PID!


KEY POINTS:
- PID is more common than we may think – largely underdiagnosed and treated
- PID has more causes than we think (not just gonorrhea and chlamydia!)
- PID can cause significant morbidity, especially in terms of fertility, even if treated properly

PATHOPHYSIOLOGY AND MICROBIAL CAUSES
- More than 85% of acute infections due to sexually transmitted cervical pathogens or BV-associated microbes and approx. 15% due to respiratory or enteric organisms that colonize lower genital tract
- Subclinical PID similar causes as above and may be twice as common
- Chronic (>30d duration) is chronic infection due to mycobacterium tuberculosis or actinomyces species
- About 15% of untreated chlamydial infections progress to PID, with risk of PID after gonorrhea even higher
- Bacterial vaginosis is associated with degradation of cervical mucus and thus may increase risk of ascending infection
- Infection leads to inflammatory damage which leads to scarring, adhesions and possibly obstruction of fallopian tubes – can lead to infertility and pelvic pain

CLINICAL MANIFESTATIONS AND DIAGNOSIS
- Wide range of manifestations –mild to severe pain, discharge, intermenstrual or post-coital bleeding, dyspareunia, dysuria, RUQ pain with Fitz-Hugh-Curtis
- Can have asymptomatic infection of upper genital tract which can lead to infertility, though this could also be mildly symptomatic disease not diagnosed as PID
- Clinical diagnosis: pelvic organ tenderness (CMR, adnexal, uterine) in conjunction with signs of lower genital tract inflammation (cervical mucopus, cervical friability, increased number of WBCs on wet prep).
• Pelvic tenderness has high sensitivity for PID (>95%) but has poor specificity. Findings of lower genital tract inflammation increase the specificity of diagnosis.

• Diagnosis is imprecise – only 75% on women with clinical diagnosis of PID have laparoscopic confirmation of salpingitis. Imaging and invasive procedures (laparoscopy, endometrial sampling) can confirm but expensive, invasive.

• 10-25% of women who are thought to have PID may have other diagnosis such as ovarian cyst, endometriosis, ectopic, acute appendicitis

• Recommendations for evaluation: gonorrhea/chlamydia testing, wet prep (if WBCs plus clue cells, suggests PID not just BV), pregnancy test, HIV testing (HIV increases risk of TOA), +/- ESR/CRP (can increase specificity of PID)

TREATMENT
Per CDC:

<table>
<thead>
<tr>
<th>Table 2. First-Line Antimicrobial Treatment Recommended by the Centers for Disease Control and Prevention (CDC) for Pelvic Inflammatory Disease.†</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outpatient regimen for mild-to-moderate pelvic inflammatory disease</strong></td>
</tr>
<tr>
<td>Doxycycline (100 mg orally twice daily for 2 wk) with or without metronidazole (500 mg orally twice daily for 2 wk), plus one of the following:</td>
</tr>
<tr>
<td>Ceftriaxone (250 mg intramuscularly in a single dose)</td>
</tr>
<tr>
<td>Cefoxitin (2 g intramuscularly) with probenecid (1 g orally) concurrently in a single dose</td>
</tr>
<tr>
<td>Other parenteral third-generation cephalosporin (cefotaxime or ceftriaxone)</td>
</tr>
<tr>
<td><strong>Inpatient regimen for moderate-to-severe pelvic inflammatory disease with or without tubo-ovarian abscess†</strong></td>
</tr>
<tr>
<td>One of the following:</td>
</tr>
<tr>
<td>Cefotetan (2 g intravenously every 12 hr) plus doxycycline (100 mg orally or intravenously every 12 hr)</td>
</tr>
<tr>
<td>Cefoxitin (2 g intravenously every 6 hr) plus doxycycline (100 mg orally or intravenously every 12 hr)</td>
</tr>
<tr>
<td>Clindamycin (900 mg intravenously every 8 hr) plus gentamicin (3 to 5 mg per kilogram of body weight intravenously once daily)</td>
</tr>
</tbody>
</table>

* Complete treatment information, including alternative regimens and additional considerations, is available at the CDC website.33
† Transition to oral therapy can usually be initiated within 24 to 48 hours after clinical improvement, and oral therapy should be continued to complete 2 weeks of therapy.

• Indications for admission: pregnancy, inability to r/o competing diagnoses, severe illness combined with inability to take oral meds, or TOA

• Removal of IUD does not hasten resolution (may delay it) and in most cases IUD is left in place
LONG-TERM REPRODUCTIVE OUTCOMES

- More than 90% of patients will have response to CDC-recommended tx, but long-term outcome is still suboptimal – infertility around 11-18%, also large percent of recurrence and chronic pelvic pain. Could be because of delay in care vs injury to tubes occurring before infection diagnosed.

PREVENTION

- Screening for and treating cervical C. trachomatis can reduce risk of PID by 30-50% over 1 year

- CDC and other groups recommend screening for all sexually active women younger than 25 and older women at high risk (multiple or new sex partners, also living in communities with high prevalence of disease)
- Other important factors to reduce infection: condom use to prevent reinfection or repeat infection, treatment of sex partners (including empiric treatment of partner without exam)

UNANSWERED QUESTIONS AND UNADDRESSED NEEDS

- Need for:
  - noninvasive or minimally invasive test to confirm infection of fallopian tubes or inflammatory changes increasing risk for long term disease
  - biomarkers – can use CA-125 and E-cadherin in serum to track response but further research needed before can adopt for practice
  - studies to determine role of MRI, U/S, Doppler in diagnosis and treatment
  - finding other microbial sources of infection, including role of M. genitalium and BV-associated microbes
  - inexpensive, POC diagnostic tests to use in low-resource settings
  - development of vaccines

- An ongoing trial is also evaluating benefit of adding metronidazole to PID treatment (as BV may be contributory and underdiagnosed)