Pelvic inflammatory disease

Jonathan D C Ross

Abstract

Pelvic inflammatory disease (PID) is a common cause of morbidity in young women and is usually secondary to a sexually transmitted infection. The diagnosis is based on clinical history and examination, but is inaccurate and leads to overdiagnosis of the condition. Despite this, empirical antibiotic treatment based on a clinical assessment is still recommended because failure to treat PID can result in infertility, ectopic pregnancy or chronic pelvic pain in up to 40% of women. It is important to exclude an ectopic pregnancy before starting treatment for PID. Screening and treatment of male partners is important to prevent re-infection, which is associated with an increased risk of long-term sequelae.

Keywords Chlamydia; chronic pelvic pain; ectopic pregnancy; gonorrhoea; infertility; pelvic infection; pelvic inflammatory disease; salpingitis

Pelvic inflammatory disease (PID) is a common condition affecting young women; one study reported that 1 in 45 consultations by this group with their GP were related to pelvic inflammatory disease. Pelvic infection has unpleasant, short-term, physical and psychological affects, and also serious long-term sequelae in the form of chronic pelvic pain, increased risk of ectopic pregnancy and tubal factor infertility. The public health importance of many sexually transmitted infections (STIs), including gonorrhoea and chlamydia, includes their ability to cause PID and its complications, which are costly to treat and may justify primary prevention through screening for predisposing infections.

Epidemiology

Accurately measuring how many women have PID, their distribution and the factors associated with the disease is hampered by our inability to make an accurate clinical diagnosis and the multiple clinical settings in which they may present. In many developed countries, there has been a decline in the number of inpatient and outpatient diagnoses, although in the UK outpatient rates of infection continue to rise (Figure 1). Pelvic infection rates may be reduced in the future as a result of increased testing for chlamydia and gonorrhoea, increased public awareness of the risks of these STIs and the early use of effective antimicrobial therapy.

The main risks associated with PID are similar to those for any other sexually acquired infection — young age, multiple concurrent sexual partners and lack of barrier contraception use. Women taking the oral contraceptive pill appear to be at lower risk of developing severe PID, although this effect may be limited to those infected with chlamydia. Some, although not all, studies suggest that a delay of more than a few days between the onset of symptoms and receiving antimicrobial therapy is associated with a subsequent increased risk of impaired fertility.

Vaginal douching has been previously linked with pelvic infection. In particular, women presenting with PID are more likely to give a history of douching compared to those without PID. However, two studies that prospectively followed women with a history of douching suggested that they are at no increased risk of developing PID and it is likely that the symptoms of PID, such as offensive vaginal discharge, may lead to increased douching rather than vice versa.

The microbial causes and associated clinical presentation of PID vary in different geographical regions, reflecting differences in the local prevalence of STIs.

Aetiology

PID occurs when pathogens spread from the lower genital tract through the cervix to produce an endometritis, before spreading to the fallopian tubes to cause salpingitis (Figure 2). An exception to this is tuberculosis, which may often infect the pelvis via the lymphatic system or blood.

Chlamydia trachomatis and *Neisseria gonorrhoeae* are the two pathogens most closely linked with pelvic infection and inflammation. The exact proportion of cases caused by these pathogens varies according to geographical location, but in developed countries gonorrhoea causes around 2–5% of infections, and chlamydia 15–40%. The mechanism by which gonorrhoea and chlamydia cause damage to the fallopian tubes differs. In gonococcal PID there is direct infection and destruction of the epithelial lining of the tube with an acute inflammatory response usually leading to acute symptoms. Women with chlamydial disease have a more indolent clinical picture where much of the tubal damage occurs secondary to the immune response to infection, possibly via cross-reactivity between human and chlamydia heat shock protein 60.

The microbial aetiology of the cases not caused by gonorrhoea or chlamydia remains unclear. Although a number of pathogens may have a role, including *Mycoplasma genitalium*, anaerobes, *Trichomonas vaginalis*, *Gardnerella vaginalis*, *Mobiluncus* and herpes simplex virus, some women carry the same organisms without going on to develop PID (Table 1).[1,2] Of these, the evidence is strongest for *M. genitalium* and anaerobes (such as *Prevotella*).

Women with pelvic infection often also have bacterial vaginosis. In bacterial vaginosis there is an imbalance in the vaginal flora with loss of lactobacilli and an increase in other bacterial species, including *Gardnerella*, *Mobiluncus* and anaerobes, associated with an offensive vaginal discharge. Women presenting initially with bacterial vaginosis do not appear to be at an increased risk of developing PID, with two exceptions. First, those who have large quantities of Gram-negative anaerobes in the vagina have a slightly increased risk of developing upper genital tract infection; and second, those with bacterial vaginosis who subsequently acquire gonorrhoea or chlamydia are also at increased risk of subsequent salpingitis.[3]

Clinical presentation (Table 2)

Asymptomatic infection of the fallopian tubes is common and can lead to future tubal factor infertility in the absence of a

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Pelvic inflammatory disease diagnoses in sexual health clinics in England

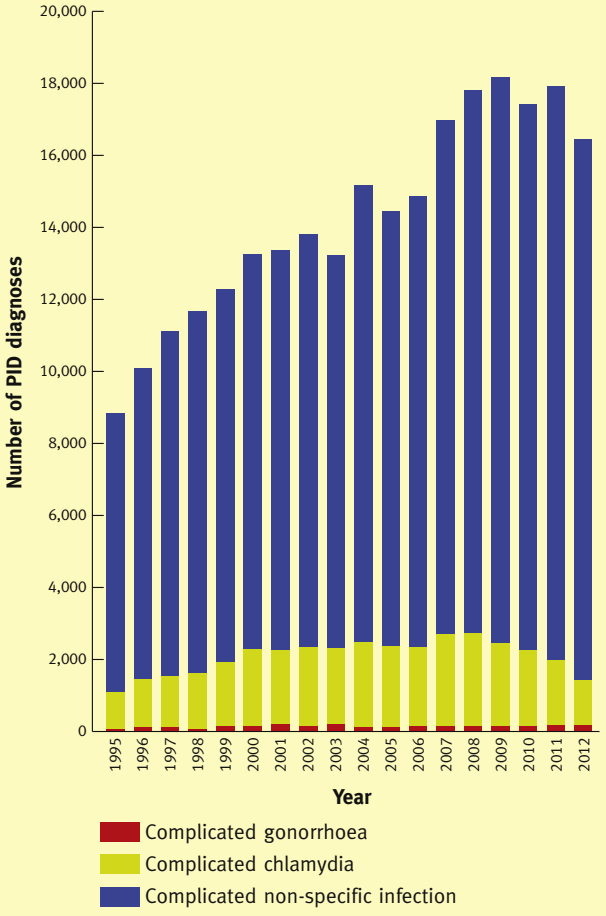
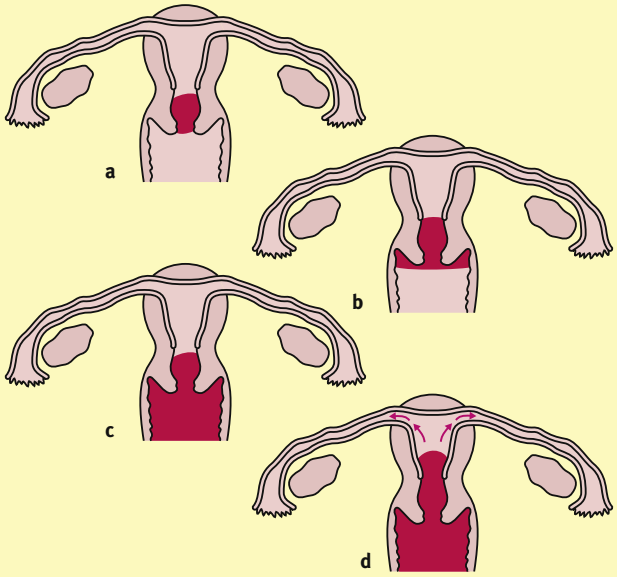


Figure 1

Pathogenesis of pelvic inflammatory disease

PID begins with cervicitis (**a**). This is followed by a change in the cervicovaginal micro-environment (**b**) that leads to bacterial vaginitis (**c**). Finally, the original cervical pathogens, the flora causing bacterial vaginitis or both ascend into the upper genital tract (**d**). The red areas indicate the affected portions of the genital tract.



McCormack W M. *N Engl J Med* 1994; **330:** 115–19.

Figure 2

history of clinical PID, particularly following chlamydia infection. When symptoms are present, the patient often complains of bilateral, recent-onset lower abdominal pain associated with dyspareunia, vaginal discharge and postcoital/intermenstrual bleeding. Those with more severe PID also manifest systemic features, such as fever, malaise, nausea and vomiting. Around 5% of women develop an associated perihepatitis producing right upper quadrant abdominal pain and tenderness (Fitzhugh–Curtis syndrome).

Abdominal and pelvic examination should be performed. Abdominal and adnexal tenderness is often present with pain noted on movement of the cervix in severe disease (cervical excitation). A fever is uncommon in mild-to-moderate PID, but occurs more frequently in severe disease.

Further investigations may help in making a diagnosis. Erythrocyte sedimentation rate (ESR) and serum C-reactive protein (CRP) are useful markers of severity of disease, but have poor specificity. All patients should be screened for STIs, including gonorrhoea and chlamydia, using nucleic acid amplification tests where possible. A pregnancy test should be performed to help exclude an ectopic pregnancy. Ultrasound imaging is useful to detect a tubo-ovarian abscess, hydrosalpinx or pyosalpinx, but is operator dependent and lacks sensitivity for PID unless a pelvic collection is present. Computerized tomography (CT) and magnetic resonance imaging (MRI) of the pelvis have not yet been fully validated and their role in the diagnosis of PID remains uncertain. A transcervical endometrial biopsy can provide histological evidence of endometritis that supports the diagnosis of PID, but is not used routinely because of difficulties in ensuring consistent interpretation of the biopsy and the delay while waiting for biopsy processing and reporting.

Microbial aetiology of pelvic inflammatory disease

Pathogen	Associated features
Chlamydia trachomatis	Indolent, asymptomatic infection
Neisseria gonorrhoeae	Severe, acute-onset infection
Mycoplasma genitalium	Probable cause of pelvic inflammatory disease
Anaerobes	Often detected in tubo-ovarian abscess
Trichomonas vaginalis	Role as primary pathogen uncertain
Gardnerella vaginalis	Role as primary pathogen uncertain
Mobiluncus	Role as primary pathogen uncertain
Herpes simplex virus	Role as primary pathogen uncertain

Table 1

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Clinical features of pelvic inflammatory disease

Symptoms	Features
Lower abdominal pain	Usually bilateral and of recent onset
Vaginal discharge	Secondary to cervicitis, endometritis or bacterial vaginosis
Vaginal bleeding	Intermenstrual or postcoital
Dyspareunia	Deep dyspareunia associated with adnexal inflammation
Nausea/vomiting	Associated with severe pelvic inflammatory disease
Signs	
Fever	Not common in mild/moderate pelvic inflammatory disease
Adnexal tenderness	Common but non-specific
Adnexal mass	Possible hydrosalpinx, pyosalpinx or tubo-ovarian abscess

Table 2

Common alternative causes of lower abdominal pain in a young woman include appendicitis, urinary tract infection and irritable bowel syndrome. Ectopic pregnancy is uncommon but important to exclude. Ovarian cysts are usually asymptomatic unless they rupture or undergo torsion. Endometriosis usually leads to a more chronic history, possibly with intermittent exacerbations of pain.

Laparoscopy allows direct visualization of the fallopian tubes and has previously been considered to be the gold standard test in making a diagnosis (Figure 3).[4] However, because infection spreads through the fallopian tube wall from the inside to the outside, early infection can be missed. There is also significant inter- and intra-observer variation in how the visual appearances at laparoscopy are interpreted; although it is a fairly specific test, laparoscopy therefore lacks sensitivity.

Treatment

In clinical practice it is appropriate to consider treatment for PID in any sexually active woman presenting with lower abdominal pain who has adnexal tenderness on vaginal examination. This will result in over-treatment but the risks associated with antibiotic treatment are usually small and offset by the potentially serious sequelae that can follow untreated infection. Antibiotics are effective in reducing short-term morbidity, but despite their use a significant number of women will go on to develop long-term complications (Figure 4).

Appropriate advice should be given to the patient following a diagnosis of PID. This should include how the infection was acquired, the potential long-term consequences of PID, and how future infections can be prevented through the use of barrier contraception and effective treatment of sexual partners. Written information for the patient should also be provided (e.g. the Royal College of Obstetricians and Gynaecologists patient information leaflet available at www.rcog.org.uk).

General advice should be given to the patient regarding rest for those with severe disease and the use of appropriate analgesia. Unprotected sexual intercourse should be avoided until the patient and her partner(s) have completed treatment and follow-up.

The indications for inpatient care and use of parenteral antibiotics is shown in Table 3. With these exceptions, outpatient care is recommended.

Recommended outpatient antibiotic therapy is shown in Table 4 and should be given for 14 days.[5,6] A ceftriaxone-based regimen should be used in women at high risk of gonococcal PID, which includes those with a partner infected with gonorrhoea, in clinically severe disease or if there is a history of sexual contact abroad. Metronidazole is used to provide cover for anaerobic bacteria, but in women with mild-to-moderate pelvic inflammatory disease it may be discontinued if patients are unable to tolerate it, since it adds uncertain additional efficacy in less severe disease.

Inpatient antibiotic therapy is summarized in Table 5 and parenteral therapy should be continued until 24 hours after clinical improvement, and followed by oral therapy to complete a 14-day course.

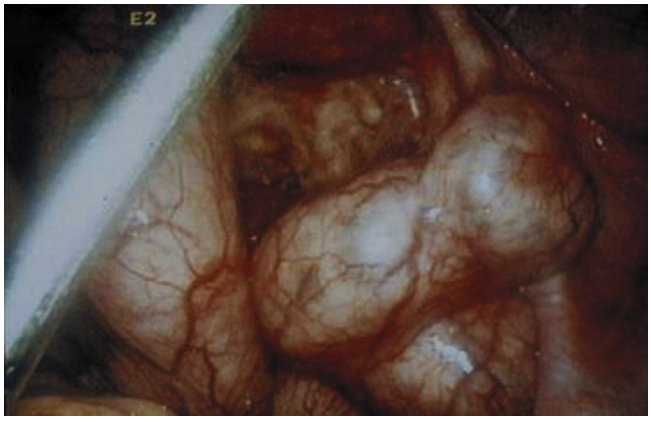

Figure 3 Laparoscopic view of severe pelvic inflammatory disease.

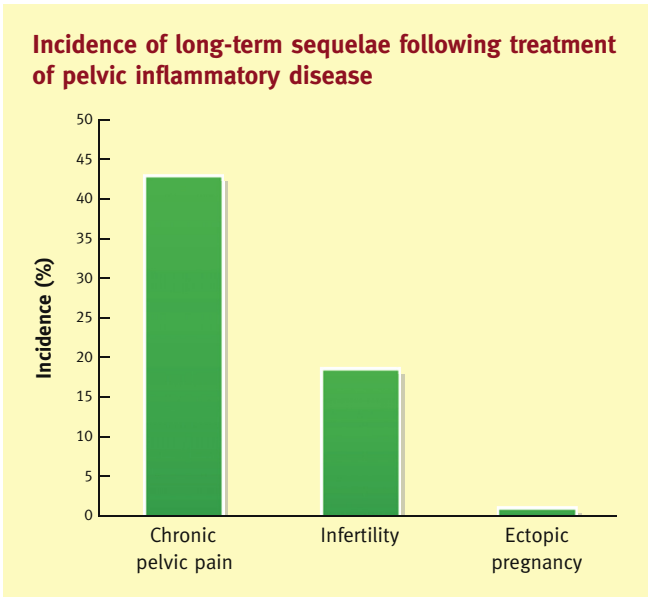

Figure 4

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Indications for inpatient management of pelvic inflammatory disease

Surgical emergency cannot be excluded
Clinically severe disease
Tubo-ovarian abscess
Pregnancy
Lack of response to oral therapy
Intolerance to oral therapy

Table 3

PID in pregnancy is uncommon, but since tetracyclines and quinolone antibiotics should be avoided in pregnant women, a combination of cefotaxime, azithromycin and metronidazole for 14 days may be used.

The presence of an intrauterine contraception device (IUD) does not increase the risk of PID beyond the first few weeks after insertion. However, if an IUD is present when PID is diagnosed, its removal should be considered. Removal has been associated with an improvement in short-term resolution of symptoms and signs but needs to be balanced against the risk of pregnancy in women who have had recent unprotected intercourse.

Women who are immunosuppressed secondary to HIV are at increased risk of severe PID but treatment recommendations are unaltered.

Male partners of women with PID should be offered screening for gonorrhoea and chlamydia and treated empirically with single-dose azithromycin.

Long-term sequelae

The symptoms and signs of acute PID often resolve following antimicrobial therapy but women remain at risk of long-term sequelae; indeed, the correlation between short- and long-term response to therapy is not particularly strong.[7] Chronic pelvic pain is the commonest long-term problem affecting over a third of women. Fallopian tube damage leading to blockage and infertility is particularly common following repeated episodes of pelvic infection (approximately 15%) but women can be reassured that, following a single episode of mild-to-moderate PID, which is treated promptly with appropriate antibiotics, fertility rates remain very similar to that of the general population.

Outpatient antibiotic therapy

Oral ofloxacin 400 mg twice daily plus oral metronidazole 400 mg twice daily[a]
Intramuscular ceftriaxone 500 mg single dose followed by oral doxycycline 100 mg twice daily plus oral metronidazole 400 mg twice daily
Oral moxifloxacin 400 mg once daily[b]

[a] ofloxacin should be avoided if gonorrhoea is a likely cause of PID.
[b] moxifloxacin is licenced for use in PID but can rarely cause severe liver toxicity and is usually used as a second-line treatment.

Table 4

Inpatient antibiotic therapy

IV ceftriaxone 2 g daily and doxycycline[a] 100 mg twice daily followed by oral doxycycline 100 mg twice daily oral metronidazole 400 mg twice daily
IV clindamycin 900 mg three times daily plus IV gentamicin[b] (2 mg/kg loading dose followed by 1.5 mg/kg 3 times daily [a single daily dose of 7 mg/kg may be substituted]) followed by oral doxycycline 100 mg twice daily and oral metronidazole 400 mg twice daily
IV ofloxacin 400 mg twice daily plus IV metronidazole 500 mg three times daily followed by oral ofloxacin 400 mg twice daily and oral metronidazole 400 mg twice daily

[a] Intravenous doxycycline is available from IDIS World Medicines; oral doxycycline can be substituted if tolerated.
[b] Parenteral gentamicin is used then serum drug levels and renal function should be monitored.

Table 5

Women who have had PID are also at an increased relative risk of ectopic pregnancy in the future, but the absolute risk of ectopic pregnancy fortunately remains small (<1%).

Follow-up

Women with clinically severe PID should be reviewed within 72 hours to ensure that symptoms and signs are improving, since failure to improve suggests an alternative diagnosis or the need for a change in antibiotic therapy. It is also helpful to review the patient after three to four weeks to check that they have completed their antibiotics, that their partners have been seen and that they understand the importance of avoiding recurrent infection (Figure 5).

Primary prevention of PID can be achieved through the use of barrier contraception, screening young sexually active women for chlamydia infection and reducing risk-taking sexual behaviour.[8] For those women who have already had PID, secondary prevention should be attempted through the use of barrier contraception and effective contact tracing.

Risk of impaired fertility following repeat pelvic inflammatory disease

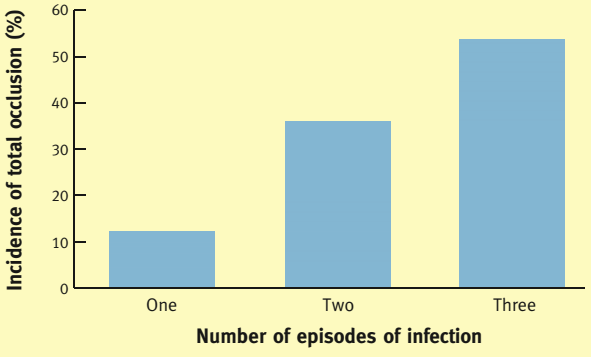

Figure 5

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Summary

Pelvic infection remains a common cause of morbidity in young women. Its control requires effective health education to reduce high-risk sexual behaviour, more effective screening for predisposing infections and the use of effective antibiotic therapy, given without delay. ◆

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USEFUL WEBSITES

British Association for Sexual Health and HIV — www.bashh.org.
Clinical evidence — www.clinicalevidence.com.
Royal College of Obstetrics and Gynaecology — www.rcog.org.uk.

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