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| **PELVIC INFLAMMATORY DISEASE From Diagnosis to Prevention**[**Dermatologic Clinics**](http://www.mdconsult.com.p.atsu.edu/das/journallist/view/266165575-2/home/0733-8635/0?issn=0733-8635) - [Volume 16, Issue 4](http://www.mdconsult.com.p.atsu.edu/das/journallist/view/266165575-2/issue/8835?ANCHOR=126905&issn=0733-8635) (October 1998)  -  Copyright © 1998 W. B. Saunders Company  -  [About This Journal](http://www.mdconsult.com.p.atsu.edu/about/journal/266165575-2/about0der.html) Add Journals Issue Alert  |

**747**

**SEXUALLY TRANSMITTED DISEASES**

**PELVIC INFLAMMATORY DISEASE
From Diagnosis to Prevention**

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**Pelvic inflammatory disease (PID) refers to infection of the uterus, fallopian tubes, and adjacent pelvic structures that is not associated with surgery or pregnancy [**[**20**](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747020)**] ; however, the terminology is not uniform, and in addition to PID, many other terms are commonly used to describe different manifestations of pelvic infection, including:**

**Endometritis**

**Salpingitis**

**Salpingo-oophoritis**

**Adnexitis**

**Parametritis**

**Pyosalpinx**

**Tubo-ovarian abscess**

**Tubo-ovarian complex**

**Pelvic peritonitis**

**Perihepatitis**

**Periappendicitis**

**PID causes major medical, social, and economic problems worldwide. Long-term sequelae, specifically tubal factor infertility and its management and ectopic pregnancy, are common and extremely costly. [**[**46**](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747046)**] Tubal factor infertility is a major global health care problem. For instance, in the United States, at least $5.5 billion are spent on PID and its sequelae annually. This is difficult to accept because PID and its sequelae should be preventable.**

**RISK FACTORS**

Risk factors for PID include young age, multiple sexual partners, intrauterine device insertion, vaginal douching, tobacco smoking, chlamydial and gonococcal infection, and bacterial vaginosis (BV). Barrier contraceptive use protects against PID. Oral contraceptive (OC) use modifies the manifestations of PID toward less symptomatic disease. [[45](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747045)] [[52](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747052)] Some studies suggest that OC use in fact protects against manifest PID. [[53](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747053)]

**RECENT PID TRENDS**

One important trend is the shift in the microbial etiology of PID. The relative role of *Chlamydia trachomatis* in the cause of PID has increased, whereas the role of *Neisseria gonorrhoeae* has decreased. In many developed countries, gonorrhea is now a rare disease, whereas chlamydia rates are still high or on the rise [(Fig. 1)](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#F074701) . Thus, *C. trachomatis* is now the predominant sexually transmitted disease (STD) organism causing PID. [[24](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747024)]

Another recent trend is the shift from inpatient PID toward outpatient PID. Hospitalizations of women with PID have rapidly decreased [(Fig. 2)](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#F074702) , probably because of a change in the clinical manifestations of PID; however, this does not necessarily mean that the overall incidence of PID has decreased [(Fig. 3)](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#F074703) .

Recently, a new clinical PID entity, so-called "silent" or "subclinical" PID, has been described. [[54](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747054)] Minimally symptomatic patients usually delay in seeking medical care, which

**748**

**Figure 1.** *Chlamydia trachomatis-*reported rates in the United States, 1984-1995 (STD Surveillance, NIH, 1995).

may increase the risk for tubal damage and long-term sequelae. [[13](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747013)] Studies have shown that not only clinical PID but also subclinical PID is associated with permanent tubal damage. [[30](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747030)] Thus, symptomatic PID is not a prerequisite for eventual development of tubal damage.

**PATHOGENESIS**

PID is an ascending infection in which pathogenic microorganisms ascend from the vagina and cervix to the upper genital tract (Fig. 4) (Figure Not Available) . Most cases of severe PID develop during or shortly after a menstrual period. Age is another important risk factor for PID. This suggests that there are specific age-related hormonal or other factors in the cervix or cervical mucus that determine whether a cervicovaginal infection ascends to the upper genital tract, causing PID.

Endometritis is an early manifestation of PID, and most but not all women with PID have endometritis. [[28](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747028)] The histopathologic diagnosis of endometritis is based on the presence of plasma cells in the endometrial stroma. [[25](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747025)] Next, salpingitis develops [(Figs. 5](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#F074705) and [6)](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#F074706) , which sometimes leads to pyosalpinx

**Figure 2.** Pelvic inflammatory disease (PID) hospitalizations of women 15-44 years of age in the United States, 1980-1993 (STD Surveillance, NIH, 1995).

**749**

**Figure 3.** PID initial visits to physicians' offices by women 15-44 years of age in the United States, 1980-1995 and the Healthy People Year 2000 objective (STD Surveillance, 1995).

formation [(Fig. 7)](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#F074707) and sometimes to tubo-ovarian abscess formation. Perihepatitis can be associated with PID [(Fig. 8)](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#F074708) .

**ETIOLOGY**

The most important causative micro-organisms are *C. trachomatis, N. gonorrhoeae*, and microorganisms associated with BV. The proportion of PID caused by *C. trachomatis* or *N. gonorrhoeae* reflects the background prevalence of these organisms in the population. Recently, gonorrhea rates have rapidly decreased in most developed countries, making *C. trachomatis* the major cause of PID. Approximately 30% of women with chlamydial cervicitis develop manifest PID. [[40](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747040)]

Bacterial vaginosis is the most prevalent cause of abnormal vaginal discharge. The role of BV in the cause of PID may have been underestimated. [[28](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747028)] [[36](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747036)] [[41](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747041)] BV represents a complex change in vaginal ecosystem characterized by a massive shift of vaginal microflora. There is reduction in the prevalence and concentration of hydrogen peroxide-producing lactobacilli and a massive increase in the prevalence and concentration of *Gardnerella vaginalis*, *Mobiluncus* spp., genital mycoplasmas, and anaerobic gram-negative rods. Increased overall concentration of microorganisms leads to a massive increase in the concentration of microbial by-products and virulence factors. These virulence factors are also thought to overcome cervical host defense barriers, leading to ascent of microorganisms and their byproducts to the upper genital tract. Besides PID, BV has also been linked to plasma cell endometritis, [[15](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747015)] postpartum fever, [[48](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747048)] posthysterectomy vaginal cuff infection, [[37](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747037)] and postabortion endometritis. [[16](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747016)] Most nonchlamydial nongonococcal microorganisms detected in the upper genital tract of women with laparoscopically proven PID are microorganisms associated with BV. [[28](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747028)] [[36](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747036)] [[41](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747041)]

**CLINICAL CHARACTERISTICS**

The clinical spectrum of PID is extremely wide, ranging from subclinical endometritis to frank salpingitis, pyosalpinx, tubo-ovarian abscess, pelvic peritonitis, and perihepatitis. Bilateral lower abdominal pain is the most common presenting symptom. Perihepatitis causes right quadrant upper abdominal pain mimicking acute cholecystitis. Other common symptoms are abnormal vaginal discharge, metrorrhagia, postcoital bleeding, abnormal uterine bleeding (endometritis), dysuria, fever, and nausea or vomiting; however, severe symptomatic PID represents only the tip of the iceberg. In recent years, severe symptomatic "textbook" PID has become a rare disease.

Increasing attention has recently been paid to so-called "atypical" or "silent" PID. [[6](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747006)] [[54](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747054)] Only a fraction of women with tubal factor infertility have a history of frank PID that highlights the impact of silent PID in the development of permanent tubal damage. In one study, 64% of women who had chlamydial

**750**

**751**

**Figure 4.** (Figure Not Available) Pathogenesis of pelvic inflammatory disease (PID). PID begins with chlamydial and/or gonococcal cervicitis *(A)*. This is followed by an alteration in the cervicovaginal microenvironment *(B)*, leading to bacterial vaginosis *(C)*. Finally, the original cervical pathogens, the flora causing bacterial vaginosis, or both ascend into the upper genital tract *(D)*. The cross-hatched areas indicate the affected portions of the genital tract. *( Modified from McCormack WM: Pelvic inflammatory disease. N Engl J Med 330:115-119, 1994; with permission.)*

**Figure 5.** Laparoscopic view of salpingitis. Note edema and inflammation of the fallopian tube.

**Figure 6.** Histopathology of salpingitis. Note severe inflammation.

**Figure 7.** Laparoscopic view of pyosalpinx. Note enlarged fallopian tube proximal from the fimbriated end.

**Figure 8.** Laparoscopic view of perihepatitis. Note violin string adhesions.

**Figure 9.** (Figure Not Available) Incidence of ectopic pregnancy in Finland 1967-1994. *( From Makinen J: Ectopic pregnancy falls in Finland. Lancet 348:129-130, 1996; with permission.)*

**752**

| **TABLE 1** -- SENSITIVITY OF THE CLINICAL DIAGNOSIS OF PID: SELECTED LAPAROSCOPIC STUDIES (1969-1997) |
| --- |
| **Author** | **Reference No.** | **No. Total (%)** |
| Jacobson and Westrom, 1969 | 14 | 532/814 (65%) |
| Chaparro et al, 1978 | 8 | 103/223 (46%) |
| Wasserheit et al, 1986 | 47 | 22/36 (61%) |
| Paavonen et al, 1987 | 28 | 30/45 (67%) |
| Sellors et al, 1991 | 35 | 44/95 (46%) |
| Bevan et al, 1995 | 3 | 104/147 (71%) |
| Molander et al, 1997 | 21 | 21/30 (70%) |

cervicitis and no symptoms or signs of PID had plasma cell endometritis consistent with subclinical PID. [[26](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747026)]

**DIAGNOSIS**

The most useful major criteria for the clinical diagnosis of PID are lower abdominal tenderness, bilateral uterine and adnexal tenderness, cervical motion tenderness, and signs of lower genital tract infection. Additional criteria include fever, elevated C-reactive protein (CRP) concentration (or elevated erythrocyte sedimentation rate), increased amount of white cells on vaginal wet mount examination, and leukocytosis [[11](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747011)] [[38](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747038)] [[49](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747049)] ; however, clinical diagnosis of PID has severe limitations. The clinical criteria are insensitive and nonspecific, and false-positive and false-negative diagnosis is common. In most studies, the sensitivity of the clinical diagnosis by pelvic examination is only 60% to 70% when laparoscopy is used as the gold standard for diagnosis [(Table 1)](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#T074701) . To increase the sensitivity of the clinical diagnosis, clinicians should always have a high index of suspicion of PID while evaluating women with pelvic pain.

Increasing concern about the silent PID has changed the recommendation for PID diagnosis, that is, moving away from laboratory-based and laparoscopy-based diagnosis toward so-called "syndromic diagnosis," which includes:

Lower abdominal tenderness

Bilateral adnexal tenderness

Cervical motion tenderness

No evidence of competing diagnosis

Negative pregnancy test

Risk assessment and syndromic diagnosis may increase diagnostic sensitivity and lead to earlier therapy, although on the other hand it may also lead to unnecessary antimicrobial therapies. [[31](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747031)]

Laparoscopy was introduced in 1960s as the gold standard for PID diagnosis [[14](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747014)] ; however, direct visual diagnosis is not always feasible, requires general anesthesia, and is costly. Endometrial biopsy, [[25](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747025)] [[28](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747028)] endovaginal ultrasound, [[5](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747005)] and magnetic resonance (MR) imaging [[43](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747043)] are other techniques introduced to increase the sensitivity of clinical diagnosis. Endometrial biopsy using an aspiration catheter is a simple outpatient procedure for histopathologically proven PID diagnosis (plasma cell endometritis), although the results are not readily available. Endovaginal ultrasound is another bedside procedure but requires skills and is highly observer dependent. In the author's recent study, [[43](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747043)] MR imaging was more accurate than endovaginal ultrasound in the diagnosis of inpatient PID when laparoscopy was used as the gold standard [(Table 2)](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#T074702) . There is no doubt that laparoscopy should always be recommended if there is any doubt of the diagnosis. In cases with proven PID (true positive), additional operative procedures can be performed during laparoscopy, such as liberation of adhesions, peritoneal lavation, drainage, and lavation of abscesses. These procedures seem to shorten the need for hospitalization and may improve fertility outcome. On the other hand, in non-PID cases (false-positive), operative laparoscopy greatly facilitates diagnosis and treatment of other gynecologic or nongynecologic conditions

| **TABLE 2** -- MAGNETIC RESONANCE IMAGING AND ENDOVAGINAL ULTRASOUND VERSUS LAPAROSCOPY IN THE DIAGNOSIS OF PID *From Molander P, Cacciatore B, Sjoberg J, et al: Laparoscopic management of acute pelvic inflammatory disease. Submitted.* |
| --- |
| **Diagnostic Method** | **PID(*n* = 21)**[**\***](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#T074702.01) | **No PID(*n* = 9)** |
| Endovaginal ultrasound | 17 (81%) | 2 (22%) |
| MR imaging | 19 (90%) | 0 (-) |
| MR, magnetic resonance. |

\*Laparoscopic diagnosis.

**753**

that have caused differential diagnostic problems. For instance, endometriomas, ruptured ovarian cysts, adnexal torsions, and appendicitis can all be treated laparoscopically. [[21](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747021)] Thus, laparoscopy greatly augments the management of non-PID cases that are difficult to discriminate from acute PID by clinical criteria alone.

**TREATMENT**

Current treatment guidelines call for broad-spectrum antimicrobial coverage [(Table 3)](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#T074703) . Although the recommended antibiotic therapies are very effective in achieving short-term clinical cure, their success in preventing sequelae is not known. Furthermore, the guidelines have not been critically evaluated in large, randomized, multicenter clinical trials. Another problem is that the guidelines have not been effectively implemented or followed by clinicians as demonstrated by recent audits. [[1](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747001)] [[12](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747012)] [[44](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747044)]

The author's experience is that, in most situations, combination treatment with doxycycline plus metronidazole is an effective treatment for inpatient and outpatient PID. This antimicrobial combination therapy is generally well tolerated; easy to administer (orally or intravenously); rarely causes major gastrointestinal problems, such as enterocolitis; and is not very costly. One important disadvantage is, of course, that it does not provide adequate coverage against gonorrhea, which may be a problem in populations with high background prevalence of *N. gonorrhoeae*. Then, a single-dose therapy for gonorrhea should be provided (e.g., ciprofloxacin, 500 mg, or cefixime, 1-g oral single dose). Intrauterine devices should be removed once antimicrobial treatment has begun and contraceptive counseling should be provided.

Most patients with PID are now managed as utpatients. Hospitalization of PID patients is recommended in specific situations, including:

Uncertain diagnosis

Pelvic abscess

Pregnancy

Adolescent patient

Severe illness precluding outpatient treatment

No response to outpatient management

Unable to arrange follow-up

However, the proportion of all PID patients treated as inpatients varies largely from one country to another. Whether inpatient treatment improves the long-term outcome of PID is not known.

**PELVIC INFLAMMATORY DISEASE IN PATIENTS WITH HUMAN IMMUNODEFICIENCY VIRUS INFECTION**

In developed countries, a minority of patients with PID are also infected with HIV; however, in African countries, the HIV positivity

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| **TABLE 3** -- TREATMENT GUIDELINES FOR PELVIC INFLAMMATORY DISEASE *From Centers for Disease Control and Prevention: 1993 sexually transmitted diseases treatment guidelines. MMWR 42 (No. RR-14), 1993; with permission.* |
| **Inpatient treatment** |
|     Regimen A |
|         Cefoxitin, 2 g intravenously every 6 hours or cefotetan, 2 g intravenously every 12 hours; plus doxycycline, 100 mg intravenously or orally every 2 hours |
|         Note: This regimen should be continued for at least 48 hours after the patient demonstrates substantial clinical improvement, after which doxycycline, 100 mg orally two times a day, should be continued for a total of 14 days. |
|     Regimen B |
|         Clindamycin, 900 mg intravenously every 8 hours, plus gentamicin, loading dose intravenously or intramuscularly (2 mg/kg of body weight), followed by a maintenance dose (1.5 mg/kg) every 8 hours  |
|         Note: This regimen should be continued for at least 48 hours after the patient demonstrates substantial clinical improvement, then followed with doxycycline, 100 mg orally two times a day, or clindamycin, 450 mg orally four times a day, to complete a total of 14 days of therapy.  |
| **Outpatient treatment** |
|     Regimen A |
|         Cefoxitin, 2 g intramuscularly, plus probenecid, 1 g orally in a single dose concurrently; or ceftriaxone, 250 mg intramuscularly or other parenteral third-generation cephalosporin (e.g., ceftizoxime or cefotaxime); plus doxycycline, 100 mg orally two times a day for 14 days |
|     Regimen B |
|         Ofloxacin, 400 mg orally two times a day for 14 days; plus either clindamycin, 450 mg orally four times a day, or metronidazole, 500 mg orally two times a day for 14 days |

**754**

rate may be as high as 33% to 39% (Craig Cohen, MD, personal communication, 1997). HIV-positive patients with PID are more likely to have pelvic abscesses, require prolonged hospitalization, respond more slowly to antimicrobial therapy, and more often require change of antibiotics. Hospitalization and intravenous antimicrobial therapy are recommended for all HIV-positive patients with PID. [[2](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747002)]

**OUTCOME**

The sharp worldwide increase in the incidence of PID during the past few decades has led to the secondary epidemics of infertility and ectopic pregnancy. The proportion of tubal factor infertility of all infertility ranges from 37% in developed countries to 85% in developing countries. [[55](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747055)] After a single episode of PID, the relative risk for tubal factor infertility is 7.0%. [[50](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747050)] Each repeat episode of PID doubles the risk so that it is 16.2% after two episodes and 28.3% after three or more episodes. Tubal factor infertility remains the most common indication for in vitro fertilization. Ectopic pregnancy is the main cause of maternal mortality in the first trimester of pregnancy in developing countries. In the United States, ectopic pregnancy accounts for 9% of all pregnancy-related deaths. [[22](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747022)] Women with a history of PID have sevenfold to tenfold increased risk for tubal pregnancy compared with women with no history of PID. [[51](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747051)] The incidence of ectopic pregnancy has been increasing during the past 2 decades (Fig. 9) (Figure Not Available) . [[18](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747018)] Ectopic pregnancy is a marker of subsequent repeat ectopic pregnancy and infertility. The recurrence rate of ectopic pregnancy is approximately 20%. [[19](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747019)]

In addition to infertility and ectopic pregnancy, other morbidity is associated with history of PID, such as chronic pain. Chronic pelvic pain following PID occurs in 24% to 75% of women. [[32](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747032)] Women with a history of PID are 10 times more likely to be admitted for abdominal pain, and the hysterectomy rate is eight times higher than in control women. [[4](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747004)] Thus, women with PID suffer substantial long-term gynecologic morbidity later in their lives.

**PREVENTION**

PID is a common complication of cervicitis. Upper genital tract infection can develop in patients without clinical findings suggestive of PID. [[23](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747023)] [[26](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747026)] [[39](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747039)] It is likely that symptomatic acute PID represents only the tip of the iceberg of all upper genital tract infections. Silent or atypical PID accounts for a significant proportion of tubal factor infertility and tubal pregnancy. Because *C. trachomatis* is the most common sexually transmitted pathogen and a major cause of PID, it is logical to focus preventive efforts on chlamydia. [[56](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747056)]

Therefore, screening for cervicitis and for cervicitis-causing microorganisms, most notably *C. trachomatis*, is of paramount importance in the prevention of long-term sequelae associated with PID. STD control programs should include development of diagnostic services with proper quality control, guidelines for clinicians in the clinical diagnosis and management of cervicitis, screening to identify asymptomatic carriers of *C. trachomatis*, establishment of surveillance systems, training of health care workers, periodic monitoring and evaluation of control measures, routine evaluation of sex partners, and effective patient education on behavioral aspects and contraception.

Disease prevention can be primary, secondary, or tertiary. Tertiary prevention of acute and chronic chlamydial infections of the upper genital tract has largely failed because substantial tubal damage has already occurred by the time symptoms develop. Delay of care is another critical factor predicting permanent tubal damage. [[13](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747013)] Although patients respond to antimicrobial therapy, the risk for tubal-factor infertility or ectopic pregnancy may still be high.

Primary prevention involves preventing both exposure to and acquisition of chlamydial infection through lifestyle counseling and health education. Clinicians have an important role in primary prevention by asking questions about high-risk sexual behavior, encouraging screening tests for those at risk, ensuring that male sex partners are evaluated and treated, and counseling about safe sex practices. Primary prevention of STDs by health education has not proven to be very effective so far; however, studies of the efficacy of primary prevention are slow and extremely complicated to conduct. Clearly, more emphasis should be directed to primary prevention. Effective health education programs should be implemented among adolescents.

Secondary prevention by universal screening is likely to have a critical role in the prevention of PID and its long-term sequelae. [[27](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747027)] [[42](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747042)]

**755**

Secondary prevention means early detection of subclinical disease by screening to prevent lower genital tract infection from becoming upper genital tract infection. Chlamydial infection fills the general prerequisites for disease prevention by screening because chlamydial infections are highly prevalent, are associated with significant morbidity, can be diagnosed, and are treatable. One recent randomized controlled trial has provided strong evidence that intervention with selective screening for chlamydial infections effectively reduces the incidence of PID. [[34](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747034)] Recent technologic advances should further enhance efforts to prevent chlamydial infection. [[9](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747009)] These include single-dose therapy using azithromycin, amplification tests, and the first-void urine specimens for the diagnosis [[9](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747009)] [[17](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747017)] [[29](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747029)] [[33](http://www.mdconsult.com.p.atsu.edu/das/article/body/266165575-2/jorg%3Djournal%26source%3D%26sp%3D10450557%26sid%3D0/N/126905/1.html?issn=0733-8635&issue_id=8835#R0747033)] ; however, whether such intervention will also have a significant effect on the incidence of ectopic pregnancy and tubal factor infertility remains to be seen.

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**756**

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