ADULT PELVIC INFLAMMATORY DISEASE

Background
1. Definition – polymicrobial infection in women of the upper genital tract.
   - Includes salpingitis, endometritis, parametritis, oophoritis, peritonitis and tubo-ovarian abscess.\(^1\)
2. General Information
   - Spectrum of disease may vary from subclinical, asymptomatic infection to severe, life-threatening illness.
   - Most common gynecological reason in US for admission to hospital\(^2\)
   - Etiology: STI (sexually transmitted infection) organisms, especially \(N.\) gonorrhoae and \(C.\) trachomatis, and vaginal flora microorganisms (e.g., anaerobes, \(G.\) vaginalis, \(H.\) influenzae, enteric Gram-negative rods, and \(S.\) agalactiae)\(^3\)

Pathophysiology
1. Pathophysiology of Disease – Infections such as Neisseria gonorrhea and Chlamydia trachomatis cause epithelial damage and allow opportunistic infections from other bacteria.\(^3\)
   - PID believed to result from direct canalicual spread of these organisms from the endocervix to mucosa of endometrium and fallopian tube.\(^5\)
   - Four factors may contribute:\(^5\)
     - Uterine instrumentation (e.g., the insertion of an intrauterine device (IUD)). Limited to first 3 weeks post-insertion
     - Hormonal changes during menses, as well as menstruation itself, leads to cervical alterations decreased mechanical barrier preventing ascent.
     - Retrograde menstruation
     - Individual organisms may have potential virulence factors associated with pathogenesis of acute chlamydial and gonococcal PID.\(^5\)
2. Incidence, Prevalence – estimated 600,000 to 1 million cases annually in U.S\(^7\)
3. Risk Factors\(^1,\,2\)
   - young age
   - recent new sexual partner
   - low socioeconomic status
   - lower educational attainment
   - previous episode of PID
   - early age sexual intercourse
   - presence of a sexually transmitted infection
   - high number of sexual partners
   - alcohol use
4. Morbidity/Mortality –
   - About 40% of affected women develop chronic pelvic pain
   - About 20% of affected women become infertile
   - 1% who conceive have an ectopic pregnancy
   - Repeated episodes: four-six fold increase in risk of permanent tubal damage.\(^2\)
Diagnostics

1. History
   - Abdominal/pelvic pain
   - Abnormal vaginal discharge
   - Intermenstrual bleeding
   - Postcoital bleeding
   - Urinary frequency
   - Lower back pain
   - Nausea/vomiting
   - Fever
   - Dyspareunia
   - In some women, symptoms are mild or absent.

2. Physical Examination
   - Abdominal examination may reveal diffuse tenderness greatest in lower quadrants.
   - Rebound tenderness, decreased bowel sounds. Marked right upper quadrant tenderness in about 10% of patients with perihepatitis.
   - May be asymptomatic
   - Bimanual pelvic examination: cervical motion and/or uterine tenderness
   - Presence of palpable adnexal mass likely to represent a tubo-ovarian abscess complicating PID.
   - Cervix: green or yellow mucopus and friability.

3. Diagnostic Testing – Invasive diagnostic tests, such as laparoscopy, may sometimes be needed.

4. Laboratory Evaluation
   - Human chorionic gonadotropin: r/o ectopic pregnancy
   - Leukocytosis
   - Elevated acute phase reactants: ESR>15mm/hr, C-reactive protein
   - Endocervical cultures for N. gonorrhoeae and C. trachomatis
   - Gram stain of endocervical exudates: > 30 polymorphonuclear cells /hpf suggests GC of Chlamydia
   - Fallopian tube aspirate or peritoneal exudates culture if laparoscopy

5. Diagnostic Imaging
   - Transvaginal ultrasound: tubal wall thickness greater than 5 mm, fluid in the cul-de-sac, incomplete septae within fallopian tube, and cogwheel sign (cogwheel appearance on cross-section tubal view).
   - CT pelvis (if ultrasound indeterminate): may show subtle changes pelvic floor fascial planes, inflammatory changes of tubes or ovaries, thickened uterosacral ligaments, and abnormal fluid collection.
   - MRI: tubo-ovarian abscess, a pyosalpinx, a fluid-filled fallopian tube, or polycystic-like ovaries with free pelvic fluid.

6. Other Studies
   - Endometrial biopsy: endometritis can be diagnosed from histologic exam of specimens
   - Laparoscopy: allows direct visualization of ovaries, uterus, fallopian tubes, and other abdominal structures.
7. Diagnostic Criteria
   - CDC Diagnostic Criteria:
     - PID should be suspected and treatment initiated if:
       - Patient at risk of PID and
       - Patient has uterine, adnexal, or cervical motion tenderness with no other apparent causes.
     - Findings that support the diagnosis:
       - Cervical or vaginal mucopurulent (green or yellow) discharge
       - Elevated erythrocyte sedimentation rate or C-reactive protein
       - Laboratory confirmation of gonorrheal or chlamydial infection
       - Oral temperature of 101°F (38.3°C) or greater
       - WBC’s on vaginal secretion saline wet mount
     - Most specific criteria for the diagnosis:
       - Endometritis on endometrial biopsy
       - Thickened, fluid-filled tubes apparent on trans-vaginal ultrasound or magnetic resonance imaging
       - Laparoscopic abnormalities consistent with PID (e.g. tubal erythema, adhesions, edema, purulent exudates or cul-de-sac fluid, abnormal fibriae)

Differential Diagnosis
1. Key Differential Diagnosis:
   - Gastrointestinal: appendicitis, cholecystitis, constipation, inflammatory bowel disease, gastroenteritis
   - Renal: urethritis, nephrolithiasis, pyelonephritis, cystitis
   - Obstetric/Gynecologic: ectopic pregnancy, dysmenorrhea, ruptured ovarian cyst, ovarian torsion, endometriosis, adenomyosis, tuboovarian abscess

Therapeutics
1. Acute Treatment: In women with PID of mild to moderate severity, parenteral and oral therapies appear to have similar efficacy.
   - Criteria for hospitalization:
     - surgical emergencies (e.g. appendicitis) cannot be excluded
     - pregnant
     - does not respond clinically to oral antimicrobial therapy in 72 hours
     - unable to follow or tolerate an outpatient oral regimen
     - severe illness, nausea and vomiting, or high fever
     - tubo-ovarian abscess suspected
   - Recommended parenteral regimen A:
     - Cefotetan 2g iv q12h OR
     - Cefoxitin 2g iv q 6h PLUS
     - Doxycycline 100mg po or iv q 12h
   - Recommended parenteral regimen B:
     - Clindamycin 900 mg iv q8h PLUS
     - Gentamicin loading dose iv or im (2mg/kg of body weight), followed by a Maintenance dose (1.5 mg/kg) q8h. Single daily dosing (3 to 5 mg/kg) can be substituted.
Alternative parenteral regimens:
- Ampicillin/subactam 3g iv q6h PLUS
- Doxycycline 100mg po or iv q12h

Outpatient oral treatment: (CDC does not recommend routine use of fluoroquinolones)

Recommended regimen
- Ceftriaxone 250 mg im in a single dose PLUS
  - Doxycycline 100 mg po bid for 14 days WITH or WITHOUT
  - Metronidazole 500 mg po bid for 14 days OR
- Cefoxitin 2 g im in a single dose and Probenacid, 1 g po administered concurrently in a single dose PLUS
  - Doxycycline 100 mg po bid for 14 days WITH or WITHOUT
  - Metronidazole 500 mg po bid for 14 days OR
- Other parenteral third-generation cephalosporin (e.g ceftizoxime or cefotaxime) PLUS
  - Doxycycline 100 mg po bid for 14 days WITH or WITHOUT
  - Metronidazole 500 mg po bid for 14 days

2. Further Management (24 hrs): Transition to oral therapy usually within 24-48 hours of clinical improvement.
   - If patient has tubo-ovarian abscess, at least 24 hours of direct in-patient observation recommended.

3. Long-Term Care: In hospitalized patients receiving intravenous therapy, significant clinical improvement characterized by defervescence, decreased abdominal, adnexal, uterine and cervical motion tenderness within 3-5 days.
   - If no clinical improvement occurs, further diagnostic tests required, including possible surgical intervention.
   - After discharge from hospital, oral antibiotics continued for 10-14 days total.

Follow-Up
1. Return to Office: follow-up within 48-72 hours to ensure clinical improvement if outpatient oral regimen chosen.
2. Admit to Hospital: no clinical improvement within 48-72 hours of outpatient therapy,
   - Hospitalization for parenteral therapy and further diagnostic evaluation for alternative diagnosis recommended.
   - Antimicrobial regimen should be reassessed and diagnostic laparoscopy for consideration of an alternative diagnosis recommended.
3. High rate of reinfection in women who have documented chlamydia or gonococcal infections
   - Repeat testing recommended 3-6 months after treatment regardless of whether their sex partners were treated.

Prevention
1. Primary prevention: avoiding acquisition of sexually transmitted infections.
2. Secondary prevention: preventing lower-genital-tract infection from ascending
3. Tertiary prevention: preventing upper-genital-tract infection from leading to tubal dysfunction/obstruction and functional or structural damage to other abdominal/pelvic organs.

4. Recommended Strategies for Communities:
   - Community health promotion and education
   - Appropriate clinical services
   - Partner notification
   - Training of health-care providers
   - Detecting asymptomatic STD’s

5. Recommended Strategies for Individuals:
   - Maintain healthy sexual behavior
   - Use barrier methods
   - Adopt appropriate health-care-seeking behavior
   - Influence sex partners to be evaluated

6. Recommended Strategies for Health-care Providers:
   - Maintain up-to-date knowledge about the prevention and control of STD/PID
   - Provide appropriate preventive services
   - Provide appropriate medical management for illness
   - Provide risk-reduction counseling
   - Ensure evaluation of sex partners

References
2. Ross, JD. Pelvic Inflammatory Disease. BMJ. 2008: 1606
5. www.cdc.gov/mmwr/preview/mmwrhtml/00031006
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