Anaerobes in Pelvic Inflammatory Disease: Implications for the Centers for Disease Control and Prevention’s Guidelines for Treatment of Sexually Transmitted Diseases


In preparing the 1998 sexually transmitted disease treatment guidelines of the Centers for Disease Control and Prevention, we reviewed evidence regarding the need to eradicate anaerobes when treating pelvic inflammatory disease (PID). Anaerobes are present in the upper genital tract during an episode of acute PID, with the prevalence dependent on the population under study. Vaginal anaerobes can facilitate acquisition of PID and cause tissue damage to the fallopian tube, either directly or indirectly through the host inflammatory response. Use of several broad-spectrum regimens appears to result in excellent clinical cure rates, despite the fact that some combinations fall short of providing comprehensive coverage of anaerobes. There are limited data on the long-term effects of failing to eradicate anaerobes from the upper genital tract. Concern that tissue damage may continue when anaerobes are suboptimally treated has prompted many experts to caution that therapeutic regimens should include comprehensive anaerobic coverage for optimal treatment of women with PID.

Pelvic inflammatory disease (PID) is the most common gynecologic disorder necessitating hospitalization for women of reproductive age in the United States, at a rate of 49.3 per 10,000 hospital discharges [1]. This represents only the tip of the iceberg, as the majority of women are treated for PID as outpatients [2], and many women with subacute or asymptomatic disease are never identified [3, 4].

The pathogenesis of PID is incompletely understood but involves some single event or set of circumstances that results in disruption of standard host immunity, which under normal circumstances protects the upper genital tract from the anaerobes and gram-negative bacteria of the vagina. How this happens remains largely speculative. Damage to cervical mucous and tubal ciliated epithelium by both Neisseria gonorrhoeae and Chlamydia trachomatis has been well-documented. N. gonorrhoeae attaches to and penetrates mucosal epithelial cells, directly causing cell destruction and irreversible damage to ciliary motility [5–7]. In contrast, it is the host immune response to C. trachomatis that causes tubal scarring [8, 9]. However, little is known about the role of anaerobes in this process.

In addition, the clinical features of PID are often enigmatic, making diagnosis difficult. Studies in which laparoscopic confirmation was used have shown that up to 54% of women meeting the clinical and laboratory criteria for PID in fact do not have PID, but rather have evidence of another separate pathological process or a normal pelvis [10–15]. Furthermore, there is evidence that many women with PID experience minimal or no discernable symptoms [16]. Kahn and colleagues have demonstrated that no single historical, clinical, or laboratory finding or combination thereof had both high sensitivity and specificity for the diagnosis of PID [17]. Finally, serious adverse reproductive sequelae are common. Rates of infertility range from 11% to 43% after one and three episodes of PID, respectively, and rates of ectopic pregnancy range from 6% to 22% [18].

These points emphasize how little we understand about PID and suggest why we rely less upon incomplete evidence and more on consensus and theoretical concerns to form the basis for our treatment regimen choices. However, current expert recommendations are inconsistent with respect to the treatment of anaerobes. Although many authorities have concerns that inadequate anaerobic coverage may allow persistent microbes to smolder, perhaps increasing the rates of long-term sequelae, not all recommended regimens are held to the same theoretical standards. Furthermore, there is no consensus on what level of coverage should be considered adequate.

In this article, we explore the role of anaerobes in PID in order to guide the development of treatment recommendations.
Specific questions need to be answered to resolve controversies in case management, including the following. (1) What is the prevalence of anaerobes in the upper genital tracts of women with PID? (2) Are anaerobes involved in the pathogenesis of PID? (3) Is it necessary that antibiotic regimens provide adequate coverage of anaerobes in order to prevent long-term sequelae in women with PID? (4) Are there special circumstances in which coverage of anaerobes is particularly important for women with PID? (5) What are the data concerning safety and patients’ acceptance of an oral regimen of metronidazole plus doxycycline?

**Methods**

A list of pertinent articles written in the English language was compiled from a search of the MEDLINE PLUS (National Library of Medicine, Bethesda, MD) databases for the years between 1966 and 1997. Key words included pelvic inflammatory disease, PID, salpingitis, and anaerobes. In addition, we reviewed the bibliography from a recent review on the subject [19] and PID chapters in standard references [16, 20, 21] for additional articles.

**Results**

**What Is the Prevalence of Anaerobes in the Upper Genital Tracts of Women with PID?**

Investigators using laparoscopy have recovered a variety of microbes from the upper genital tracts of women with PID [12–15, 22–25]. Pathogens include *N. gonorrhoeae, C. trachomatis, anaerobes, and gram-negative organisms* (table 1). Although anaerobic bacteria have been consistently isolated from the genital tract specimens of women with PID, the proportion of women with these microorganisms varies from 13% to 78%, as noted in table 2 [12–15, 22–24, 26–33]. Explanations of such observed variances include differences in patient populations, severity of disease at presentation, and microbiological techniques.

Personal behaviors, including specific sexual and feminine hygiene practices, may be responsible for differences in populations of women with PID. For example, there is wide racial and ethnic variation in the prevalence of douching, which has been found to be an independent risk factor for PID [34]. According to a national survey, while one-third of American women overall douche regularly, two-thirds of black American women douche regularly [35].

Another potential explanation for the wide variation in the prevalence of anaerobes in women with PID is that it is an artifact of study design. Subject recruitment for studies of women with PID may occur in multiple settings. Women enrolled from outpatient settings, such as gynecology or sexually transmitted disease (STD) clinics, may be expected to have a milder presentation than women who present to an urgent care or emergency department. It is conceivable that the microbiological profiles of these populations may vary.

Variations in microbiological methods may be at fault for their failure to identify anaerobes in some studies. Microbiological techniques vary widely for the acquisition and processing of samples in order to identify anaerobes. Specimens may be collected by culdoscopy, by endometrial biopsy, or laparoscopically with peritoneal lavage, swabbing, or tissue biopsy. Culdoscopy has been shown to result in contamination of the upper genital tract with microbes from the vagina [22, 36]; studies using this methodology have therefore overestimated the presence of anaerobes in PID. Conversely, peritoneal lavage or swabbing may result in underestimation of the presence of anaerobes, as tissue biopsy specimens tend to be superior for evaluation. Finally, the facilities and techniques, as well as the experience of the personnel, at the laboratories processing the specimens have a direct effect on the ability to isolate anaerobes [37, 38].

### Table 1. Bacteria isolated from the upper genital tracts of women with pelvic inflammatory disease (PID).

<table>
<thead>
<tr>
<th>Type of bacteria</th>
<th>Isolates</th>
</tr>
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<tbody>
<tr>
<td>Aerobes</td>
<td>Coagulase-negative staphylococci, Group B streptococci, α-Hemolytic streptococci, Nonhemolytic streptococci, <em>Neisseria gonorrhoeae</em>, <em>Escherichia coli</em>, <em>Gardnerella vaginalis</em>, <em>Streptococcus faecalis</em></td>
</tr>
<tr>
<td>Anaerobes</td>
<td><em>Prevotella species</em>, <em>Prevotella bivia</em>, <em>Prevotella disiens</em>, <em>Peptostreptococcus anaerobius</em>, <em>Peptostreptococcus asaccharolyticus</em>, <em>Peptococcus species</em></td>
</tr>
<tr>
<td>Mycoplasmas, bacteria</td>
<td><em>Mycoplasma hominis</em>, <em>Ureaplasma urealyticum</em></td>
</tr>
<tr>
<td>Intracellular</td>
<td><em>Chlamydia trachomatis</em></td>
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**Are Anaerobes Involved in the Pathogenesis of PID?**

Several authors have described the complex interplay of mechanical, microbiological, hormonal, and immunologic micro-environments that influence susceptibility, infectiousness, and risk of sequelae in women with PID [39, 40]. There are two components to this question. (1) Do anaerobes participate in the compromise of normal host immunity, thereby facilitating acquisition of infection? (2) Do anaerobes cause tissue damage at the level of the fallopian tube?

Soper and colleagues have postulated that bacterial vaginosis (BV) alone may alter host defense mechanisms in the cervicovaginal environment to such a degree that ascending infection results [15]. There are several pieces of evidence that support this position. First, BV is commonly diagnosed in women with PID. In one study, BV was more common in women with PID...
The mere presence of anaerobes in the upper genital tracts of women with PID does not prove that they play a pathological role. There are limited data, however, which suggest that anaerobes do cause damage to the upper genital tract. In postcesarean section endomyometritis, it has been shown clearly that failure to treat against anaerobes often results in abscess formation [55]. Hare and Barnes have shown that bacteroides infection of human fallopian tube explants results in damage to the delicate structure of cilia [56]. Landers and colleagues have shown similar results in the mouse by infecting ovarian bursas with mixed anaerobes; furthermore, they have documented low rates of subsequent fertility in mouse uterine horns infected with Peptostreptococcus anaerobius and Bacteroides fragilis [57]. It is not clear whether this tissue damage occurs primarily via the direct effects of the anaerobes themselves, as in gonococcal infection, or secondarily via the host inflammatory response, as in chlamydial infection.

Is It Necessary That Antibiotic Regimens Provide Adequate Coverage for Anaerobes in Order to Cure Women with PID?

Adequacy of treatment response can be assessed on the basis of several key outcomes. Clinical cure is defined as significant or complete improvement in the signs and/or symptoms that combined to indicate the diagnosis. Microbiological cure is defined as eradication of N. gonorrhoeae and C. trachomatis, as indicated by posttreatment follow-up sampling of all women who were positive for the organisms on initial presentation. Although the presence and distribution of anaerobes in the upper genital tract at initial presentation may be described in clinical trials, their persistence following treatment has rarely been sought in a routine or methodical fashion. The prevention of sequelae, such as infertility, chronic pelvic pain, and ectopic pregnancy, is considered another key outcome; however, this has not been studied well.

Clinical and microbiological cure rates are excellent for several regimens that lack optimal theoretical anaerobic coverage [25, 58–64]. A meta-analysis of antimicrobial regimen efficacy for the treatment of acute PID evaluated 21 of 34 trials published between 1966 and 1992, and it found roughly equivalent short-term clinical and microbiological cure rates for all but one of the regimens [19]. This study did not include assessment of anaerobic bacterial eradication.

Table 3 presents an updated review of the individual and pooled clinical and microbiological cure rates from this meta-analysis. It was expanded to include data from the five clinical

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Table 2. Laparoscopic retrieval of anaerobes and facultative bacteria from the upper genital tracts of women with PID.

<table>
<thead>
<tr>
<th>Reference</th>
<th>No. of patients</th>
<th>No. of isolates</th>
<th>Percentage of patients from whom anaerobes were isolated</th>
</tr>
</thead>
<tbody>
<tr>
<td>[22]</td>
<td>380</td>
<td>267</td>
<td>70</td>
</tr>
<tr>
<td>[12]</td>
<td>25</td>
<td>28</td>
<td>78</td>
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<td>[13]</td>
<td>23</td>
<td>11</td>
<td>44</td>
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<td>[23]</td>
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<td>24</td>
<td>69</td>
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<td>[24]</td>
<td>50</td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td>[15]</td>
<td>84</td>
<td>12</td>
<td>13</td>
</tr>
<tr>
<td>[25]</td>
<td>138</td>
<td>7</td>
<td>NS</td>
</tr>
</tbody>
</table>

NOTE: NS = not stated.

toward the cervix during menstruation. Investigators using vaginal sonography have described a series of abnormal uterine peristalsis forms that may be associated with the development of endometriosis [51], and retrograde menstruation has been considered a likely candidate in the pathogenesis of this disease [52]. In addition, anaerobes may translocate across the bowel wall [53] and, rarely, there may be direct extension of infection or inflammation from active appendicitis [54] or Crohn’s disease [53].

than in matched controls [23], and another noted that women with BV are more likely to have signs and/or symptoms of PID [41]. Korn and colleagues reported that women with symptomatic BV were more likely to have plasma-cell endometritis and BV-associated organisms recovered from the endometrium than were symptomatic women without BV [42]. Second, women with PID frequently have BV-associated microorganisms isolated from their upper genital tracts [15, 43]. Third, McGregor and colleagues provided a mechanism by which BV may compromise host immunity. They showed that anaerobic bacteria from the female lower genital tract produce a variety of mucolytic enzymes, including mucinases and sialidases, that are able to damage cervical mucus [44].

Other investigators contend that PID does not require an antecedent lower genital tract infection to breach host immunity [31, 32, 45]. It has been well documented that high estrogen levels in the midcycle and loss of the cervical mucus plug during menstruation enhance the penetrability of the endocervical canal [46]. Behaviors such as douching may facilitate entry of vaginal microbes into the upper genital tract by altering vaginal pH and transiently eradicating protective vaginal secretions that contain native microbial flora and host immune components [34]. Finally, instrumentation of the upper genital tract, including dilation and curettage, hysterosalpingography or hysteroscopy [47], and placement of an intrauterine device [48], bypasses cervical defenses and may result in contamination of the endometrium with vaginal flora.

Once the cervical barrier has been violated, microbes can be swept from the vagina to the upper genital tract. Both particulate matter and dyes have been shown to rise spontaneously to the level of the fallopian tube after placement in the vagina [49]. MRI of the uterus has identified an inner subendometrial portion of the myometrium, called the junctional zone, that is responsible for uterine contractions throughout the menstrual cycle in nonpregnant women [50]. During the follicular phase of a normal woman, these contractions move from the cervix toward the fundus and increase in amplitude and frequency until the time of ovulation; they become dysrhythmic during the luteal phase and reverse direction to move from the fundus
Antimicrobial therapy dramatically reduced morbidity and virtually abolished deaths due to PID. Then, in the era before 
*C. trachomatis* was recognized as having a central role in the pathogenesis of PID, many recommended regimens failed to 
eradicate this microbe. Sweet and colleagues documented that chlamydial organisms may persist and cause ongoing damage 
Despite suposed clinical cure in patients receiving single-agent 
cephalosporins [70]. Anaerobes can persist and cause ongoing damage in the upper genital tract following treatment with suboptimal antibi 

<table>
<thead>
<tr>
<th>Drug regimen</th>
<th>No. of studies</th>
<th>No. of patients</th>
<th>Percentage of patients cured clinically/ microbiologically</th>
</tr>
</thead>
</table>

**Inpatient**

- Clindamycin and aminoglycoside: 11/470, 91/97
- Cefoxitin and doxycycline: 8/427, 91/98
- Cefotetan and doxycycline: 3/174, 95/100
- Ceftriaxone and tetracycline: 1/18, 88/100
- Cefotaxime and tetracycline: 1/19, 94/100
- Ciprofloxacin: 4/90, 94/96
- Doxycycline: 1/36, 100/97
- Sulbactam/ampicillin and doxycycline: 1/37, 95/100
- Amoxicillin/clavulanic acid: 1/32, 93/NS
- Metronidazole and doxycycline: 2/36, 75/71

**Outpatient**

- Cefoxitin, probenecid, and doxycycline: 3/219, 89/93
- Ofloxacin: 2/165, 95/100
- Amoxicillin/clavulanic acid: 1/35, 100/100
- Sulbactam/ampicillin: 1/36, 70/70
- Ceftriazone and doxycycline: 1/64, 95/100
- Ciprofloxacin and clindamycin: 1/67, 97/94

NOTE: NS = not stated. Table is adapted from [19]; additional data are from [25, 65–68].

Are There Special Circumstances in Which Coverage of Anaerobes Is Particularly Important for Women with PID?

There are at least three situations in which enhanced coverage of anaerobes in women with PID may be warranted. The first involves women in whom a tubo-ovarian abscess is identified. The other two involve women who have PID and coexistent infection with BV or HIV.

Between 7% and 16% of women hospitalized with PID have tubo-ovarian abscesses [72]. The microbiology of these abscesses is mixed, with *B. fragilis* and other *Bacteroides* and *Prevotella* species predominating. Tissue destruction, vascular compromise, large concentrations of anaerobes and their by-products, and local immunologic factors combine to result in an abscess milieu that is relatively impermeable to many antimicrobial agents [73]. Some antibiotics, including penicillin, ampicillin, first-generation cephalosporins, ticarcillin, carbenicillin, and chloramphenicol, may be destroyed by enzymatic products of anaerobes. Other agents, especially clindamycin, work well in extracellular spaces, reaching high concentrations as a result of active transport into the abscess by polymorphonuclear leukocytes [74, 75].

Metronidazole, cefoxitin, and moxalactam may also reach therapeutic concentrations within abscesses. In a study that measured reduction in bacterial counts in subcutaneous abscesses, the most active antimicrobials, in order of decreasing activity, were metronidazole, clindamycin, moxalactam, and cefoxitin [76]. In the absence of comparative trials, parenteral treatment is advocated, as is the recommendation to complete the 14-day course of treatment with oral metronidazole and doxycycline.

As noted above, BV is commonly associated with PID. Irrespective of the role of BV in the pathogenesis of PID or one’s
certainty about the need to cover anaerobes adequately to treat PID. Antimicrobial treatment must be sufficient to eradicate BV when these two infections coexist. Because metronidazole is the recommended treatment for BV, a regimen including metronidazole is preferred in this situation.

HIV-infected women who develop PID are no more likely than seronegative controls to have coexistent BV [77] or to have pathogenic bacteria, such as N. gonorrhoeae, C. trachomatis, or G. vaginalis, recovered from the upper genital tract [78]. In addition, while they may present with slightly more severe symptoms than HIV-uninfected controls, they respond equally well to standard antimicrobial therapy [77, 79].

**What Are the Data Concerning Safety and Patients’ Acceptance of an Oral Regimen of Metronidazole Plus Doxycycline?**

Doxycycline is the antibiotic used most commonly to complete the 14-day treatment courses of oral and parenteral regimens against PID. Although this drug has excellent efficacy against C. trachomatis, it has limited coverage against other nonsexually transmitted pathogens associated with PID. Hasselquist and Hillier reported doxycycline resistance rates of 93% for facultative bacteria and 56% for anaerobes recovered from the upper genital tracts of women with PID [80].

For regimens of drugs such as ceftriaxone and doxycycline that are associated with limitations in anaerobic coverage but excellent clinical performance data, the addition of a 7- to 14-day course of oral metronidazole has been suggested as an ideal solution. This would result in a 2-week course of metronidazole and doxycycline. There is some concern regarding potential synergy between the gastrointestinal toxicities of each drug. Data from multiple sources suggest that this may not be a serious problem, however. There do not appear to be safety issues with the combination of a 7- to 14-day course of metronidazole plus doxycycline with a single dose of ceftriaxone or cefoxitin.

This combination has been evaluated in hundreds of individuals in the treatment of at least two clinical entities. Several investigators have reported use of the combination for the treatment of PID [63, 81–84]. Additional data on 7- to 28-day regimens combining metronidazole and tetracycline or doxycycline in the treatment of H. pylori infection are widely described. Many clinical trials including these two antimicrobial agents have shown an acceptable tolerance profile [85–88]. Significant adverse effects such as pseudomembranous colitis, neuropathy, and drug reactions occur rarely (0.1%–0.5% of cases), and minor side effects such as nausea, flushing, and a metallic taste occur in 30%–50% of patients [85].

Even minor side effects may result in failure to use the medication correctly. In one study, while nearly 70% of patients without side effects completed their prescribed erythromycin or tetracycline regimen as directed, fewer than 50% of those with gastrointestinal side effects were compliant [89]. In a more recent study of individuals prescribed doxycycline, only 25% were strictly adherent, 24% were noncompliant, and 51% used their medication outside of the recommended dosing schedule [90]. While these data present astonishing compliance information, it is not clear that effectiveness suffers. Another study, measuring cure rates for chlamydia among women randomized to receive azithromycin vs. doxycycline, revealed comparable levels of use-effectiveness [91].

**Discussion**

The process of developing treatment guidelines involves a combination of evidence-based medicine and consensus-building. Given the paucity of data, it is not surprising that the process of generating recommendations for the treatment of PID was a true challenge. Moreover, because clinical and theoretical microbiological conclusions often contradicted one another, care was taken to consider regimens that provide broad-spectrum antimicrobial activity. The most recent STD treatment guidelines published by the Centers for Disease Control and Prevention are listed in table 4 [92]. Changes from the 1993 guidelines are listed below.

1. Cefotetan is listed above cefoxitin in parenteral regimen A because of its easier dosing schedule.
2. Single daily dosing has been included as an option for gentamicin administration, on the basis of data concerning its use in the treatment of other serious polymicrobial infections.
3. Data supporting the use of alternative parenteral regimens are excellent, though limited. The three-drug ciprofloxacin regimen was added because it was studied in four trials and because some hospital formularies recommend only one fluoroquinolone.
4. Parenteral therapy may be discontinued 24 hours after a patient’s condition improves clinically. However, the optimal duration of parenteral therapy should be determined by the health care provider.
5. Ofloxacin plus metronidazole was moved to become regimen A because of excellent clinical trial data and because of the theoretical advantages of its broad coverage.

As noted above, although all of the recommended regimens cover N. gonorrhoeae and C. trachomatis, not all provide theoretically optimal anaerobic coverage. Oral and parenteral ofloxacin have been studied as single agents for the treatment of PID in several well-designed randomized, controlled trials that revealed excellent clinical and microbiological cure rates despite a limited anaerobic spectrum of activity. Although clinical data support the use of ofloxacin as a single agent, many experts recommend the addition of metronidazole to enhance the anaerobic coverage of this regimen, on the basis of theoretical concerns.

In addition, a recent multicenter study was the first to demonstrate the clinical and microbiological efficacy of ceftriaxone plus doxycycline in the treatment of PID [25]. Aside from the surprising fact that these are the first data to support the efficacy of this common treatment regimen, it is important to note that a single intramuscular dose of ceftriaxone and a 14-day course of doxycycline were associated with excellent clinical response, despite rather poor anaerobic coverage for this soft-tissue pelvic...
Table 4. The 1998 guidelines of the Centers for Disease Control and Prevention for treatment of pelvic inflammatory disease.

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Agent(s) and dosage</th>
</tr>
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<tbody>
<tr>
<td>Parenteral regimen A</td>
<td>Cefotetan, 2 g iv every 12 h, or Cefoxitin, 2 g iv every 6 h, plus doxycycline, 100 mg po or iv every 12 h.</td>
</tr>
<tr>
<td>Parenteral regimen B</td>
<td>Clindamycin, 900 mg iv every 8 h, plus gentamicin loading dose iv or im (2 mg/kg), followed by a maintenance dose (1.5 mg/kg) every 8 h; single daily dosing may be substituted.</td>
</tr>
<tr>
<td>Alternative parenteral regimens</td>
<td>Ofloxacin, 400 mg iv every 12 h, plus metronidazole, 500 mg iv every 8 h, or Ampicillin/sulbactam, 3 g iv every 6 h, plus doxycycline, 100 mg po or iv every 12 h, or Ciprofloxacin, 200 mg iv every 12 h, plus doxycycline, 100 mg po or iv every 12 h, plus metronidazole, 500 mg iv every 8 h.</td>
</tr>
<tr>
<td>Oral regimen A</td>
<td>Ofloxacin, 400 mg po twice a day for 14 d, plus metronidazole, 500 mg po twice a day for 14 d.</td>
</tr>
<tr>
<td>Oral regimen B</td>
<td>Ceftriaxone, 250 mg im once, or Cefoxitin, 2 g im, plus probenecid, 1 g po in a single concurrent dose, or Other parenteral third-generation cephalosporin (e.g., ceftriaxone or cefotaxime), plus doxycycline, 100 mg po twice a day for 14 d.</td>
</tr>
</tbody>
</table>

NOTE. Table is adapted from [92]. Parenteral therapy may be discontinued 24 hours after a patient’s condition improves clinically, and oral therapy with doxycycline (100 mg twice daily) should continue until completion of a 14-day course. When tubo-ovarian abscess is present, many health care providers use clindamycin or metronidazole with doxycycline for continued therapy rather than doxycycline alone because it provides more effective anaerobic coverage.

infection. The addition of a 14-day course of metronidazole may enhance the anaerobic coverage of this regimen without compromising safety.

We conclude from this review that the prevalence of anaerobes in the upper genital tracts of women with PID is variable. BV is commonly associated with PID. Data on the role of anaerobes in the pathogenesis of PID are limited but suggest strongly that anaerobes facilitate acquisition of infection and cause local tissue damage at the level of the fallopian tube. Treatment trials have documented excellent clinical and microbiological cure rates both for regimens that offer adequate anaerobic coverage and for regimens that do not. However, various studies indicate that upper genital tract damage may continue to occur when anaerobes are incompletely eradicated during treatment. Thus, current recommendations for antimicrobial regimens used in the treatment of PID should provide broad-spectrum antimicrobial coverage.

Future research is needed to generate additional information to guide the recommendations for optimal antimicrobial regimens for the treatment of PID. The proposed research agenda includes the following questions. (1) In women with laparoscopically proven PID, how do rates of long-term sequelae differ between those randomized to regimens that comprehensively cover anaerobes and those randomized to regimens that do not? (2) Are there any short-term key outcomes that correlate well with long-term ones, such as infertility, chronic pelvic pain, and ectopic pregnancy? (3) How might molecular methods be utilized to improve the sensitivity of tests to identify anaerobes in the upper genital tract at baseline and following treatment for PID? (4) With use of updated technology, what is the prevalence of BV and upper genital tract anaerobes in differing populations of women with PID? (5) What are the cure rates for the upper genital tract anaerobic infections for each antibiotic regimen currently recommended for use by women with PID?

(6) Does parenteral therapy have any advantage over oral regimens in eradicating anaerobes from the upper genital tracts of women with PID? (7) Using anaerobic cure and prevention of long-term sequelae as the key outcomes, what is the optimal duration for oral and parenteral antibiotic regimens? (8) How can animal models be used to elucidate the roles of anaerobes and the host immune response to anaerobic infection in the pathogenesis and natural history of PID?

References


