namely, *E. coli* and *Klebsiella* spp. In addition, because of the common association of tuboovarian abscess formation, antimicrobial coverage of anaerobic bacteria is mandatory. Box 1 lists several regimens that are acceptable for the treatment of postmenopausal PID. These antimicrobial regimens possess a broad spectrum of activity against aerobic and anaerobic microorganisms and should penetrate abscess cavities well.

TABLE I. Suggested antimicrobial regimens for the treatment of postmenopausal PID[a,b]

Regimen A	Regimen B
Clindamycin, 900 mg intravenously every 8 hours, plus Gentamicin, intravenous loading dose (2 mg/kg body weight) followed by a maintenance dose (1.5 mg/kg) every 8 hours, plus Ampicillin, 1 g intravenously every 4 hours	Ofloxacin, 400 mg intravenously every 12 hours, plus Clindamycin, 900 mg intravenously every 8 hours or Metronidazole, 500 mg intravenously every 8 hours

[a]Modified from Centers for Disease Control and Prevention. 1998 Guidelines for treatment of sexually transmitted diseases. MMWR Morb Mortal Wkly Rep 1998;47(RR-1):79–86.
[b]Other options include the extended spectrum penicillins with beta lactamase inhibitors (ticarcillin/clavulanate, ampicillin/sulbactam, and piperacillin/tazobactam), extended spectrum cephalosporins (cefotetan and cefoxitin), and the carbapenems (imipenem/cilastatin and meropenem).

Early surgical intervention in the management of postmenopausal women with PID should be entertained after excluding the possibility of cervical carcinoma. These patients commonly have severe disease characterized by tuboovarian abscess formation, and many have complicating medical illnesses, such as diabetes and coronary heart disease. As a group, they are less resilient than are younger women with PID and are more likely to manifest severe systemic signs of sepsis, including shock. Mortality rates of 25% have been reported despite adequate antimicrobial and surgical treatment.[18] Moreover, the common association of inflammatory bowel disease, other extragenital pathology, and genital tract malignancies with PID in this age group allows surgical exploration to be both diagnostic and therapeutic. Percutaneous drainage of pelvic abscesses has become more common in the treatment of tuboovarian abscess following failed antimicrobial therapy; however, this treatment mo-

dality has not been evaluated in postmenopausal women with tuboovarian abscess.

SUMMARY

Pelvic inflammatory disease is a rare entity in postmenopausal women. Extragenital pathology in addition to genital tract malignancies must be considered in these patients. The microbiology in postmenopausal women is not typically associated with the sexually transmitted disease microorganisms. Tuboovarian abscess formation is common. Broad-spectrum antimicrobial therapy should be initiated, and appropriate imaging studies obtained. Serious consideration of surgical exploration should be entertained if the patient does not clinically improve within 48 hours. Aggressive treatment of these seriously ill women may lead to a decrease in the morbidity and mortality associated with this disease.

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