A FOGSI President's Initiative

TOG IPP

Infection Practice Points

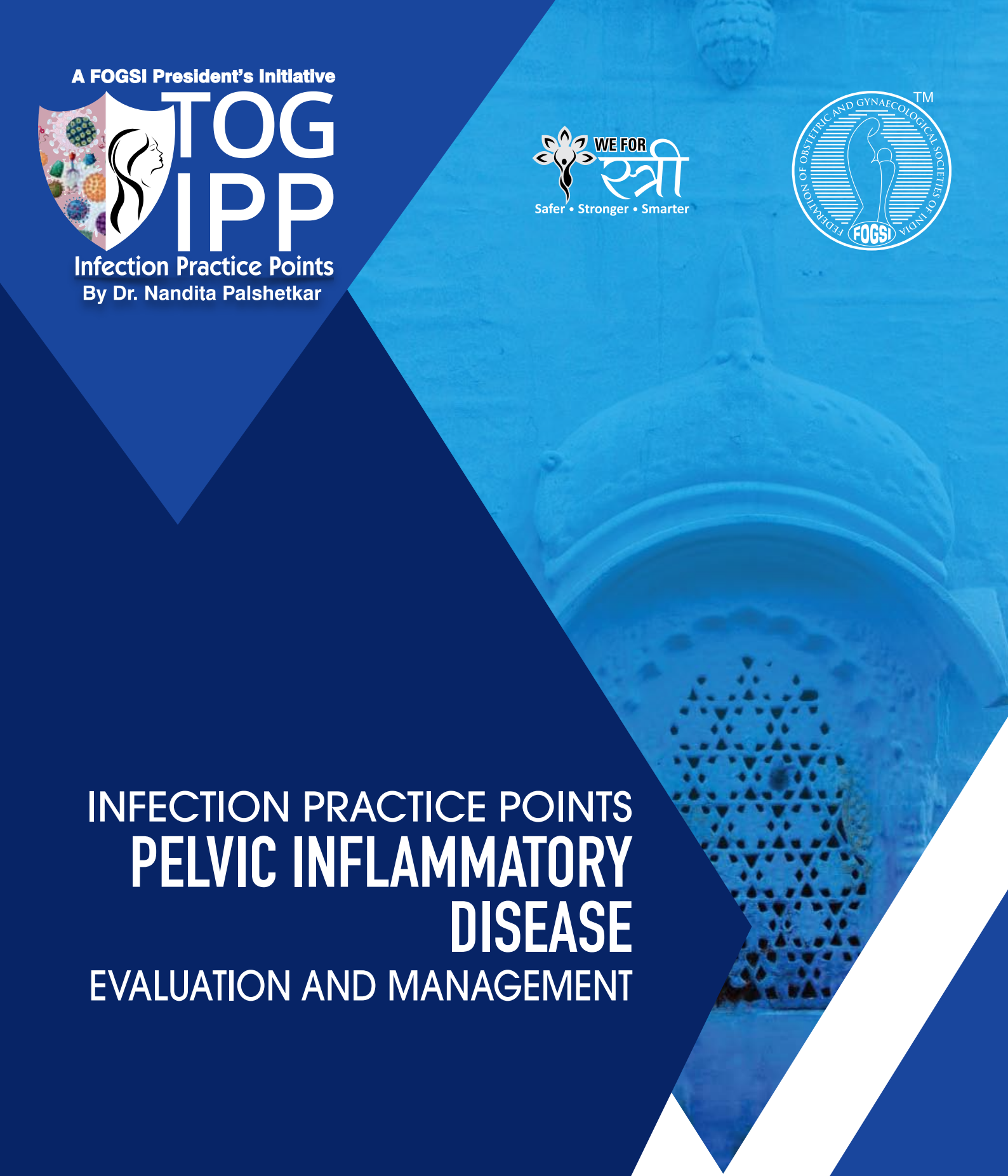
By Dr. Nandita Palshetkar

WE FOR स्त्री

Safer • Stronger • Smarter

FEDERATION OF OBSTETRIC AND GYNAECOLOGICAL SOCIETIES OF INDIA TM

FOGSI



INFECTION PRACTICE POINTS

PELVIC INFLAMMATORY DISEASE

EVALUATION AND MANAGEMENT

Zuventus Healthcare Ltd.

science integra®

For the 1ST TIME IN INDIA

Presenting

Her Best Companions To Take Care of Intimate Health

A **Unique Probiotic Vaginal** Tablets

EvaNew Probiotic Vaginal Tablets

Atleast 1 Billion CFU of Mix Lactobacilli: *L. brevis CD2, L. salivarius FV2 & L. plantarum FV9* / Vaginal Tablet

Re-establishes and Maintains Healthy Vaginal Flora

Specifically selected Lactobacilli with Proven Adherence to Vaginal Epithelium

- **Resolves Vaginal Infections**
- **Improves Reproductive Outcomes**
- **Reduces Relapse in Antibiotic Treated Patients**

Dosage:

- 1 tablet intra-vaginal at bedtime for 8 days every month preferably from 8th day of menstrual cycle for 3 consecutive months(Not to be given concomitantly with anti-infective pessaries)

Storage:

- Maintain Cold Chain (Store between 2^0 C-8^0 C. Do not freeze)

An Easy, Quick & Reliable Method for Measuring Vaginal pH in Outpatients

EvaNew Gloves

Test Glove with pH indicator

Checks Vaginal pH... Instantly & Accurately

Helps in Quick Assessment of vaginal infections

- Bacterial Vaginosis
- Protozoal Infections (Trichomoniasis)
- Vaginal Candidiasis

For Hypoestrogenemia Induced Vulvovaginal Atrophy

ISEREN® gel vaginal

Glycine MAX (Soya Isoflavones) 0.5%

Relieves Vulvovaginal Atrophy...Effectively...Safely

"Isoflavone Vaginal Gel Proved As Good Treatment Option For Relief of Vulvovaginal Atrophy"

- **Corrects Local Histology**
- **Free From Side Effects of Local Estrogen**
- **Relieves Vaginal Atrophy Symptoms**
  - Itching
  - Burning
  - Dyspareunia
  - Dryness
  - Irritation

For The Management of Vaginal Dryness

pelvik™ Gel

Transparent Vaginal Hydrating & Lubricating Gel with Hyaluronic Acid 0.05%

A Comprehensive Solution To Ease Vaginal Dryness With Efficacy & Safety

Hyaluronic acid releases water molecules to the tissues, relieves dryness without irritating vaginal mucosa

After 10 Applications significant improvement in

- Dryness by 84.44%
- Itching by 86.23 %
- Burning by 85.83 %

Under Exclusive Licence from OPKO Health Europe, Spain S.L.U.

Zuventus

Dear FOGSIANs,

The theme of FOGSI this year is "We for Stree". I would like to thank every FOGSIAN who has helped making every woman Safer, Stronger and Smarter. Through various academic and social programs FOGSI aims to uplift the quality of care that is given to every woman who comes to us.

TOG IPP (Infection Practice Points) is one such conclave that brings to light some of challenging health issues like Vaginitis, Pelvic inflammatory disease (PID) and Urogenital infections.

I would like to thank Zuventus for their contributions towards the TOG IPP Conclave.

We, as clinical practitioners are always busy, therefore the TOG IPP that is released has been a quick and easy way to update you with the latest evidence in the field of Infections. This year we ask all FOGSIANs to focus on the Stree and help make them safer, smarter and stronger.

Select FOGSIANs across India came together to deliberate and create these practice points. I am sure that you will appreciate the efforts which has gone into preparing the Infection Practice Points and find them useful in your day to day practice.

Best wishes!

Nandita P. Palshetkar

Dr. Nandita Palshetkar

MD, FCPS, FICOG
President 2019 - Federation of Obstetrics & Gynecological Societies of India (FOGSI)

PELVIC INFLAMMATORY DISEASE
EVALUATION AND MANAGEMENT

FOGSI President : **Dr. Nandita Palshetkar**

Moderators : **Dr. Rishma Dhillon Pai, Dr. Pratik Tambe**

Panelists : **Dr. Nozer Sheriar, Dr. Dibyendu Banerjee, Dr. Shyamal Sett, Dr. Madhuri Patel, Dr. Anshu Jindal, Dr. Seema Mehta, Dr. Adarsh Bhargava, Dr. Rakhi Singh, Dr. Pragya Mishra, Dr. Arun Nayak, Dr. Parzan Mistry, Dr. Bipin Pandit, Dr. Nita Mishra**

Clinical Reporter : **Dr. Ritu Hinduja**

From left to right: Dr. Nita Mishra, Dr. Pratik Tambe, Dr. Rakhi Singh, Dr. Parzan Mistry, Dr. Rishma Dhillon Pai, Dr. Nandita Palshetkar, Dr. Anshu Jindal, Dr. Shyamal Sett, Dr. Pragya Mishra, Dr. Madhuri Patel, Dr. Ritu Joshi

A FOGSI President's Initiative
TOG IPP
Infection Practice Points

PELVIC INFLAMMATORY DISEASE
Evaluation and Management

Definition

Pelvic inflammatory disease (PID) refers to acute infection of the upper genital tract structures in women, involving any or all of the uterus, fallopian tubes and ovaries and may involve the neighboring pelvic organs.[1]

Mild-to-moderate PID is defined as the absence of a tubo-ovarian abscess. Severe disease is defined as severe systemic symptoms or the presence of tubo-ovarian abscess.[2]

Introduction

- Pelvic infection is one of the most common, serious infections in non-pregnant women or reproductive age[3]
- Pelvic infection are usually the result of infection ascending from the endocervix causing endometritis, salpingitis, parametritis, oophoritis, tubo-ovarian abscess and/or pelvic peritonitis[3]
- PID is reported to occur in 1% of the 15-25 year age group of young adults around the world and affects around 24%–32% of women in India[4]
- In developed countries, the annual incidence is estimated to be 10–13 per 1000 women, with 20 per 1000 women being in the age group of 20–24 years[4]

Cause of PID[3]

- *Neisseria gonorrhea* and *Chlamydia trachomatis (C. trachomatis)* have been identified as the causative agents
- *C. trachomatis* is the commonest identified cause accounting for 14%–35% of cases, whilst *Gardnerella vaginalis*, anaerobes and other organisms commonly found in the vagina may also be implicated
- *Mycoplasma genitalium* has been associated with upper genital tract infections in women and is a very likely cause of PID
- Genital tuberculosis is one of the causes of PID in India[5]
- The insertion of an intrauterine device (IUD) increases the risk of developing PID but only for 4–6 weeks after insertion. This risk is probably highest in women with pre-existing gonorrhoea or *C. trachomatis*[3]

CAUSES

- *Neisseria gonorrhea* and *Chlamydia trachomatis* are identified as the causative agents of PID
- *Gardnerella vaginalis*, anaerobes and other organisms commonly found in the vagina may also be implicated
- *Mycoplasma genitalium* has been associated with upper genital tract infections in women and is a very likely cause of PID
- Insertion of an IUD increases the risk and is highest in women with pre-existing gonorrhoea or *C. trachomatis*

Risk factors[4,6,8,9]

- Instrumentation of the uterus / interruption of the cervical barrier
  - » Termination of pregnancy, insertion of IUD within the past 4 months, hysterosalpingography, *In vitro* fertilization, intrauterine insemination (IUI), hysteroscopy
- Young < 25 years
- Menstruating women
- Multiple sexual partners
- Recent new partners
- Past history of sexually transmitted infections (STIs) in the patient or their partner
- No h/o of contraception use
- Living in an area of high prevalence of PID
- Tampons use (forgotten)
- Poor menstrual hygiene
- Bacterial vaginosis
- However, in Indian scenarios the commonest causes are abortions, puerperal sepsis and IUD insertions

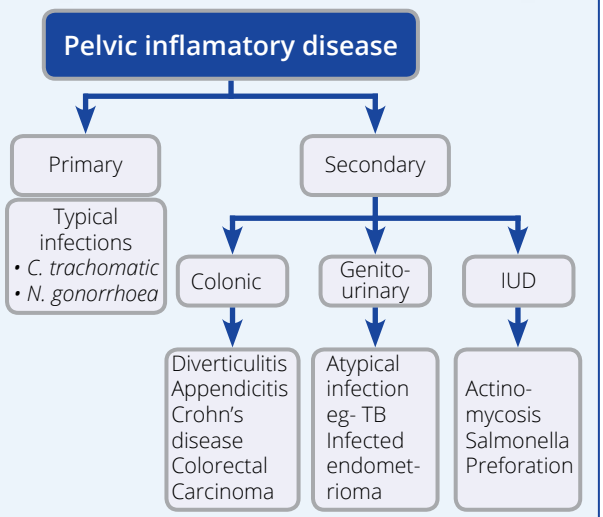
Pathogenesis of PID[4,6,8,9]

- Ascending
- Hematogenous
- Local spread

Most cases of PID occur in 2 stages.

1. Acquisition of a vaginal or cervical infection, which is often sexually transmitted and may be asymptomatic
2. Direct ascent of microorganisms from the vagina or cervix to the upper genital tract, with infection and inflammation of these structures

Figure 1. Flow diagram of causes of primary and secondary pelvic inflammatory disease[7]



TB: tuberculosis; IUD: intrauterine device.

- Infection of the fallopian tubes initially affects the mucosa, but inflammation may rapidly become transmural. This inflammation, which appears to be mediated by complement, may increase in intensity with subsequent infections
- Inflammation may extend to uninfected parametrial structures, including the bowel
- Infection may extend via spillage of purulent materials from the fallopian tubes or via lymphatic spread beyond the pelvis to produce acute peritonitis and acute perihepatitis (Fitz-Hugh–Curtis syndrome)

Other factors responsible for influencing occurrence of PID are:

- Cervical mucus provides a functional barrier against upward spread, but vaginal inflammation and hormonal changes that occur during ovulation and menstruation decrease the efficacy of this barrier
- Antibiotic treatment of sexually transmitted infections can also disrupt the balance of endogenous flora in the lower genital tract,

causing normally nonpathogenic organisms to overgrow and ascend

- Opening of the cervix during menstruation, along with retrograde menstrual flow, may also facilitate ascent of microorganisms
- Intercourse may contribute to the ascent of infection through rhythmic uterine contractions occurring during orgasm. Bacteria may also be carried along with sperm into the uterus and fallopian tubes

Clinical features[3,9]

PID should be considered in a patient with the clinical signs and/or symptoms as below.

Symptoms[3]

PID may be symptomatic or asymptomatic. The following features are suggestive of a diagnosis of PID:

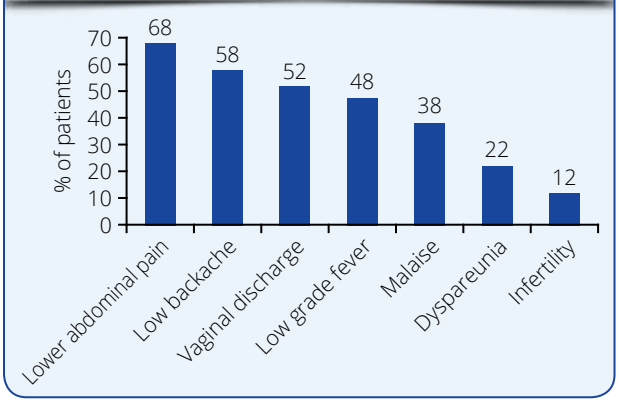
- Lower abdominal pain which is typically bilateral (but can be unilateral)
- Abnormal vaginal or cervical discharge which is often purulent
- Deep dyspareunia particularly of recent onset
- Abnormal vaginal bleeding, including post coital bleeding, inter-menstrual bleeding and menorrhagia
- Secondary dysmenorrhoea
- Abnormal vaginal or cervical discharge – as a result of associated cervicitis, endometritis or bacterial vaginosis

Physical signs[3]

- Lower abdominal tenderness which is usually bilateral
- Adnexal tenderness on bimanual vaginal examination – a tender mass is sometimes present
- Cervical motion tenderness on bimanual vaginal examination
- Fever (>38°C) in moderate to severe disease

A recent study conducted in Indian women with PID demonstrated signs and symptoms as shown in Figure 2 below.[10]

Figure 2. Signs and symptoms in studied cases



Centre for Disease Control and Prevention (CDC) Criteria for PID[11]

Table 1. PID diagnostic criteria per 2015 CDC guidelines

Minimal clinical criteria[a]	• Cervical motion tenderness • Uterine tenderness • Adnexal tenderness
Additional criteria[b]	• Oral temperature greater than 101°F (38.3°C) • Abnormal cervical mucopurulent discharge or cervical friability • Abundant white blood cells on microscopic evaluation of vaginal fluid • Elevated erythrocyte sedimentation rate • Elevated C-reactive protein • Laboratory documentation of cervical infection with *Neisseria gonorrhoea* or *Chlamydia trachomatis*
Specific criteria[c]	• Endometrial biopsy with histopathologic evidence of endometritis • Transvaginal ultrasound or magnetic resonance imaging showing thickened, fluid-filled tubes with or without free pelvic fluid or tubo-ovarian complex, or • Doppler studies suggesting pelvic infection • Laparoscopic findings consistent with PID

Notes: Reproduced from CDC. 2015 Sexually Transmitted Diseases Treatment Guidelines. Atlanta, GA: Department of Health and Human Services; 2015.
[a]Initiate treatment if one or more of these criteria are met.
[b]In addition to one or more minimal criteria, one or more of the additional criteria increases specificity of the diagnosis of PID.
[c]One or more of these criteria provides the most specific diagnosis of PID.

Abbreviations: CDC, US Centers for Disease Control and Prevention; PID, pelvic inflammatory disease.

Vaginal pH assessing gloves as easy quick diagnosis tool

Vaginal infections may be associated with PID and now assessing vaginal infections with gloves is an easy diagnostic tool

Rationale for use

- A move away from normal vaginal pH especially pH≥5.0 may be suggestive of altered vaginal flora and PID
- In such situations, the clinical signs and symptoms may not be obvious and the patient may present with only a vaginal discharge
- In such a clinical scenario, a simple digital vaginal assessment using specially developed gloves can be utilized

Procedure

- Wash and dry your hands
- Insert your right hand in the glove
- Insert your forefinger in the vagina for a few seconds and take out
- Immediately press together your forefinger find the thumb, making sure the absorbing pad is pressed against the pH indicator

3.5	4.0	4.5	5.0	5.5	6.0
The normal vaginal pH is between 3.8 and 4.5. An altered vaginal pH is indicative of vaginal infection					
pH	≤ 4.5	< 4.5	> 4.5	≥ 5.0	
Vaginal discharge	+/-	+ (white, thick, clumpy discharge)	+ (white/grey, thin, clumpy discharge)	+ (Greenish-yellow, frothy discharge)	
Malodour	-	-	+	+	
Itching	-	+	-	+	
Burning	-	+	-	+	
	Normal	Candidiasis	Bacterial vaginosis	Trichomoniasis	

Diagnosis

Laboratory evaluation[8]

- Urine pregnancy test (always rule out ectopic)
- CBC: WBC > 10000/microl (<50% cases- not amongst the diagnostic criteria's)
- ESR> 40mm/hr
- CRP: Elevated CRP> 60 mg/l
- Vaginal smear: Abundant WBC on vaginal smears (>10 WBC/hpf , >1 WBC/ epithelial cell) absence of endocervical or vaginal pus cells is a good negative predictive value (95%) but presence has a low positive predictive value of 17%)
- Culture of vaginal secretions: Culture-Blood agar and McConkeys agar at 37^0C for 24 hours. Blood culture plays no role in diagnosis of PID
- DNA probes: Gonorrhea and chlamydia probes (recovery rates of 5%–56%) have a high specificity of 100% on diagnosis
- Nucleic Acid Amplification Test (NAAT)-positive supports diagnosis, however negative NAAT does not exclude the diagnosis. Performed 3–6 months after Rx to rule out reinfection
- PCR
- Chlamydia Antibodies: IgG and IgM
- Test for other infections: Syphilis, HIV and UTI

Transvaginal ultrasound

- Predictor: Thickened >5 mm fluid filled tubes, indistinct borders, moderate to large fluid filled in pouch of Douglas, multiple cysts in ovaries. Cogwheel appearance of tubes on cross section

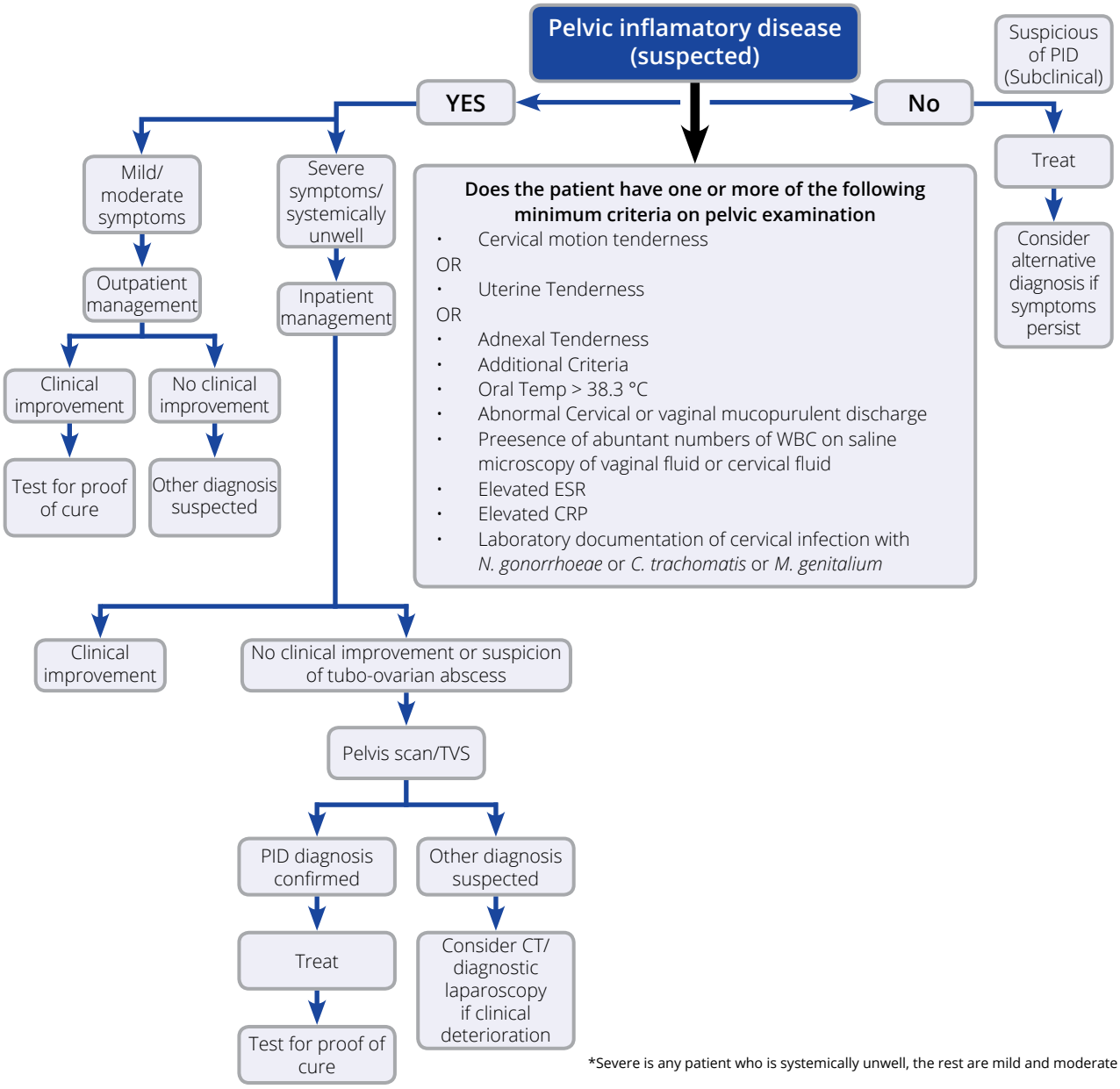
CT scan

- Not better than USG

Endoscopy and laparoscopy

- Not routinely recommended as first line investigations
- When imaging not definitive
- When no relief of symptoms after post outpatient treatment
- Tubal wall edema, hyperemia, exudates
- Direct visualization of tubo-ovarian abscess
- Fitz-Hugh-Curtis Syndrome
- Materials obtained simultaneously for histology and culture

Clinical diagnosis of PID: Flowchart[12]



*Severe is any patient who is systemically unwell, the rest are mild and moderate

Complications[3,9]

- The main complications of PID include tubo-ovarian abscesses and pelvic peritonitis
- A tubo-ovarian abscess should be suspected in patients who are systemically unwell and/or have severe pelvic pain
  - » The palpation of an adnexal mass, or lack of response to therapy, should prompt pelvic imaging with ultrasound, computed tomography (CT) or magnetic resonance imaging (MRI)
  - » Tubo-ovarian abscess is an indication for hospital admission for parenteral antimicrobial therapy, with appropriate anaerobic cover and to monitor for signs of rupture or sepsis

Staging of PID[13]

IDSOG STAGES

Stage 1

- Women who fulfill the CDC major diagnostic criteria and ≥1 of its minor criteria, but who do not have overt peritonitis and who do not have prior documented STD upper tract infections

Stage 2

- The above said criteria plus peritonitis

Stage 3

- Women with demonstrable tubo-ovarian complex or tubo-ovarian abscess evident on physical or ultrasonographic examination

Stage 4

- Women with ruptured tubo-ovarian abscesses

IDSOG: Infectious Diseases Society for Obstetrics and Gynaecology

- The Fitz-Hugh-Curtis syndrome comprises right upper quadrant pain associated with perihepatitis which occurs in some women with PID, especially by *C. trachomatis*
- PID is uncommon in pregnancy, but has been associated with an increase in both maternal and fetal morbidity, therefore parenteral therapy is advised
- Women with HIV may have more severe symptoms associated with PID but respond well to antibiotic therapy, although parenteral regimens may be required
- In women with an contraceptive IUD *in situ*, consider removing the IUD since this may be associated with better short-term improvement in symptoms and signs
  - » The decision to remove the IUD needs to be balanced against the risk of pregnancy in those who have had otherwise unprotected intercourse in the preceding 7 days
  - » Emergency hormonal contraception following removal of an IUD may be appropriate for some women in this situation

COMPLICATIONS OF PID

- Tubo-ovarian abscesses and pelvic peritonitis–indication for hospital admission for parenteral antimicrobial therapy, with appropriate anaerobic cover
- Fitz-Hugh-Curtis Syndrome
- Maternal and fetal morbidity in pregnancy
- HIV women may have severe symptoms
- Consider removal of *in situ* IUD for improving symptoms and signs
- Septicaemia

DIFFERENTIAL DIAGNOSIS[9,14]

The differential diagnosis of lower abdominal pain in a young woman includes:

- Ectopic pregnancy
- Acute appendicitis
- Endometriosis
- Irritable Bowel Syndrome (and less commonly, other gastrointestinal disorders)
- Complications of an ovarian cyst such as rupture or torsion
- Urinary tract infection
- Functional pain (pain of unknown physical origin)

PID in adolescents[15]

- Adolescents and young adults 15–24 years of age represent approximately 25% of the sexually active population, but account for nearly half of all new sexually transmitted infection (STI) cases
- Adolescents have the highest incidence of *Neisseria gonorrhea* and *Chlamydia trachomatis* among any sexually active age group
- This population also has an elevated risk of subsequent STIs after initial PID, thus putting them at increased risk of associated reproductive health sequelae such as infertility, ectopic pregnancy and chronic abdominal pain
- **Meeting adolescents where they interact with healthcare professionals:** Talking to adolescents about sex in a confidential manner, screening appropriately, notifying patients with positive results and treating both the patients and their partners to prevent reinfection should be the standard of care

AAP RECOMMENDS

- **The American Academy of Pediatrics (AAP) recommends at least one preventive health visit per year**
- The AAP, American Medical Association and Society for Adolescent Medicine recommend that **physicians discuss sexuality with youth as part of routine healthcare**

- According to the Society for Adolescent Medicine, "**Confidentiality protection** is an essential component of health care for adolescents because it is consistent with their development of maturity and autonomy and without it, some adolescents will forgo care"
- The AAP has endorsed a position paper by the Society for Adolescent Health and Medicine supporting the use of expedited partner therapy (EPT) as a treatment option for heterosexual sex partners of adolescents with gonorrhea and chlamydia when other partner treatment methods are impractical or unsuccessful

Counselling and prevention of adolescent PID[15]

- Make right choices
- Prevention of disease
- Adolescent education
- Menstrual hygiene
- School and college education
- Adolescent friendly clinics

Management[9]

Aim of management is:

- Symptomatic relief
- Treatment of acute condition
- Prevention of sequelae

Information, explanation and advice for the patient[6]

- Rest is advised for those with severe disease
- Appropriate analgesia should be provided
- Patients should be advised to avoid oral or genital intercourse until they and their partner(s), have completed their treatment
- A detailed explanation of their condition with particular emphasis on the long term implications for the health of themselves and their partner(s) should be provided
- Appropriate information should include:
  - » Fertility is usually well preserved in women with first-episode of PID who receive prompt appropriate antimicrobial therapy
  - » The risk of impaired fertility increases significantly with each subsequent episode of PID (approximately doubling with each new presentation)
  - » The risk of impaired fertility is increased in clinically more severe PID and chronic pelvic pain of varying severity affecting around 30% of women following PID
  - » PID increases the relative risk of a subsequent pregnancy being an ectopic, but the absolute risk of ectopic pregnancy remains low at around 1%

Admission for parenteral therapy, observation, further investigation and/or possible surgical intervention should be considered in the following situations:

- Diagnostic uncertainty
- Lack of response to oral therapy
- Clinically severe disease
- Presence of a tubo-ovarian abscess
- Intolerance to oral therapy
- Pregnancy

Recommended regimens[9]

- Broad spectrum antibiotic therapy is required to cover *N. gonorrhoeae, C. trachomatis* and anaerobic infection
- It is also desirable to include microbiological cover for other possible pathogens (*M. genitalium, streptococci, staphylococci, E. coli, H. influenzae*)

GENERAL ADVICE

- Rest is advised for those with severe disease (Evidence level IV, C)
- If there is a possibility that the patient could be pregnant, a pregnancy test should be performed (Evidence level IV, C)
- Appropriate analgesia should be provided (Evidence level IV, C)
- Intravenous therapy is recommended for patients with more severe clinical disease
- Oral or genital intercourse should be avoided until treatment completion to avoid reinfection

Admission for parenteral therapy, observation, further investigation and/or possible surgical intervention should be considered in the following situations:

- Diagnostic uncertainty
- Lack of response to oral therapy
- Clinically severe disease
- Presence of a tubo-ovarian abscess
- Intolerance to oral therapy
- Pregnancy

RECOMMENDED REGIMENS

Choice of treatment regimen should be influenced by the following:

- Mild and moderate cases should be treated as outpatients with oral therapy (Evidence level Ib, A)
- Intravenous therapy, when given, should be continued until 24 h after clinical improvement and then switched to oral therapy (Evidence level IV, C)
- Dosage recommendations may need to be adjusted depending on local licensing regulations and the availability of drug formulations, e.g. metronidazole may be dosed at 400 or 500 mg
- The optimal duration of treatment is not known but most clinical trials report a response to 10–14 days of therapy

Outpatient regimens[9]	Inpatient regimens[9]
First line therapy • IM ceftriaxone 500 mg single dose followed by • Oral doxycycline 100 mg twice daily plus metronidazole 500 mg twice daily for 14 days (Evidence level Ia, A) **Second line therapy** • Oral ofloxacin 400 mg twice daily plus oral metronidazole 500 mg twice daily for 14 days (ofloxacin may be replaced by levofloxacin 500 mg once daily) (Evidence level Ib, A) • Oral moxifloxacin 400 mg once daily for 14 days (Evidence level Ia, A)	• IV/IM ceftriaxone 1 g once daily + IV doxycycline 100 mg twice daily (oral doxycycline may be used if tolerated) followed by » Oral doxycycline 100 mg twice daily + oral metronidazole 500 mg twice daily to complete 14 days (Evidence level Ia, A) • IV clindamycin 900 mg three times daily plus IM/IV gentamicin (3–6 mg/kg as a single daily dose with renal monitoring) followed by » Either (oral clindamycin 450 mg four times daily to complete 14 days) or (oral doxycycline 100mg twice daily plus oral metronidazole 500 mg twice daily to complete 14 days) (Evidence level Ia, A)
Alternative regimens[9] The evidence for alternative regimens is less robust than the regimens above. • IV ofloxacin 400 mg twice daily plus IV metronidazole 500 mg three times daily for 14 days (Evidence level Ib, A) • IM ceftriaxone 500 mg single dose plus oral azithromycin 1 g single dose followed by a second dose of oral azithromycin 1 g after one week (Evidence level Ib, A)	
Where the above regimens are not available antibiotic therapy should be given for 14 days and attempt to cover: • *N. gonorrhoeae*, e.g. cephalosporins • *C. trachomatis*, e.g. tetracyclines, macrolides • Anaerobic bacteria, e.g. metronidazole	

CDC's treatment recommendations[9,16]

Treatments are generally targeted toward the causative pathogens. Anaerobic coverage is indicated if tubo-ovarian abscess is present.

Oral treatment regimens for pelvic inflammatory disease
Ceftriaxone 250 mg IM in a single dose PLUS Doxycycline 100 mg orally twice a day for 14 days WITH or WITHOUT Metronidazole 500 mg orally twice a day for 14 days
OR
Cefoxitin 2 g IM in a single dose and Probenecid, 1 g orally administered concurrently in a single dose PLUS Doxycycline 100 mg orally twice a day for 14 days WITH or WITHOUT Metronidazole 500 mg orally twice a day for 14 days
OR
Other parenteral third-generation cephalosporin (e.g., ceftizoxime or cefotaxime) PLUS Doxycycline 100 mg orally twice a day for 14 days WITH or WITHOUT Metronidazole 500 mg orally twice a day for 14 days
Adapted from Workowski KA, Berman S; Centers for Disease Control and Prevention (CDC). Sexually transmitted diseases treatment guidelines, 2010 [published correction appears in MMWR Morb Mortal Wkly Rep. 2011;60(1):18]. MMWR Recomm Rep. 2010;59(RR-12):66.

Parenteral treatment regimens for pelvic inflammatory disease
Regimen A
Cefotetan 2 g IV every 12 hours OR Cefoxitin 2 g IV every six hours PLUS Doxycycline 100 mg orally or IV every 12 hours
Regimen B
Clindamycin 900 mg IV every eight hours PLUS Gentamicin: Loading dose IV or IM (2 mg per kg), followed by a maintenance dose (1.5 mg per kg) every eight hours; a single daily dose (3 to 5 mg per kg) can be substituted
Alternative regimen
Ampicillin/sulbactam 3 g IV every six hours PLUS Doxycycline 100 mg orally or IV every 12 hours

β-lactam/β-lactamase inhibitor combinations

- Although, β-Lactam/β-lactamase inhibitor combinations generally, do not constitute reliable therapy against extended-spectrum β-lactamase producers, their substitution in place of cephalosporins appears to reduce emergence of the latter pathogens
- Their use may also curtail the emergence of other resistant pathogens such as *Clostridium difficile* and vancomycin-resistant enterococci
- Sulbactam is combined with either ampicillin or cefoperazone

Evidence for efficacy of Amoxycillin + Clavulanic acid in PID

In women with PID with 3 days of treatment, more patients in the amoxycillin/clavulanic acid group showed diminution of symptoms of pain and discharge ($p \leq 0.05$) compared to the triple combination group (oral ampicillin, intramuscular gentamicin and metronidazole tablets/pessaries).

Complete cure or satisfactory improvement was recorded at the end of treatment.

BETA-LACTAM

- Oral amoxycillin/clavulanic acid reduces symptoms and is a convenient alternative to the triple drug regimen for the treatment of PID

Patients admitted with severe PID and/or tubo–ovarian abscess are recommended to be discharged on a broad-spectrum oral antimicrobial regimen to complete a 14-day course. Owing to excellent polymicrobial coverage, the oral regimens recommended for discharge include amoxicillin/clavulanate (875 mg twice daily) or the combination of trimethoprim/sulfamethoxazole (160/800 mg twice daily) and metronidazole (500 mg twice daily).[20,21]

The most frequently recommended treatment to eradicate these organisms are:[22]

1. Amoxicillin and Clavulanic acid 2–3 g/day + doxycycline (200 mg/day)
2. Amoxicillin and Clavulanic acid 2–3 g/ day + ofloxacin (400 mg/day)

When PID is associated with risk factors such as IUD, hysterosalpingography, D and C, post-partum and post abortion, the bacteria usually isolated is Enterobacteriaceae, anaerobes, Haemophilus and streptococcus. The initial recommended treatment is therefore amoxicillin with clavulanic acid 2–3 g/day+ofloxacin 200 mg i.v. twice every 24 hours.

Beigi, *et al* has shown that Amoxicillin/Clavulanic acid plus doxycycline has acceptable efficacy.[23]

Amoxicillin/clavulanate in combination with doxycycline was associated with excellent clinical cure rates of 95% in the treatment of PID. The microbiologic cure rates were also observed to be excellent (>95%) for *N. gonorrhoeae*, *C. trachomatis, M. hominis* and anaerobes.[24]

Moreover, Amoxicillin/Clavulanic acid combination was considered as a satisfactory alternative to the penicillin-aminoside metronidazole combination in the treatment of upper genital infections in women.[25]

Cefoperazone + Sulbactam combination for PID

- Sulbactam–cefoperazone has been used in several nosocomial infections, including mild-to-moderate and severe nosocomial pneumonia, intra-abdominal infections, including biliary sepsis, intra-abdominal abscesses, pelvic inflammatory disease, gynecological infections, sepsis, infections in burn patients and infections in febrile neutropenic patients[26,27]

CEFOPERAZONE + SULBACTAM

- The addition of sulbactam to either ampicillin or cefoperazone does not compromise the safety of these β-lactam antibiotics[26,27]
- Sulbactam/cefoperazone is effective and safe for the treatment of moderate-to-severe bacterial infections caused mainly by β-lactamase—producing organisms[26,27]

Evidences favouring Cefoperazone + Sulbactam combination

Cefoperazone is safe and effective for the treatment of common obstetric and gynecologic infections.[28]

- Symptomatic cures were achieved in 91% of patients and 96% of isolated pathogens were eradicated during the therapy
- Adverse drug-related reactions occurred in only 4% of the patients (Table 2)

Intravenous administration of sulbactam/ cefoperazone to patients with various kinds of gynecological infectious diseases demonstrated a clinical and bacteriological efficiency rate of 100% and 75%, respectively. No remarkable side effects were observed, except for 1 buccal exanthema and 1 genital candidiasis detected during the course of drug administration.[29]

Sulbactam/cefoperazone combination demonstrated an effectiveness rate of 91.7%.[30]

Combined sulbactam/cefoperazone covers a much wider range than cefoperazone only.[31]

Reports have revealed that combined sulbactam/cefoperazone administered at a daily dosage of 2 g in two divided doses is considered to be a highly effective antibiotic with clinical efficacy in obstetric and gynecological infections.[32]

The efficacy rate was 100% for all conditions due to single or mixed infection, due to aerobic Gram-negative, -positive or anaerobic bacteria. In a study, patients with Obstetric and Gynecologic Infections (post cesarean section endometritis, post-hysterectomy cuff, pelvic cellulitis, or both, acute salpingitis and endometritis after vaginal delivery or incomplete abortion) demonstrated good clinical response (92%) to cefoperazone. Cefoperazone appeared to be as effective as clindamycin-gentamicin and was observed to be safe and efficacious in women with polymicrobial pelvic infections.[33, 34]

In the treatment of 31 cases of gynecological infections, the clinical efficacy of sulbactam/cefoperazone was assessed as excellent in 9 cases and effective in 22 cases.[35]

- β-Lactam/β-lactamase inhibitor combinations are particularly useful against mixed infections
- Owing to excellent polymicrobial coverage, the oral regimen recommended at discharge is amoxicillin/clavulanate (875 mg twice daily) for those with severe PID
- Amoxicillin and clavulanic acid 2–3 g/day + doxycycline (200 mg/day) or amoxicillin and clavulanic acid 2–3 g/ day + ofloxacin (400 mg/day) are the most frequently recommended treatment to eradicate *N. gonorrhoeae and C. trachomatis*
- The initial recommended treatment is amoxicillin with clavulanic acid 2–3 g/day + ofloxacin 200 mg IV twice every 24 hours for PID associated with risk factors such as IUD, hysterosalpingography D and C, postpartum and post abortion
- Amoxicillin-clavulanic acid combination is considered as a satisfactory alternative to the penicillin-aminoside metronidazole combination in the treatment of upper genital infections in women
- Cefoperazone is safe and effective for the treatment of common obstetric and gynaecologic infections
- Sulbactam/cefoperazone combination demonstrated high efficacy rate in infections caused by β-lactamase producing organisms
- The efficacy rate of sulbactam/cefoperazone was reported to be 100% for all infections due to single or mixed infection, due to aerobic Gram-negative, -positive or anaerobic bacteria

Treatment in pregnancy[31]

A pregnancy test should be performed in all women suspected of having PID to help exclude an ectopic pregnancy.

- In an on-going intrauterine pregnancy, PID is extremely rare, except in the case of septic abortion. Cervicitis may occur, however and is associated with increased maternal and fetal morbidity including pre-term delivery
- Treatment regimens will be dependent upon the organisms isolated. Drugs known to be toxic in pregnancy should be avoided e.g.- Tetracyclines
- Erythromycin and amoxycillin are not known to be harmful in pregnancy
- A combination of cefotaxime, azithromycin and metronidazole for 14 days may be used. The risks associated with metronidazole are uncertain but no confirmed associations with adverse outcomes have been reported

Table 2. Results of cefoperazone therapy in patients with obstetric and gynecologic infections							
		No. of patients with clinical response			No. of patients with bacteriologic response		
Type of infection	No. of patient studied	Cure	Improvement	Failure	Satisfactory	Unsatisfactory	Undetermined
Uterine	65	59	3	3	62	–	3
PID	21	59	1	–	18	–	3
Postoperative	14	11	2	1	13	1	–
Miscellaneous*	7	7	–	–	7	–	–
Totals	107	97	6	4	100	1	6
PID: pelvic inflammatory disease; *Chorioamnionitis, septicemia and tubo-ovarian abscess							

Treatment in a woman with an intrauterine contraceptive device[36]

- An intrauterine contraceptive device (IUCD) may be left *in situ* in women with clinically mild PID but should be removed in cases of severe disease and, especially, if symptoms have not resolved within 72 hours

Treatment in a woman with HIV[36]

- Women with PID who are also infected with HIV should be treated with the same antibiotic regimens as women who are HIV negative
- Potential interactions between antibiotics and anti-retroviral medication need to be considered on an individual basis. Low CD4 count is an indication for hospitalization

Surgery[36]

Surgical treatment should be considered in severe cases or where there is clear evidence of a pelvic abscess.

- Laparotomy/laparoscopy may help early resolution of the disease by division of adhesions and drainage of pelvic abscesses
- Ultrasound-guided aspiration of pelvic fluid collections is less invasive and may be equally effective
- It is also possible to perform adhesiolysis in cases of peri-hepatitis due to chlamydia although there is no evidence as to whether this is superior to antibiotic therapy alone

Follow-up of patients[31]

- In the outpatient setting, review at 72 hours is recommended particularly for those with a moderate or severe clinical presentation
- Failure to improve suggests the need for further investigations, parenteral therapy and / or surgical intervention
- Further review four weeks after therapy may be useful to ensure:
  - » Adequate clinical response to treatment
  - » Compliance with oral antibiotics
  - » Screening and treatment of sexual contacts
  - » Awareness of the significance of PID and its sequelae
- If PCR is used as a test of cure, it should not be repeated before 3 weeks as persistent gonococcal and chlamydial DNA may lead to false positive results
- If microscopy and culture are used as a test of cure, specimens should be taken at least 72 hrs after completion of treatment
- A full screen for all STDs including Hepatitis B & HIV should be offered for persistent infections

Prevention[11,37]

Primary prevention

- Patient education
- Opportunistic screening
- Secondary prevention
- Adherence of compliance to treatment
- Follow up of treatment
- Tracing of partner and partner treatment
- Completion of entire antibiotic course

Prevention of PID falls broadly into the following two categories:

1) Prevention of the first PID episode

- Women who have had one episode of PID need to prevent STI infection given the relationship between recurrent STIs, such as *C. trachomatis* and infertility

- The CDC recommends annual chlamydia and gonorrhea screening in all sexually active women <25 years of age and in sexually active women ≥25 years of age at increased risk (who have a new sex partner, those who have more than one sex partner, those whose sex partner has concurrent partners, or those with a sex partner who has an STI)
- The CDC also recommends considering regular screening for *Trichomonas vaginalis* in women receiving care in high STI prevalence settings and women engaged in high risk behaviors (such as sex with multiple partners, exchanging sex for money or drugs, use of illicit drugs and prior history of an STI)

- Women who test positive for an STI should be rescreened for STIs 3 months after STI treatment, particularly if they reside in STI-prevalent communities and/or new behavioral risks are identified at the follow-up visit

2) Prevention of recurrent disease

- Patients with recurrent PID are at risk for greater reproductive sequelae than those who avoid subsequent disease

- Reports have shown that infertility roughly doubles with each subsequent episode of PID and that women with recurrent PID were almost two times more likely to report infertility and over four times more likely to report CPP

Notification and treatment of male sexual partners[14]

Men who have had sexual contact with a woman diagnosed with PID during the 60 days prior to her onset of symptoms (or most recent sexual partner if her last sexual intercourse was >60 days) should be evaluated and treated with regimens that are effective against chlamydia and gonorrhea.

- Women should be advised to avoid sexual intercourse until they and their partners have completed the treatment course
- If adequate screening for gonorrhea and chlamydia in the sexual partner(s) is not possible, empiric therapy for gonorrhea and chlamydia should be prescribed

Grading of recommendations

A (Evidence levels Ia, Ib) – Requires at least one randomized controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation.

B (Evidence levels IIa, IIb, III) – Requires availability of well-conducted clinical studies but no randomized clinical trials on the topic of recommendation.

C (Evidence IV) – Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities. Indicates absence of directly-applicable studies of good quality.

SUMMARY

- Pelvic inflammatory disease (PID) refers to acute infection of the upper genital tract structures in women, involving any or all of the uterus, fallopian tubes and ovaries and may involve the neighbouring pelvic organs
- *Neisseria gonorrhea* and *Chlamydia trachomatis* are identified as the causative agents. *Gardnerella vaginalis*, anaerobes and other organisms commonly found in the vagina may also be implicated. *Mycoplasma genitalium* has been associated with upper genital tract infections in women and is a very likely cause of PID

Risk factors for PID

- Instrumentation of the uterus/ interruption of the cervical barrier
- Young < 25 years
- Menstruating women
- Multiple sexual partners
- Recent new partners
- No h/o of contraception use
- Living in an area of high prevalence of PID
- Tampons use (forgotten)
- Poor menstrual hygiene
- Bacterial vaginosis
- Abortions, puerperal sepsis and IUD insertions in Indian scenario

Complications of PID

- Tubo-ovarian abscesses and pelvic peritonitis– indication for hospital admission for parenteral antimicrobial therapy, with appropriate anaerobic coverage
- Fitz-Hugh-Curtis Syndrome
- Maternal and fetal morbidity in pregnancy
- HIV women may have severe symptoms
- Consider removal of *in situ* IUD for improving symptoms and signs
- Septicaemia

Differential diagnosis for lower abdominal pain in young women include

- Ectopic pregnancy
- Acute appendicitis
- Endometriosis
- Irritable bowel syndrome (and less commonly, other gastrointestinal disorders)
- Complications of an ovarian cyst such as rupture or torsion
- Urinary tract infection
- Functional pain (pain of unknown physical origin)

PID in adolescents

- The American Academy of Pediatrics (AAP) recommends at least one preventive health visit per year
- The AAP, American Medical Association and Society for Adolescent Medicine recommend that physicians discuss sexuality with youth as part of routine healthcare

SUMMARY

- According to the Society for Adolescent Medicine, "Confidentiality protection is an essential component of health care for adolescents because it is consistent with their development of maturity and autonomy and without it, some adolescents will forgo care"
- The AAP has endorsed a position paper by the Society for Adolescent Health and Medicine supporting the use of EPT as a treatment option for heterosexual sex partners of adolescents with gonorrhea and chlamydia when in the other partner treatment methods are impractical or unsuccessful

General advice on management

- Rest is advised for those with severe disease (Evidence level IV, C)
- If there is a possibility that the patient could be pregnant, a pregnancy test should be performed (Evidence level IV, C)
- Appropriate analgesia should be provided (Evidence level IV, C)
- Intravenous therapy is recommended for patients with more severe clinical disease
- Oral or genital intercourse should be avoided until treatment completion to avoid reinfection

Recommended regimen

- Mild and moderate cases should be treated as outpatients with oral therapy (Evidence level Ib, A)
- Intravenous therapy, when given, should be continued until 24 h after clinical improvement and then switched to oral (Evidence level IV, C)
- Dosage recommendations may need to be adjusted depending on local licensing regulations and the availability of drug formulations
- The optimal duration of treatment is not known but most clinical trials report a response to 10–14 days of therapy

For treatment of PID in Indian population NACO has recommended Yellow Kit – KIT 6

1. Tab Cefixime 400 X 1 tab
2. Tab Metronidazole 400 mg X (1 BD for 14 days)
3. Tab Doxycycline 100 mg (1 BD for 14 days)

β-lactam/β-lactamase inhibitor combinations for PID

- β-Lactam/β-lactamase inhibitor combinations are particularly useful against mixed infections
- β-Lactamase inhibitors when combined with certain β-lactam antibiotics, augment the potency of these against β-lactamase-producing bacteria

Amoxycillin + clavulanic acid in PID

- Owing to excellent polymicrobial coverage, the oral regimen recommended at discharge is amoxicillin/clavulanate (875 mg twice daily) for those with severe PID
- Amoxicillin and clavulanic acid 2–3 g/day +doxycycline (200 mg/day) or amoxicillin and clavulanic acid 2–3 g/ day+ofloxacin

SUMMARY

(400 mg/day) are the most frequently recommended treatment to eradicate *N. gonorrhoeae* and *C. trachomatis*

- The initial recommended treatment is amoxicillin with clavulanic acid 2–3 g/day +ofloxacin 200 mg i.v. twice every 24 hours for PID associated with risk factors such as IUD, hysterosalpingography, D and C, postpartum, post abortion

Cefoperazone + sulbactam combination

- The addition of sulbactam to either ampicillin or cefoperazone does not compromise the safety of these β-lactam antibiotics
- Sulbactam/cefoperazone is effective and safe for the treatment of moderate-to-severe bacterial infections caused mainly by β-lactamase—producing organisms
- The efficacy rate of sulbactam/cefoperazone was reported to be 100% for all infections due to single or mixed infection, due to aerobic Gram-negative, -positive or anaerobic bacteria

References

1. Wiesenfeld HC. Pelvic inflammatory disease: Treatment in adults and adolescents. UpToDate. Uptodate.com. 2019 [cited 6 August 2019]. Available from: https://www.uptodate.com/contents/pelvic-inflammatory-disease-treatment-in-adults-and-adolescents.
2. Ross J. Pelvic inflammatory disease. BMJ Clin Evid. 2013; 2013: 1606.
3. Ross J, Cole M, Evans C et al. United Kingdom National Guideline for the Management of Pelvic Inflammatory Disease (2019 Interim Update). PID Guideline
4. Vanamala VG et al. Pelvic inflammatory disease and the risk factors. Int J Reprod Contracept Obstet Gynecol. 2018; 7(9):3572–75
5. Grace GA, Devaleenal DB, Natrajan M. Genital tuberculosis in females. Indian J Med Res. 2017; 145(4):425–36.
6. Dayal S, Singh A, Chaturvedi V, et al. Pattern of pelvic inflammatory disease in women who attended the tertiary care hospital among the rural population of North India. Muller J Med Sci Res 2016;7:100–4.
7. Smith J, Daley FC, Shakur A et al. Causes and complications of female pelvic inflammatory disease: a multimodal imaging review. ECR 2018 / C-1945 doi: 10.1594/ecr2018/C-1945
8. Kristi A Tough DeSapri, Pelvic Inflammatory Disease. Medscape. 2019. Available on: https://emedicine.medscape.com/article/256448-overview
9. Ross J, Guaschino S, Cusini M, et al. 2017 European guideline for the management of pelvic inflammatory disease. Int J STD AIDS. 2018; 29(2):108–114.
10. Gopchade CA. Pelvic Inflammatory Disease in Women of Child Bearing age Group: A Prospective Study. Annals of International Medical and Dental Research. 2018; 4 (2): DOI: 10.21276/aimdr.2018.4.2.OG7
11. Das BB, Ronda J, Trent M et al. Pelvic inflammatory disease: Improving awareness, prevention and treatment. Infect Drug Resist. 2016; 9: 191–7.
12. Diagnostic Imaging Pathways - Pelvic Inflammatory Disease (Suspected). 2014. Available on: http://www.imagingpathways.health.wa.gov.au/index.php/imaging-pathways/obstetric-gynaecological/pelvic-inflammatory-disease?tmpl=component&format=pdf Assessed on: 9th Aug 2019
13. Hemsel DL, Ledger WJ, Martens M, et al. Concerns regarding the Centers for Disease Control's published guidelines for pelvic inflammatory disease. Clin Infect Dis. 2001; 32(1):103–7.
14. BMJ Best Practice. Pelvic inflammatory disease. 2018
15. Schneider K et al. Adolescents and Young Adults: Targeting the Unique Challenges of This High Risk Group. DOI: http://dx.doi.org/10.5772/intechopen.86251
16. Workowski KA, Berman S; Centers for Disease Control and Prevention (CDC).Sexually transmitted diseases treatment guidelines, 2010. MMWR Recomm Rep. 2010; 59(RR-12): 1-110.

17. NACO. STI/RTI syndromic case management. Available on: http://naco.gov.in/sites/default/files/Syndromic%20Poster_REDUCED.pdf
18. Lee N, Yuen KY, Kumana CR. Clinical role of beta-lactam/beta-lactamase inhibitor combinations. Drugs. 2003;63(14):1511–24.
19. Uri FI, Sartawi SA, Dajani YF, et al. Amoxycillin/clavulanic acid (augmentin) compared with triple drug therapy for pelvic inflammatory disease. Int J Gynaecol Obstet. 1992; 38(1):41–3.
20. Jaiyeoba O, Lazenby G, Soper DE. Recommendations and rationale for the treatment of pelvic inflammatory disease. Expert Rev Anti Infect Ther. 2011; 9(1):61–70.
21. Soper DE. Pelvic inflammatory disease. Obstet Gynecol. 2010; 116(2 Pt 1):419–28.
22. Quentin R, Lansac J. Pelvic inflammatory disease: Medical treatment. Eur J Obstet Gynecol Reprod Biol. 2000; 92(2):189–92.
23. Beigi RH, Wiesenfeld HC. Pelvic inflammatory disease: New diagnostic criteria and treatment. Obstet Gynecol Clin North Am. 2003; 30(4):777–93.
24. Sweet RL. Treatment strategies for pelvic inflammatory disease. Expert Opin Pharmacother. 2009; 10(5):823–37.
25. Buisson P, Mulard C, Baudet J, et al. [Treatment of upper genital infections in women. Multicenter study of the comparative efficacy and tolerance of an amoxicillin-clavulanic acid combination and of a triple antibiotic combination]. [Article in French] Rev Fr Gynecol Obstet. 1989; 84(10):699–703.
26. Akova M. Sulbactam-containing beta-lactamase inhibitor combinations. Clin Microbiol Infect. 2008; 14 Suppl 1:185–8.
27. Li JT, Lu Y, Hou J, et al. Sulbactam/cefoperazone versus cefotaxime for the treatment of moderate-to-severe bacterial infections: Results of a randomized, controlled clinical trial. Clin Infect Dis. 1997; 24(3):498–505.
28. Strausbaugh LJ, Llorens AS. Cefoperazone therapy for obstetric and gynecologic infections. Rev Infect Dis. 1983; 5 Suppl 1:S154–60.
29. Saito Y, Tachizaki T, Maki M. [Clinical and bacteriological efficiency of sulbactam/cefoperazone in gynecological infectious diseases]. [Article in Japanese] Jpn J Antibiot. 1984; 37(10):1919–24.
30. Chimura T, Inoue K, Morisaki N. [Clinical evaluation of sulbactam/cefoperazone for infections in the field of obstetrics and gynecology]. [Article in Japanese]. Jpn J Antibiot. 1984; 37(10):1928–33.
31. Domon H, Kodama M, Sato H, et al. [Clinical evaluation of sulbactam/cefoperazone in obstetric and gynecological infection]. [Article in Japanese] Jpn J Antibiot. 1984; 37(10):1925–7.
32. Kohara T, Matsui Y, Noda M, et al. [Experience with sulbactam/cefoperazone in the field of obstetrics and gynecology]. [Article in Japanese] Jpn J Antibiot. 1984; 37(10):1934–8.
33. Kubota K. [Fundamental and clinical studies of sulbactam/cefoperazone in obstetrics and gynecology]. [Article in Japanese] Jpn J Antibiot. 1984; 37(11):2234–42.
34. Gilstrap LC 3rd, St Clair PJ, Gibbs RS, et al. Cefoperazone versus clindamycin plus gentamicin for obstetric and gynecologic infections. Antimicrob Agents Chemother. 1986; 30(5):808-9.
35. Obata I, Ryu F, Imagawa N, et al. [Clinical studies on sulbactam/cefoperazone in the field of obstetrics and gynecology]. [Article in Japanese]. Jpn J Antibiot. 1984; 37(12):2478–94.
36. ICOG FOGSI Recommendations for Good Clinical Practice. Management of Acute Pelvic Inflammatory Disease. 2009
37. Pelvic Inflammatory Disease: Guidelines for Prevention and Management. 1991 // 40(RR-5);1-25 Available on: https://www.cdc.gov/mmwr/preview/mmwrhtml/00031002.htm

AUGPEN®

Amoxycillin + Clavulanic Acid

Tablets / I.V.

The *Platinum Standard* Co-amoxyclav

"Ensures Entrapment of Amoxyclav within SYLOID & prevents degradation by moisture"

High Clinical Cure Rates:

- 100% in PID
- 85% in UTI

The Most Dependable 1st Line in PID

Zostum®

Cefoperazone + Sulbactam (1gm+500mg / 2gm+1gm)

1.5g
3g

Designed for **Safety & Surety**

More than 80% inhibition of bacteria involved in PID

E.coli, Klebsiella, Proteus, Neisseria, Bacteroides, Staphylococcus, Peptococcus, and Peptostreptococcus

Symptomatic cure in 91% of patients & 96% bacterial eradication

Zuventus