



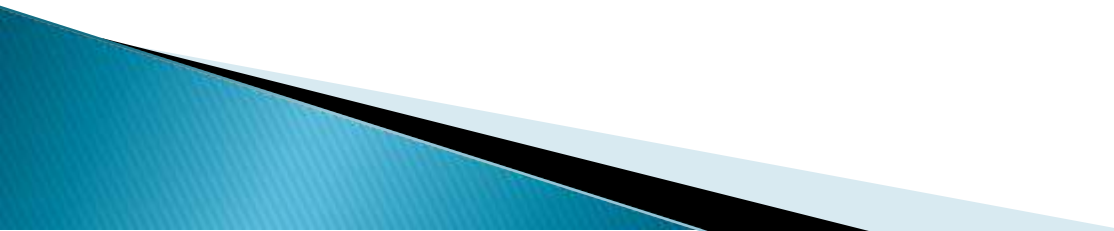
Pelvic inflammatory disease (PID)

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Pelvic inflammatory disease (PID) :

*** **Acute infection** of the **upper genital tract** structures in women, involving any or all of the uterus, oviducts, and ovaries; this is often accompanied by involvement of the neighboring pelvic organs. Involvement of these structures results in endometritis, salpingitis, oophoritis, peritonitis, perihepatitis and tubo-ovarian abscess.

By definition, PID is a **community-acquired infection initiated by a sexually transmitted agent**, distinguishing it from pelvic infections caused by medical procedures, pregnancy, and other primary abdominal processes.



PID is primarily a disease of sexually active women

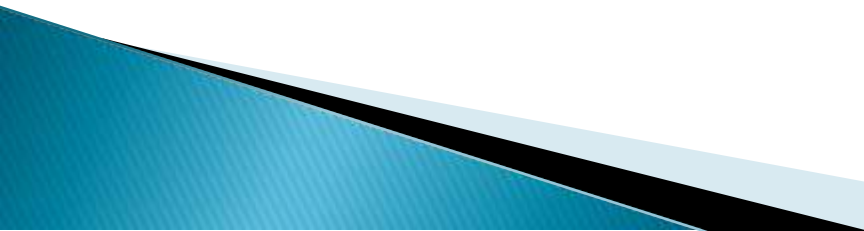


PATHOGENESIS :

The endocervical canal functions as a barrier protecting the normally sterile upper genital tract from the organisms of the dynamic vaginal ecosystem. **Disturbance of this barrier** provides vaginal bacteria with access to the upper genital organs via **canalicular routes**, infecting the endometrium, then endosalpinx, ovarian cortex, pelvic peritoneum, and their underlying stroma. This is the clinical entity of PID.

Acute PID is an ascending infection caused by cervical microorganisms (including *Chlamydia trachomatis* and *Neisseria gonorrhoeae*), as well as the vaginal microflora, including anaerobic organisms, enteric gram-negative rods, streptococci, genital mycoplasmas, and *Gardnerella vaginalis*, which is associated bacterial vaginosis. Bacterial vaginosis results in complex alterations of the normal vaginal flora, which may alter host defense mechanisms in the cervicovaginal environment

- **Up to 75 % of cases occur within seven days of menses**, during which time the quality of the cervical mucus favors the ascension of vaginal organisms. Epidemiologic data suggest that **all community-acquired agents causing disturbance of the endocervical barrier are sexually transmitted.**

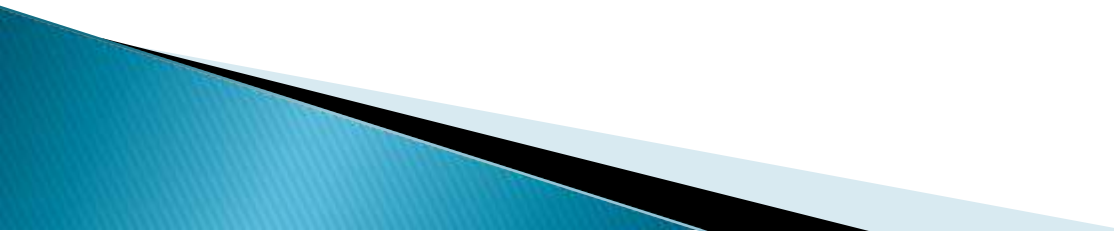


MICROBIOLOGY :

Initiating pathogens in pelvic inflammatory disease include *Neisseria gonorrhoeae* and *Chlamydia trachomatis* account for an estimated one-third of all cases of pelvic inflammatory disease, although in the majority of cases the etiology of PID is unknown.

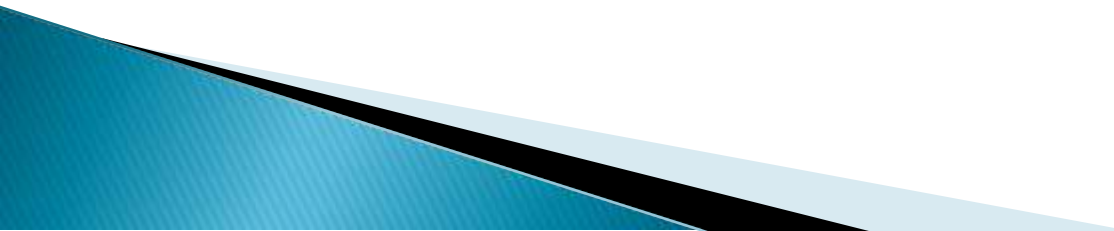
- **Mixed infection** : Regardless of the initiating event, the microbiology of PID, especially for clinical purposes, should be viewed and treated as a mixed (facultative and anaerobic) polymicrobial infection.

RISK FACTORS :

- 1) **Multiple sex partners** : The most important risk factor.
 - Celibate women are not at risk for PID.
 - Women with longstanding monogamous relationships rarely develop PID.
 - 2) **Status of the partner** : Approximately one-third of men with gonococcal or chlamydial urethritis are asymptomatic. Having a **symptomatic** (dysuria, urethral discharge) male partner greatly increases a woman's risk of PID.
 - 3) **Age**: PID occurs in highest frequency among those **15 to 25 years of age**; the incidence in women older than the age of 35 is only one-seventh that in younger women.
 - 4) **Previous PID**: approximately one in four women with PID will suffer recurrence.
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5) Contraceptive method :

- **Barrier contraception** : protects against PID. Condoms are the most effective, preventing 50 % of endocervical gonococcal and chlamydial infections.
- **Oral contraceptives**: associated with increased risk of subclinical PID.
- **Intrauterine device and tubal ligation**: Modern intrauterine devices cause little, if any, increased risk for PID. The risk of PID is primarily limited to the **first three weeks after IUD insertion** and is uncommon thereafter.
→ Long-term indwelling IUDs have been associated with pelvic actinomycosis, a rare disease that can present as a pelvic mass with weight loss and constitutional symptoms.
- **Progestin-based contraceptives**: may decrease the risk of PID because progestin thickens cervical mucus, thereby possibly providing an enhanced barrier against ascending infection.

- 6) **Bacterial vaginosis** : is more common among women with PID.
 - 7) **Sex during menses.**
 - 8) **Vaginal douching.**
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CLINICAL FEATURES :

1) **Lower abdominal pain** : Is the cardinal presenting symptom in women with PID

- The onset of pain during or shortly after menses is particularly suggestive.
- Usually bilateral and rarely of more than two weeks' duration.

2) **Abnormal uterine bleeding**: occurs in one-third or more of patients with PID.

3) **On physical examination** :

- **Fever** : about one-half of patients.

- Abdominal examination reveals **diffuse tenderness** greatest in the lower quadrants which may or may not be symmetrical.

Rebound tenderness and decreased bowel sounds are common. Marked tenderness in the right upper quadrant does not exclude PID, since approximately 10 % of these patients have perihepatitis (Fitz-Hugh Curtis syndrome).

- **On pelvic examination**, the finding of a **purulent endocervical discharge** and/or acute **cervical motion and adnexal tenderness** with bimanual examination is strongly suggestive of PID.

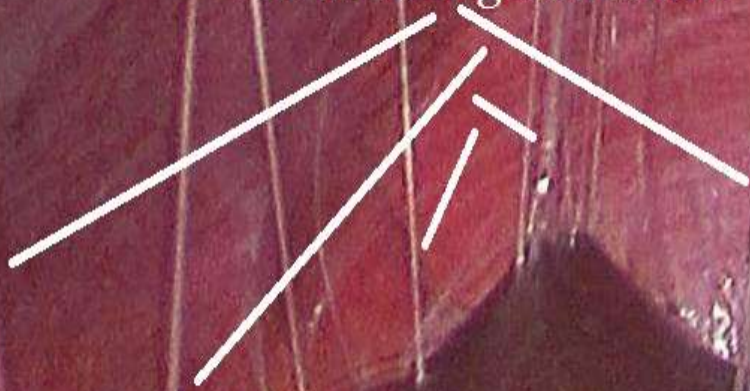
Subclinical PID :

- No symptoms.
 - Defined histologically by the presence of neutrophils and plasma cells in endometrial tissue.
 - Subclinical PID severe enough to produce significant sequelae (e.g,tubal factor infertility).
 - Subclinical episodes are particularly common among oral contraceptive users.
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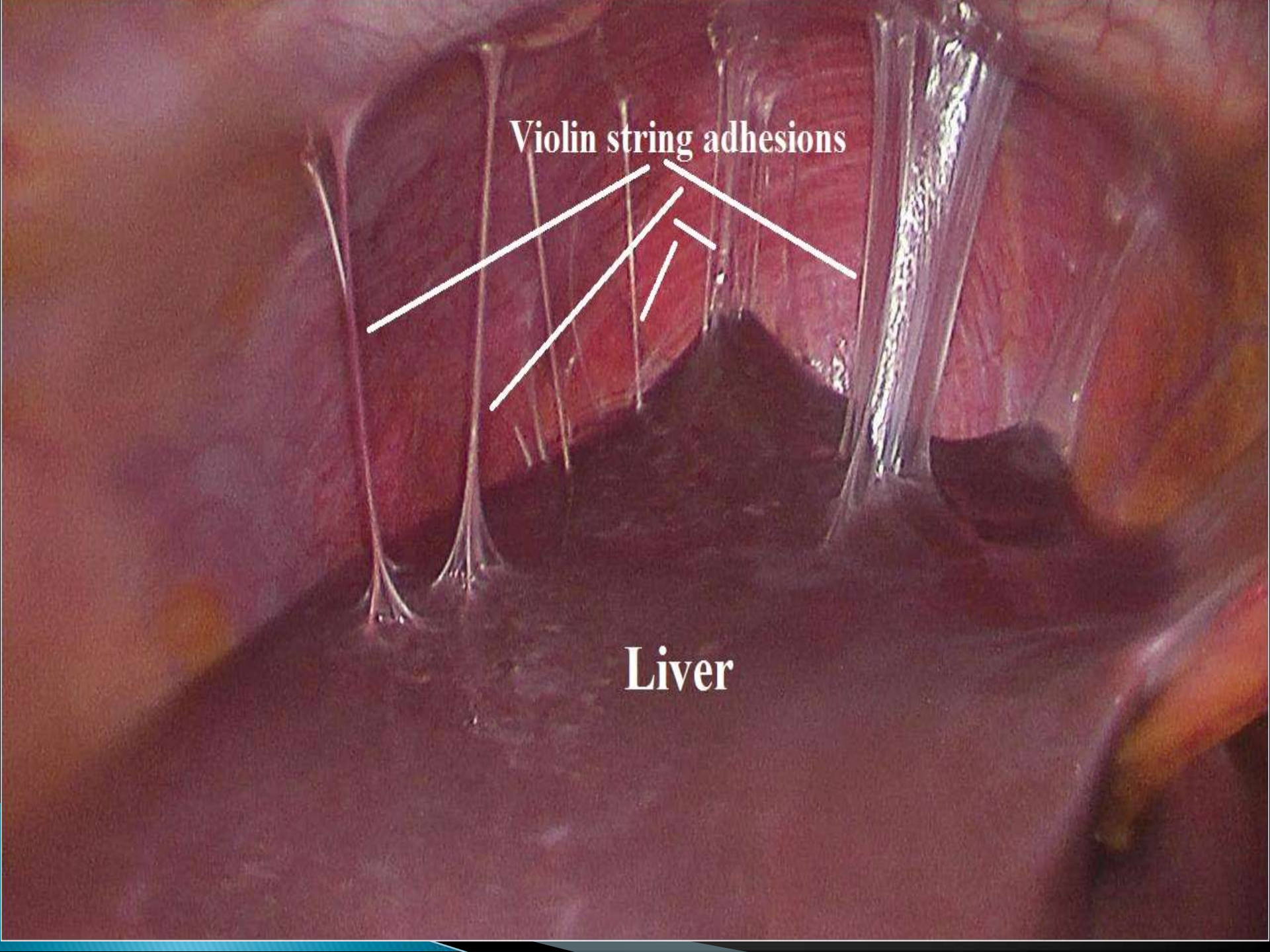
Perihepatitis (Fitz-Hugh Curtis Syndrome) :

- It consists of infection of the **liver capsule and peritoneal surfaces** of the anterior right upper quadrant, with minimal stromal hepatic involvement.
- Symptoms are typically the sudden onset of severe right upper quadrant abdominal pain with a distinct pleuritic component, sometimes referred to the right shoulder.
- Aminotransferases are also usually normal.
- By laparoscopy: manifests as a patchy purulent and fibrinous exudate in the acute phase ("**violin string**" **adhesions**), most prominently affecting the anterior surfaces of the liver (not the liver parenchyma).

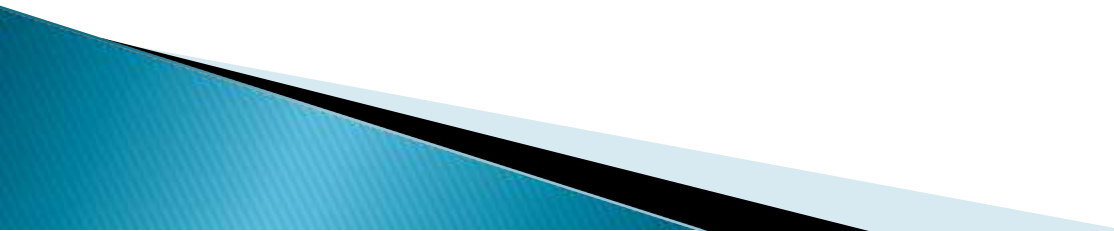
Violin string adhesions



Liver




DIAGNOSTIC CONSIDERATIONS

- PID represents a spectrum of clinical disease, from endometritis to fatal intraabdominal sepsis.
 - There are multiple gold standards in use to establish the diagnosis, because no one among them is adequate alone. Older studies defining PID by a single standard, such as laparoscopic visualization of gross salpingitis, are now felt to lack sensitivity.
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A minimal set of clinical criteria has been recommended by the CDC for empirical treatment of PID, including cervical motion tenderness or uterine or adnexal tenderness in the presence of lower abdominal or pelvic pain.

The following additional criteria can also be used to support a clinical diagnosis of PID:

- 1- Oral temperature $>101^{\circ}\text{F}$ ($>38.3^{\circ}\text{C}$). 
- 2- Abnormal cervical or vaginal mucopurulent discharge.
- 3- Presence of abundant numbers of white blood cells (WBCs) on saline microscopy of Vaginal secretions.
- 4- Elevated erythrocyte sedimentation rate (ESR).
- 5- Elevated C-reactive protein (CRP).
- 6- Demonstration of *N. gonorrhoea* or *C. trachomatis* in the genital tract

- Acute or chronic (plasma cell) endometritis or acute salpingitis on histologic evaluation of a biopsy.
- Gross salpingitis visualized at laparoscopy or laparotomy.
- Isolation of pathogenic bacteria from a clean specimen from the upper genital tract
Inflammatory/purulent pelvic peritoneal fluid without another source.

DIAGNOSTIC TESTING : Noninvasive diagnostic tests for PID include general laboratory studies looking for signs of inflammation, culture testing and microscopy of cervical or vaginal secretions, and imaging studies.

1) Laboratory tests :

- pregnancy test to rule out ectopic pregnancy and complications of an intrauterine pregnancy.
- CBC , ESR,CRP : Although PID is usually an acute process, less than half of PID patients exhibit leukocytosis.
- Swabs (high vaginal and endocervical) : for microscopic examination, gram stain and culture.(e.g., increased white blood cells (WBC) in vaginal fluid).
- Nucleic acid amplification tests for C. trachomatis and N. gonorrhoeae.
- Urinalysis.
- Others : HIV testing/Hepatitis B surface antigen and surface antibody
Testing for syphilis.

→ **Negative endocervical or high vaginal swabs screening for Chlamydia trachomatis and Neisseria gonorrhoeae does not rule out upper tract infection.**

2) Imaging techniques :

- Transvaginal ultrasound : Sonographic findings consistent with PID are **thickened fluid-filled tubes/oviducts with or without free pelvic fluid or tuboovarian complex**, are useful to support a clinical diagnosis of PID.
 - However, the absence of findings does not diminish the probability of PID and should not be used as a reason to delay treatment.

Conclusion : There was no single test or combination that was both sensitive and specific for the diagnosis of PID. However, certain combinations may have a high negative predictive value.

Health care providers should maintain a low threshold for the diagnosis of PID and that sexually active young women with the combination of lower abdominal, adnexial, and cervical motion tenderness should receive empiric treatment.

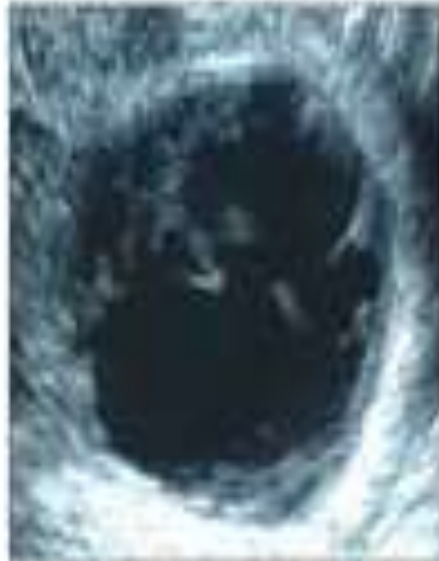
Figure 2

Examples of "Cogwheel Sign"

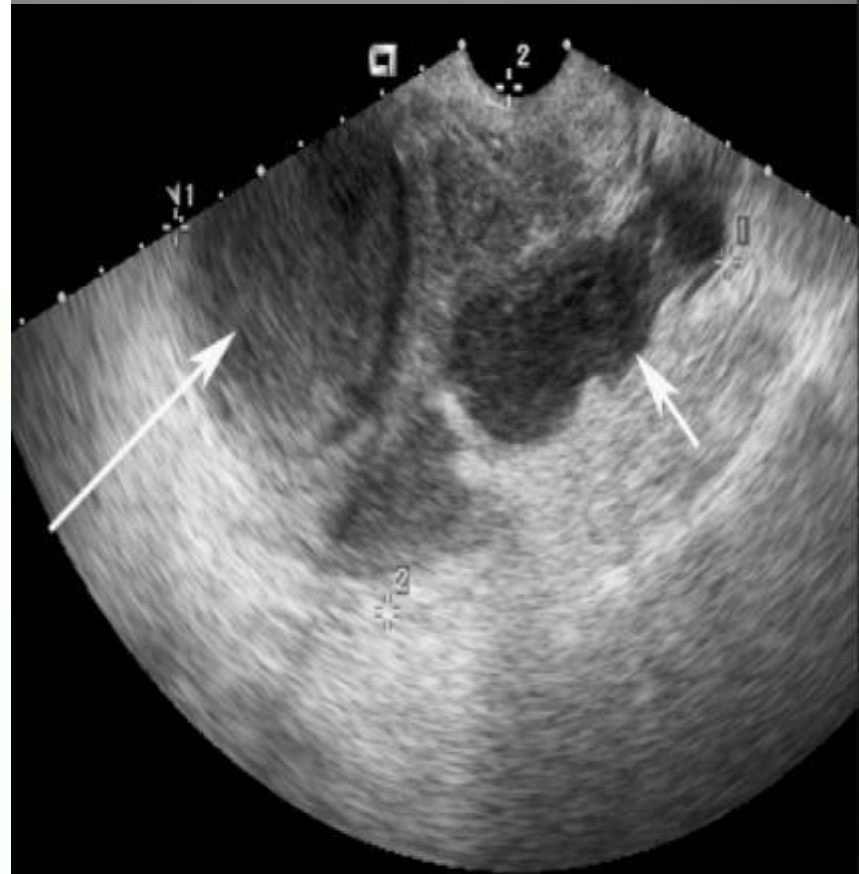
Acute salpingitis



Pyosalpinx



cross section of thick walled tube appears as sonolucent wheel shaped structure



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Dist = 12.70cm
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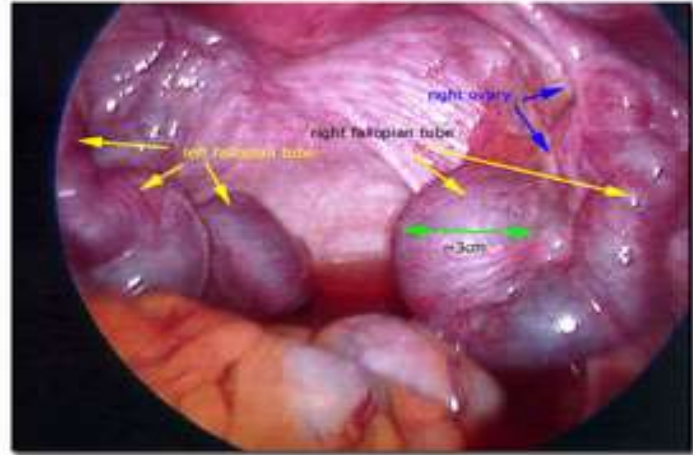
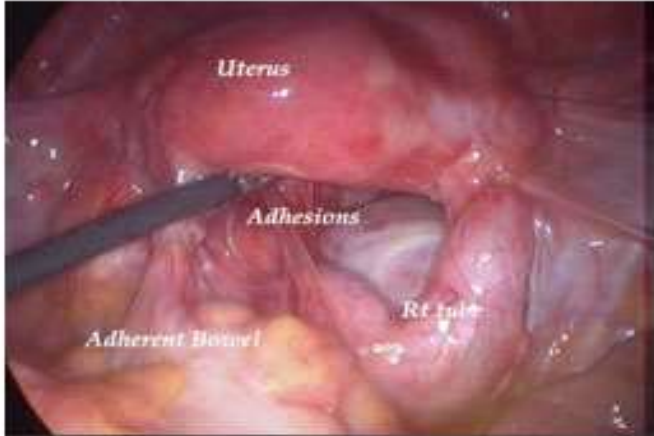
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NORMAL LAPAROSCOPY

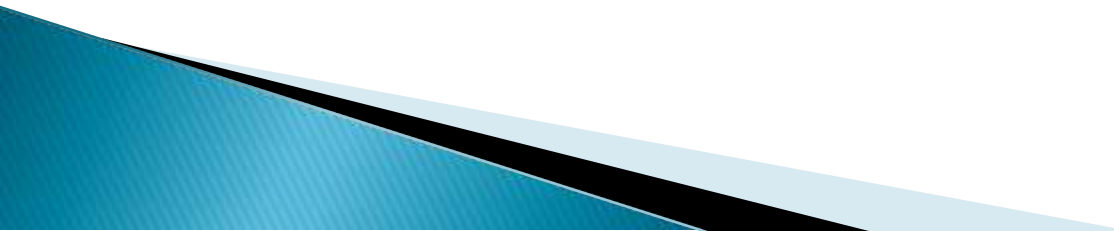
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Laparoscopy findings in chronic PID

- **Plasma cell endometritis :**

- Plasma cell endometritis (PCE) has been identified as an important component of PID.
 - PCE was documented in about **80-90%** of women with PID.
 - The density of the plasma cell infiltrate correlated with the clinical severity of disease.
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Long-term complications of PID

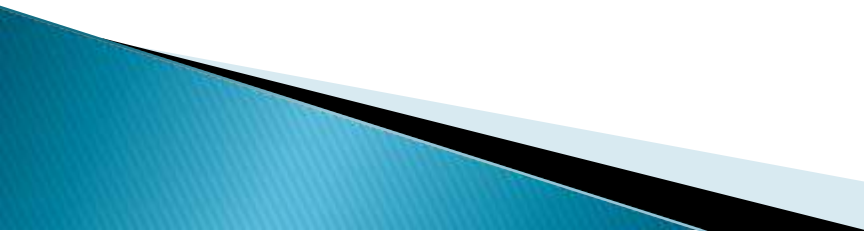
1) HYDROSALPINX :

- After PID resolves, the damaged fallopian tube can become blocked, filled with sterile fluid, and become enlarged.
- Hydrosalpinx may be associated with pain or may be asymptomatic except for tubal factor infertility.
- Hydrosalpinx in patients undergoing in vitro fertilization (IVF) has negative consequences on the rates of pregnancy, implantation, early pregnancy loss, preterm birth, and live delivery. So salpingectomy is recommended before IVF.

2) CHRONIC PELVIC PAIN :

- Defined as **menstrual or non-menstrual pain of at least six months' duration that occurs below the umbilicus and is severe enough to cause functional disability.**
- One-third of women with PID develop chronic pelvic pain.
- While the precise etiology is unknown, the pain may result from scarring and adhesions that develop from inflammation related to the infectious process.

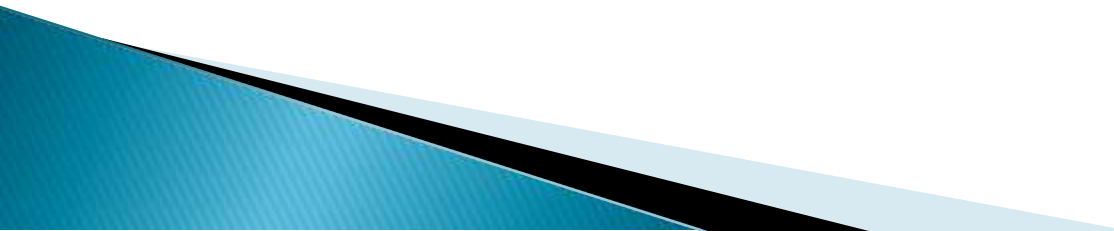
3) INFERTILITY :

- Both symptomatic and asymptomatic PID can cause permanent injury to the fallopian tube, especially the endosalpinx.
 - Changes to the fallopian tube, including loss of ciliary action, fibrosis, and occlusion, lead to tubal infertility. There may be additional mechanisms of infertility, as well.
 - *Risk factors for tubal factor infertility and other long term complications:*
 - 1- **Chlamydial infection:** Among the microorganisms that cause PID, Chlamydia trachomatis appears to carry the greatest risk of infertility. Approximately one in four women with tubal factor infertility seeking care in an infertility clinic has serum antibodies to C. trachomatis.
 - 2- **Delay in seeking care for PID :** women with PID who delayed seeking treatment ≥ 3 days were threefold more likely to be diagnosed with infertility than women who sought care in a timely manner.
 - 3- **Increasing number of PID episodes.**
 - 4- **Severity of infection.**
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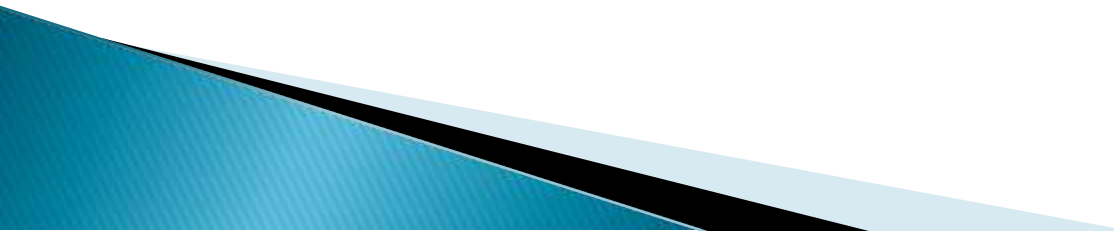
4) ECTOPIC PREGNANCY :

- Tubal damage caused by PID increases the risk of tubal pregnancy, as well as infertility, and the risk of ectopic pregnancy increased with the number of episodes and severity of PID.

5) OVARIAN CANCER:

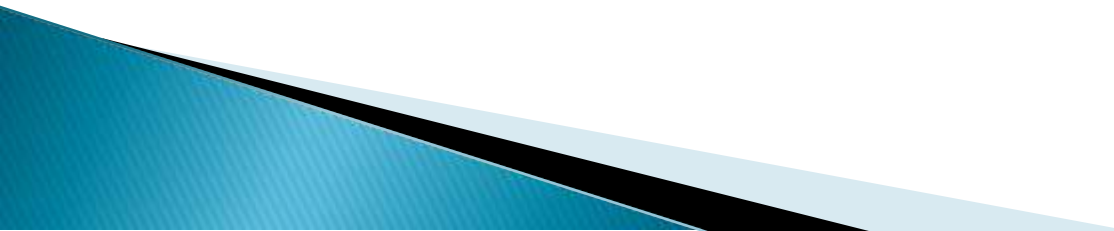
- A history of PID was associated with an almost two-fold increase in the risk of ovarian cancer, with the highest risk in women with multiple episodes of PID.
 - It is not known whether PID is an independent risk factor for ovarian cancer, as PID increases the risk of low parity, nulliparity, nulligravidity, and infertility, which are also risk factors for ovarian cancer.
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Treatment of PID

- Clinicians should maintain a low threshold of suspicion for the diagnosis and empiric treatment of PID since long-term complications are more common if treatment is delayed.
 - PID is a **polymicrobial infection**, which generally requires broad coverage, particularly among those with severe disease requiring hospitalization.
 - Treatment response is based on both short- and long-term outcomes.
 - **Clinical cure** is defined as "significant" or "complete improvement" in the signs and/or symptoms of PID.
 - **Microbiologic cure** is defined as eradication of *N. gonorrhoeae* or *C. trachomatis*, if present at baseline.
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INDICATIONS FOR HOSPITALIZATION :

Recommended indications for hospitalization and parenteral antibiotics include :

- Pregnancy
 - Lack of response or tolerance to oral medications
 - Non-adherence to therapy
 - Inability to take oral medications due to nausea and vomiting
 - Severe clinical illness (high fever, nausea, vomiting, severe abdominal pain)
 - Complicated PID with pelvic abscess (including tuboovarian abscess)
 - Possible need for surgical intervention or diagnostic exploration for alternative etiology (eg, appendicitis)
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Inpatient therapy :

Patients with severe PID should be hospitalized and treated with parenteral therapy :

First-line therapies: For patients with severe PID, the CDC recommends either of the following parenteral regimens, which result in clinical cure of acute disease in >90 % of PID cases :

- Cefoxitin (2 g intravenously every 6 hours) or cefotetan (2 g IV every 12 hours) plus doxycycline (100 mg orally every 12 hours).
- Clindamycin (900 mg intravenously every 8 hours) plus gentamicin loading dose (2 mg/kg of body weight) followed by a maintenance dose (1.5 mg/kg) every 8 hours.

Single daily intravenous dosing of gentamicin may be substituted for three times daily dosing.

These inpatient regimens provide broad coverage, including streptococci, gram-negative enteric bacilli (*E.coli*, *Klebsiella* spp, and *Proteus* spp), and anaerobic organisms (ie, bacterial vaginosis-associated flora).

--Antiemetic and antipyretic medications should be offered to those patients who are symptomatic.

Transitioning from parenteral to oral therapy can usually be started after 24 hours of sustained clinical improvement, such as resolution of fever, nausea, vomiting, and severe abdominal pain, if present.

Patients should complete a 14-day course of treatment with doxycycline (100 mg twice daily).

PREGNANT PATIENTS :

While it is quite rare to have PID during pregnancy, the infection can occur in the first 12 weeks of gestation before the mucus plug and decidua seal off the uterus from ascending bacteria. As above, pregnancy is an indication for hospitalization and parenteral antibiotics for PID.

-Use 1st line therapy but azithromycin 1gm orally instead of doxycycline.

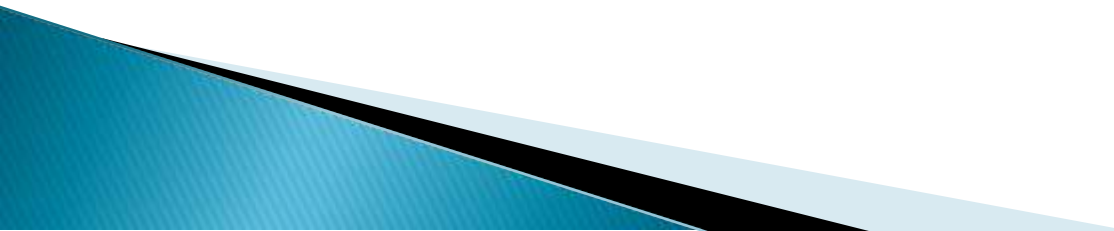
Outpatient therapy : Patients with mild or moderate PID are suitable candidates for oral therapy since clinical outcomes are equivalent with parenteral or oral therapy.

First-line regimens: The CDC recommends any of the following outpatient regimens, with or without [metronidazole](#) (500 mg twice a day for 14 days) :

- [Ceftriaxone](#) (250 mg intramuscularly in a single dose) plus [doxycycline](#) (100 mg orally twice a day for 14 days).
- [Cefoxitin](#) (2 g intramuscularly in a single dose) concurrently with [probenecid](#) (1 g orally in a single dose) plus [doxycycline](#) (100 mg orally twice a day for 14 days).
- Other parenteral third-generation cephalosporins, such as [cefotaxime](#) (1 gram intramuscularly in a single dose) or ceftizoxime (1 gram intramuscularly in a single dose) plus [doxycycline](#) (100 mg orally twice a day for 14 days).

DURATION OF THERAPY :

The optimal duration of therapy is unknown. Most studies have used **14 days** of therapy and this duration has been maintained in the 2010 STD recommendations from the CDC.



PATIENT RELATED ISSUES :

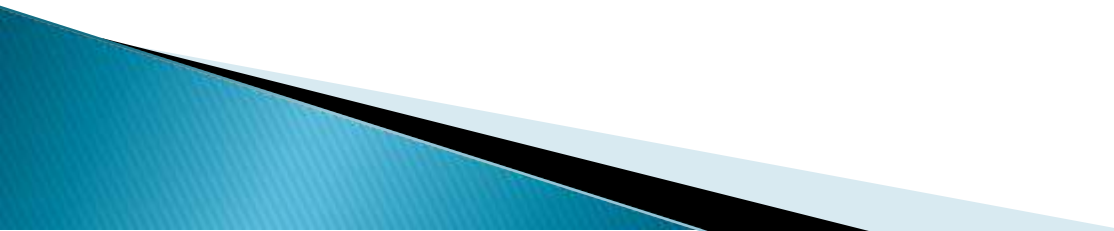
1) Patient monitoring :

If outpatient therapy is selected, it is important to see the patient within **48 to 72 hours** to be certain that clinical improvement has occurred (reduction in abdominal tenderness and reduction in cervical motion tenderness).

If no clinical improvement has occurred within 72 hours, hospitalization, parenteral therapy, and further diagnostic evaluation is recommended.

2) Medication adherence :

Compliance with a long course of oral antibiotics can be problematic. Patients should be educated about the importance of medication adherence and clinical outcomes.



3) Counseling and screening :

Clinicians should counsel patients regarding the route of acquisition for sexually transmitted infections, the concomitant need for partner treatment, and future safe sex practices.

4) Sex partners :

Male sex partners of women with PID should be examined and treated if they had sexual contact with the patient during the previous **60 days** prior to the patient's onset of symptoms, regardless of the woman's sexually transmitted infection test results.

Evaluation and treatment of the sex partner is essential to decrease the risk of reinfection. Regimens should include antibiotics with activity against *Neisseria gonorrhoeae* and *Chlamydia trachomatis*, such as ceftriaxone (250 mg) intramuscularly plus either azithromycin (1 gram) orally as a single dose or doxycycline (100 mg) orally twice daily for seven days.