

Pelvic Inflammatory Disease

**Jigna B. Patel, Pharm.D., R.Ph.
TKL Research, Inc/ Rutgers University
Post-Doctoral Fellow
Clinical Research
April 1, 2004**

Lecture Outline

- STD Overview
- Clinical Disease Course
- Epidemiology
- Financial Considerations
- Risk Assessment
- Treatment Options
- Emerging Therapies
- Prevention Techniques

STD Overview

STD Overview

- Common, costly, preventable
- 15 million new STD infections occur each year
- Examples:
 - Human Papillomavirus (HPV)
 - Trichomoniasis
 - Chlamydia
 - Gonorrhea
 - Herpes
 - Syphilis
 - Human Immunodeficiency Virus (HIV)
 - Hepatitis B
- “The Hidden Epidemic”
- Annually direct and indirect costs → \$17 billion
- ~ 65 million people in U.S. live with an incurable STD

<http://www.prevent.org>

Chlamydial Infection

- Curable STD affecting men, women, newborn babies of infected mothers
- Incidence: ~ 3 million per year
- Prevalence: ~ 2 million per year
- Cost per year $\Rightarrow$ \$ 2 billion
- Main Symptoms:
 - 1.
 - 2.
- Untreated chlamydial infections $\Rightarrow$ PID

<http://www.niaid.nih.gov/factsheets/stdclam/htm>

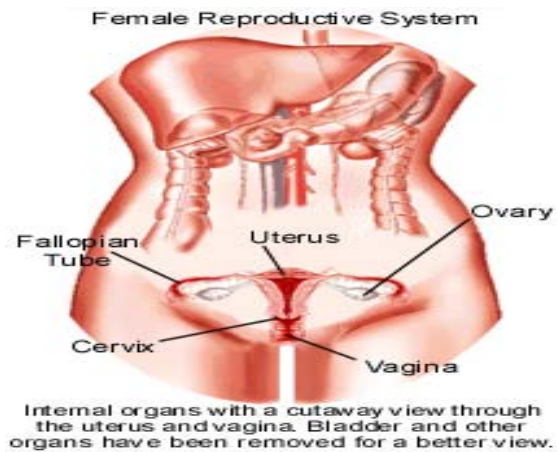
Gonococcal Infection

- Curable STD affecting men, women, newborn babies of infected mothers
- Incidence: ~ 650,000 cases per year
- Prevalence: Not available
- Main Symptom:
 - 1.
- Untreated gonococcal infections $\Rightarrow$ PID

<http://www.niaid.nih.gov/factsheets/stdclam/htm>

Clinical Disease Course

Pelvic Inflammatory Disease



Epidemiology

- Each year:
 - > 1 million people experience an episode of symptomatic pelvic inflammatory disease (PID)
 - >100,000 women become infertile each year as a result of PID
 - Large proportion of ectopic pregnancies as a result of PID
 - More than 150 women die from PID or its complications

<http://www.cdc.gov>

Pelvic Inflammatory Disease

- Occurs in women with untreated chlamydial and gonococcal infections
- Comprises a spectrum of inflammatory disorders of the upper female genital tract, including any combination of:
 - Endometritis
 - Salpingitis
 - Tubo-ovarian abscess
 - Pelvic peritonitis
- Sexually transmitted organisms:
 - *N. gonorrhoeae*
 - *C. trachomatis*
 - Vaginal flora (anaerobes, *G. vaginalis*, *Haemophilus influenzae*, enteric Gram-negative rods, and *Streptococcus agalactiae*)
 - Cytomegalovirus (CMV), *M. hominis*, *U. urealyticum*

<http://www.cdc.gov>

Risk Assessment: PID

- Risk increases in the following groups:
 - 1.
 - 2.
 - 3.
 - 4.

<http://www.niaid.nih.gov/factsheets/stdpid/html>

Pelvic Inflammatory Disease: Diagnosis

- Clinical signs and symptoms lack sensitivity and specificity
- Testing for gonorrhea and chlamydia
- Laparoscopy
- Endometrial Biopsy
- MRI of fallopian tubes

2002 guidelines for the management of
pelvic infection and perihepatitis

Pelvic Inflammatory Disease: Diagnosis

- Necessary Findings Physical examination (requires all to be present):
 - Abdominal tenderness
 - Cervical motion tenderness
 - Adnexal tenderness (unilateral or bilateral)
- Confirmatory Findings Clinical or laboratory (one must be present):
 - Fever of >101 °F
 - Abnormal cervical discharge
 - WBCs in vaginal secretions
 - Elevated ESR
 - Elevated C-reactive protein
 - Documented gonococcal or chlamydial infection of the cervix

Pelvic Inflammatory Disease. Sexually transmitted diseases treatment guidelines 2002.

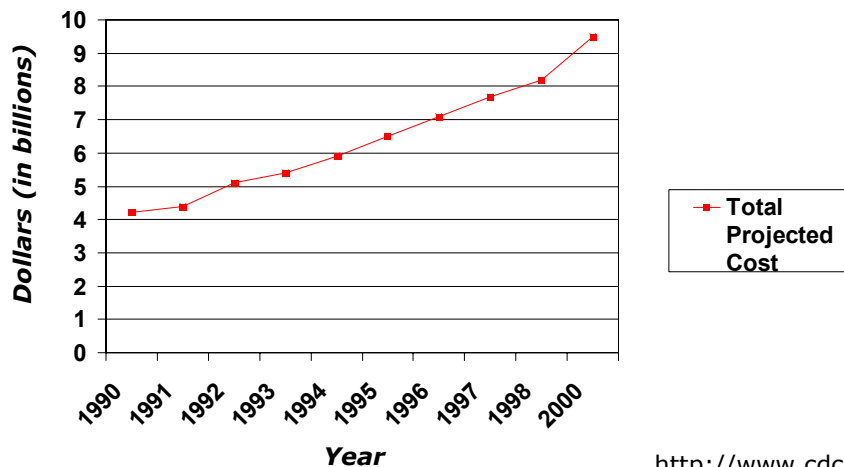
Pelvic Inflammatory Disease: Diagnosis

- Acute PID: difficult to diagnose
- Consequences of undiagnosed PID:
 - 1.
 - 2.
 - 3.
 - 4.
 - 5.

CDC: Morbidity and Mortality Report May 10, 2002, Vol.51, No. RR-6

Financial Considerations

***Total Projected Cost (Direct and Indirect)
Associated with Pelvic Inflammatory Disease,
United States, 1990-2000***



<http://www.cdc.gov>

Hospitalization

- Uncertain diagnosis
- Surgical emergencies (i.e. appendicitis)
- Pelvic/ Tubo-ovarian abscess
- Pregnant patient
- Unpredictable compliance of an adolescent patient
- Severe illness
- Unable to tolerate oral/outpatient regimen
- Failed outpatient regimen
- Immunodeficiency
- If clinical follow-up within 72 hours of starting antibiotic treatment cannot be organized

<http://www.cdc.gov>

Treatment

General Principles

- Rest advised for those with severe disease
- Pregnancy test should be performed for patient with child-bearing potential
- Provide appropriate analgesia
- Intravenous therapy is recommended for patients with more severe clinical disease
- All patients should be offered screening for sexually transmitted infections

Pelvic Inflammatory Disease. Sexually transmitted diseases treatment guidelines 2002.

Treatment Regimens

- MUST provide empiric, broad-spectrum coverage of likely pathogens:
 - *Neisseria gonorrhoeae*
 - *Chlamydia trachomatis*
 - Anaerobes
 - *Gardnerella vaginalis*
 - *Streptococcus agalactiae*
 - *Haemophilus influenzae*
 - Enteric Gram (-) rods

Pelvic Inflammatory Disease. Sexually transmitted diseases treatment guidelines 2002.

Treatment Regimens

- Depend on:
 - 1.
 - 2.
 - 3.
 - 4.
 - 5.
 - 6.
 - 7.
- Inpatient versus Outpatient regimens

Pelvic Inflammatory Disease. Sexually transmitted diseases
treatment guidelines 2002.

Inpatient Treatment Regimens

- Cefoxitin 2 gm IV every 6 hours
or
Cefotetan 2 gm IV every 12 hours
PLUS
Doxycycline 100 mg po or IV every 12 hours
- IV regimens should be given for at least 24 hours after clinical improvement of patient.
- Oral therapy should be continued for 14 days with:
Doxycycline 100mg po bid should be continued for 10 to 14 days

Pelvic Inflammatory Disease. Sexually transmitted diseases
treatment guidelines 2002.

Inpatient Treatment Regimens

- Clindamycin 900 mg IV every 8 hours

PLUS

Gentamicin (LD) IV or IM (2mg/kg of body weight) followed by a MD (1.5 mg/kg) every 8 hours (single daily dosing may be substituted)

- Continue for at least 24 hours after patient improves
- Oral therapy should be continued for 14 days with:
Doxycycline 100mg po bid or
Clindamycin 450mg po qid

Pelvic Inflammatory Disease. Sexually transmitted diseases treatment guidelines 2002.

Alternative Inpatient Treatment Regimens

- Ofloxacin 400mg IV every 12 hours

OR

Levofloxacin 500mg IV once daily +/-
Metronidazole 500mg IV every 8 hours

- Ampicillin/Sulbactam 3gm IV every 6 hours

PLUS

Doxycycline 100mg po or IV every 12 hours

Pelvic Inflammatory Disease. Sexually transmitted diseases treatment guidelines 2002.

Parenteral therapy can be discontinued
in 48 hours after the patient improves
clinically,

but _____

_____!

Pelvic Inflammatory Disease. Sexually transmitted diseases
treatment guidelines 2002.

Outpatient Treatment Regimens

- Ofloxacin 400mg po bid for 14 days

OR

Levofloxacin 500mg po qd for 14 days

+/-

Metronidazole 500mg po bid for 14 days

Pelvic Inflammatory Disease. Sexually transmitted diseases
treatment guidelines 2002.

Additional Regimens

- Ceftriaxone 250mg IM x 1 dose
- Cefoxitin 2gm IM + Probenecid 1gm po administered concurrently x 1 dose
- Other IV therapies: ceftizoxime or cefotaxime PLUS doxycycline 100 po bid for 14 days +/- metronidazole 500mg po bid for 14 days

Pelvic Inflammatory Disease. Sexually transmitted diseases treatment guidelines 2002.

PEACH Trial : Pelvic Inflammatory Disease Evaluation and Clinical Health

- Objective: Effectiveness of outpatient versus inpatient therapy in women with mild to moderate PID in terms of future fertilities and ectopic pregnancies
- Conclusion: Millions of dollars could be saved annually if used outpatient therapy in women with milder symptoms.
- Careful evaluation of symptoms is warranted to ensure cost-effectiveness

Infect Med 19(8):346-349, 2002

Follow-Up

- Clinical improvement should follow within 3 days of therapy initiation
- If no improvement within 3 days patients may:
 - 1.
 - 2.
 - 3.
- Re-screening for C.trachomatis and N. gonorrhoeae _____ weeks after therapy is completed in women with a documented infection with these pathogens is recommended.

<http://www.guideline.gov>

Treatment Counseling

- Emphasize need for taking all medication, regardless of symptoms
- Review contraindications and potential side effects
- Identify and discuss potential compliance problems
- Review the medical purpose of follow-up evaluation
- Emphasize the need to avoid sexual intercourse until treatment is completed
- Emphasize the need to refer sex partners for evaluation and treatment
- Reinforce information by providing patients with written literature on guidelines

<http://www.cdc.gov>

Emerging Therapies

- Topical microbicides
- Vaccines for gonorrhea and chlamydial infection
- Lactobacilli-containing suppository
- Diagnostic tests for gonorrhea and chlamydial infection

<http://www.niaid.nih.gov/factsheets/stdpid/html>

Management of Sex Partners

- Male sex partners of women with PID should be examined and treated if they had sexual contact with patient during 60 days before patient's onset of symptoms
- If not examined → Urethral gonococcal or chlamydial infection
- Males → asymptomatic
- Treat for both *C. trachomatis* and *N. gonorrhoeae* regardless of etiology from infected partner

<http://www.guideline.gov>

Recommendation:

PREVENTION

Prevention Techniques

- Education and counseling of persons at risk on ways to adopt safer sexual behavior
- Identification of asymptotically infected persons and of symptomatic persons unlikely to seek diagnostic and treatment services
- Effective diagnosis and treatment of infected persons
- Evaluation, treatment, and counseling of sex partners of persons who are infected with an STD
- Preexposure vaccination of persons at risk for vaccine-preventable STDs

Prevention Techniques

- **Prevention Messages:**

- Should be tailored to patient
- Describe actions to avoid spread of STDs (i.e. abstinence from intercourse)
- Adoption of safer sexual behavior if risk factors exist
- Counseling skills: respect, compassion, nonjudgmental attitude
- Open-ended questions, understandable language, reassurance of treatment despite socioeconomic status

CDC: Morbidity and Mortality Report May 10, 2002, Vol.51, No. RR-6

Prevention Techniques

- **Pre-exposure Vaccination:**

- Effective method of preventing transmission of STDs
- Examples:
 - 1.
 - 2.
- More in clinical trials

CDC: Morbidity and Mortality Report May 10, 2002, Vol.51, No. RR-6

Prevention Techniques

- **Sexual Transmission:**

- Abstinence from sexual intercourse (i.e. oral, vaginal, anal): most reliable method of STD prevention
- Long-term, mutually monogamous relationship with an uninfected partner
- Both partners should get tested for STDs, including HIV, before initiating sexual intercourse
- Use an effective method of barrier contraception
- Use a new condom if intercourse with infected partner or if infected status is unknown for each act of intercourse

CDC: Morbidity and Mortality Report May 10, 2002, Vol.51, No. RR-6

Prevention Techniques

- **Male Condom:**

- correct use and consistency yields effectiveness
- Px of STDs transmitted by fluids from mucosal surfaces
- Regulated as a medical device by FDA

- **Female Condom:**

- Reality® effective against virus transmission (i.e. HIV)
- Use if male condom cannot be used properly, not first-line compared to male condom

- **Vaginal Spermicides, Sponges and Diaphragms:**

- Vaginal Spermicides: nonoxynol-9 (N-9) – NOT effective in preventing gonorrhea, chlamydia, or HIV infection
- Sponges: Protect against gonorrhea and chlamydia
- Diaphragms: Protect against gonorrhea, chlamydia, or trichomoniasis.

- **Condoms and N-9 Vaginal Spermicides:**

- Lubricated condoms = Lubricated condoms with spermicides

CDC: Morbidity and Mortality Report May 10, 2002, Vol.51, No. RR-6

Questions...