

9.8 Pelvic inflammatory disease 1622

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ESSENTIALS Pelvic inflammatory disease is an infection of the endometrium, fallopian tubes and adnexae caused by a wide variety of bacteria, including *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Mycoplasma genitalium* and genital tract bacteria, most notably anaerobes. Pelvic inflammatory disease is often asymptomatic but clinical manifestations can range from mild pelvic pain and tenderness to severe peritonitis. Pelvic abscess formation is a serious infectious complication. However, only about 5% of patients with pelvic inflammatory disease have a fever or severe infectious manifestations. An accurate clinical diagnosis of pelvic inflammatory disease is difficult and it is commonly confused with other pelvic conditions, including ectopic pregnancy, appendicitis, and rupture or torsion of an ovarian cyst. Antibiotic therapy is aimed primarily at *C. trachomatis*, *N. gonorrhoeae*, and anaerobic bacteria, with prompt identification and treatment of pelvic inflammatory disease recommended in an attempt to reduce the 15% rate of tubal infertility and 40% risk of chronic pelvic pain following this infection. Introduction Pelvic inflammatory disease (PID) occurs when infection spreads from the vagina and cervix to the uterus, fallopian tubes, and surrounding pelvic structures. It is a common cause of morbidity in young women leading to abdominal pain, and is associated with considerable psychological distress because of the association with sexually transmitted infections and risk of infertility. Although initial treatment is relatively inexpensive, its high prevalence and the increased risk of developing long-term sequelae following PID result in a high financial burden to health services. Aetiology Most PID is caused by sexually transmitted bacteria spreading from the lower genital tract to the upper genital tract leading to endometritis, salpingitis, and oophoritis. *Chlamydia trachomatis* and *Neisseria gonorrhoeae* are the most commonly recognized pathogens but only account for around 40% of infections, although their relative contribution varies considerably in different geographical areas. Anaerobic bacteria can also be detected in the fallopian tubes in women with PID although their role as primary pathogens, as opposed to opportunistic secondary invaders, is not clear. They are important in more severe PID, particularly when a pelvic abscess forms, and indicate the need for specific antimicrobial cover. A variety of newer pathogens have been identified using nucleic acid amplification to detect bacteria which are difficult to culture using traditional microbiological techniques. *Mycoplasma genitalium* almost certainly causes PID, probably about 5–10% of cases,

and *Leptotrichia*, *Sneathia*, *Atopobium*, and 'BV-associated bacteria' (BVABs) have also been detected, although their role is less well defined. There are several possible risk factors for women to develop PID after contracting gonorrhoea or chlamydia, with the overall risk being around 10%. In animal models, infections acquired in the luteal phase of the menstrual cycle are more likely to cause PID, as are infections with a higher bacterial load. In humans, there is a link between PID and human leukocyte antigen (HLA) subtype or inherited polymorphisms affecting cytokine and immune cell expression, suggesting that some women are intrinsically at higher risk than others. Procedures such as termination of pregnancy and insertion of an intrauterine contraceptive device, which involve inserting items through the cervix, also increase the risk of introducing infection into the upper genital tract. Bacterial vaginosis, and the associated imbalance of the vaginal bacterial flora, is closely associated with PID. Bacterial vaginosis is more commonly diagnosed in women with PID and the bacteria found in the lower genital tract in bacterial vaginosis overlap considerably with those seen in the upper genital tract in PID. Prospective studies do not suggest that all women with bacterial vaginosis have an increased chance of getting PID, but certain sub-groups are at increased risk; specifically, PID is more common if there is a high bacterial load of anaerobes in the vagina or if infection with gonorrhoea or chlamydia subsequently occurs.

Epidemiology The incidence of PID is falling in many countries in those presenting both in primary and secondary care, and particularly in younger women (Fig. 9.8.1). The decline has been particularly

9.8 Pelvic inflammatory disease Jonathan D.C. Ross

9.8 Pelvic inflammatory disease 1623 marked for chlamydia PID and might reflect an increased awareness of chlamydia, in both the general population and healthcare personnel, with high rates of testing picking up early infections before they progress to cause salpingitis. The risk factors for PID are very similar to those of the underlying sexually transmitted infections, and include sex without using condoms multiple and particularly concurrent partners, and low socio-economic status. Use of the combined oral contraceptive pill reduces the risk of developing symptomatic chlamydial PID, although its effect on subclinical disease is not clear. An increase in the frequency of vaginal douching is associated with PID but prospective studies suggest that douching is not a direct cause of PID and may instead be a response to PID-related symptoms, such as genital discharge or vaginal odour.

Pathogenesis An endometrial biopsy from a woman with PID demonstrates a plasma cell infiltrate with polymorphonuclear cells and the formation of lymphoid follicles. Inflammation of the fallopian tubes causes swelling and erythema with an inflammatory exudate within the fallopian tube, mixed with blood and necrotic epithelial cells which can lead to tubal obstruction. During healing adhesions can form causing permanent blockage of the tube, and chronic inflammation can result in a pyosalpinx (abscess formation within the tube) or hydrosalpinx (fluid filled collection within the tube) if the tube becomes obstructed at both ends.

Clinical features Many women with PID are asymptomatic and might only present with the consequences of tubal damage, such as infertility or ectopic pregnancy. Of those with symptoms, most have mild to moderate lower abdominal pain which is usually bilateral, constant, and of recent onset. An associated vaginal discharge secondary to cervicitis or bacterial vaginosis is common, and there might also be a history of post-coital bleeding, intermenstrual bleeding, or menorrhagia as a result of cervicitis or endometritis. More rarely, with severe PID, the patient is systemically unwell with pyrexia, general malaise, and severe abdominal pain associated with peritonitis or a pelvic abscess. An associated perihepatitis might lead to right upper quadrant pain and tenderness (the Fitz-Hugh-Curtis syndrome). On bimanual vaginal examination there is usually bilateral adnexal tenderness and cervical excitation (discomfort on moving the cervix). An inflammatory mass or

abscess is sometimes palpable. The clinical diagnosis of PID has poor specificity with only around 60% of clinical diagnoses being confirmed if laparoscopy is performed, although the accuracy improves slightly if the examination is performed by an experienced clinician. Despite this, current guidelines recommend a low threshold for starting treatment following clinical assessment because the risks of antibiotic treatment are considered low and the sequelae of untreated infection potentially severe. PID should therefore be considered in any young sexually active women complaining of lower abdominal pain and who is found to have adnexal tenderness on examination.

Differential diagnosis The most important alternative condition to consider in a young woman with lower abdominal pain is ectopic pregnancy and a pregnancy test should, therefore, be performed. Although a pregnancy test is not reliable in very early pregnancy, an ectopic pregnancy is unlikely to present at this early stage and the patient can be recalled for repeat testing at a later date if required. Other causes of abdominal pain in young women include appendicitis, irritable

0 2000 4000 6000 8000 10000 12000 14000 16000 18000 20000 1995 1997 1999 2001 2003 2005 2007 2009 2011 2013 2015

Year No. of PID diagnoses Gonococcal PID Chlamydia PID Nonchlamydial, nongonococcal PID

Fig. 9.8.1 Pelvic infection diagnosed in sexual health clinics in England.

Section 9 Sexually transmitted diseases 1624 bowel syndrome, rupture/torsion of an ovarian cyst, endometriosis, urinary tract infection, or functional pain where no underlying cause is identified (Table 9.8.1). In older women, diverticulitis or malignancy should also be considered. Clinical investigations Microbiological testing for gonorrhoea, chlamydia and *M. genitalium* should be performed, from a vaginal or cervical swab using a nucleic acid amplification-based test (NAAT). An additional cervical sample for gonorrhoea culture should be taken to test for antibiotic sensitivities. Although a minority of women with clinical PID have gonorrhoea, chlamydia or mycoplasma, their presence makes the diagnosis more likely and, if *N. gonorrhoeae* is present, the resistance pattern might influence the choice of antibiotic therapy. Screening for HIV and syphilis should also be offered. Other blood tests have limited value in most women with PID. An elevated neutrophil count, erythrocyte sedimentation rate (ESR), or C-reactive protein is unusual in mild to moderate disease, and nonspecific in women with severe pain. Ultrasound scanning is useful when a tubo-ovarian abscess or hydrosalpinx is suspected clinically (e.g. severe pain with adnexal mass) but seldom helpful when trying to identify uncomplicated salpingitis because the inflamed tissue cannot easily be seen on the scan. Doppler ultrasound is potentially more useful by detecting the increased blood flow associated with pelvic inflammation. Computed tomography (CT) or MRI scanning can occasionally be helpful, especially in a patient with severe pain and an uncertain diagnosis, but are not used routinely. A transcervical endometrial biopsy can be taken and examined for histological evidence of endometritis, which is a reasonable proxy marker for salpingitis. However, the fixing, staining, and reporting of the sample takes several days and it is therefore not helpful in making decisions about whether to start therapy. Laparoscopy or laparotomy are seldom performed except where the diagnosis is in doubt in a patient with severe symptoms, or if antibiotic treatment has not been effective. Although directly visualizing the fallopian tubes is helpful in diagnosing moderate or severe PID, there is considerable inter and intraobserver variation in interpreting the tissue appearances in women with mild disease.

Treatment Several different antibiotic regimens are effective in treating PID, and are summarized in Table 9.8.2. Early empirical therapy, within a few days of the onset of symptoms, is important to minimize the risk of tubal damage. The choice of antibiotic regimen will be determined by patient choice and the local epidemiology of specific infections. Antimicrobial resistance in *N. gonor-*

rhoeae is common for penicillin and tetracyclines, can develop rapidly for macrolides (such as azithromycin), and is beginning to emerge for cephalosporins. Moxifloxacin should be given if *M. genitalium* is diagnosed. First-line empirical therapy might, therefore, need to be altered once the results of microbiology testing and antibiotic sensitivities are available. Inpatient care with parenteral antibiotics is needed for women with severe symptoms (e.g. temperature over 38°C, peritonitis, tubo-ovarian abscess), failure to respond to oral antibiotics within 3–4 days, or intolerance of oral treatment. Women should be given a detailed explanation about PID including the long-term prognosis, and provided with written information. A patient information leaflet is available at <https://www.bashh.org>. Sexual partners should be screened for gonorrhoea and chlamydia (and/or treated empirically with a 7 day course of doxycycline) before resuming sexual contact.

Table 9.8.1 Differential diagnoses for pelvic inflammatory disease (PID)

Ectopic pregnancy	Positive pregnancy test
Appendicitis	Pain localizes to right iliac fossa
Associated with vomiting	Irritable bowel syndrome
Associated altered bowel habit and abdominal pain	Ovarian cyst rupture/torsion
Sudden onset of pain	Endometriosis
Cyclical or chronic pain	Urinary tract infection
Urinary frequency/dysuria	

Table 9.8.2 Antibiotic treatment of PID

a Outpatient care

1. Single dose intramuscular ceftriaxone plus oral doxycycline (14 days) plus oral metronidazole (14 days)
2. Oral ofloxacin (14 days) plus oral metronidazole (14 days)
3. Oral moxifloxacin (14 days)

b Inpatient care

1. Intravenous ceftriaxone plus intravenous/oral doxycycline
2. Intravenous clindamycin plus intravenous gentamicin
3. Intravenous ofloxacin plus intravenous metronidazole
4. Intravenous ciprofloxacin plus intravenous/oral doxycycline plus intravenous metronidazole

a See also <https://www.bashh.org> for UK National Guideline for the Management of Pelvic Inflammatory Disease

b Switch to oral therapy 24 hours after symptoms improve to complete a total of 14 days treatment

9.8 Pelvic inflammatory disease

1625 A clinical review after three days is recommended if symptoms are not improving, and it might also be helpful after two to four weeks to review the treatment response, tracing of sexual partners, and microbiology results. It can take several weeks for symptoms to fully resolve, but if there is no significant improvement within the first week or two, then alternative causes of abdominal pain should be sought. If an intrauterine contraceptive device (IUD) is present, then its removal should be considered. If symptoms are not too severe, it is reasonable to leave the IUD in situ while treating with antibiotics, but it should be removed if clinical improvement has not occurred within a few days.

Prognosis The fertility of women with a first episode of PID is usually good if they are treated without delay with appropriate antibiotics, but infertility occurs overall in around 15% of patients (defined as failing to become pregnant over several months despite not using contraception). The risk is markedly increased in women who have repeated episodes of infection (Fig. 9.8.2). The most common long-term consequence of PID is chronic pelvic pain, which affects up to 40% of women. The relative risk of tubal damage leading to ectopic pregnancy is also increased, but the absolute risk remains low at about 1%. The risk of sequelae can be reduced by avoiding further infection through the use of barrier contraception such as condoms. Screening young women for chlamydia, which is often asymptomatic, and providing early treatment can also reduce rates of PID.

FURTHER READING Molander P, et al. (2001). Transvaginal power Doppler findings in laparoscopically proven acute pelvic inflammatory disease. *Ultrasound Obstet Gynecol*, 17, 233–8. Ness RB, et al. (2002). Effectiveness of inpatient and outpatient treatment strategies for women with pelvic inflammatory disease: results from the Pelvic Inflammatory Disease Evaluation and Clinical Health (PEACH) Randomized Trial. *Am J Obstet Gynecol*, 186, 929–37. Ness RB, et al. (2005). Douching, pelvic inflammatory disease, and incident gonococcal and chlamydial genital infection in a cohort of high-risk women. *Am J Epidemiol*, 161,

186-95. Ross JDC, Hughes G. (2014). Why is the incidence of pelvic inflammatory disease falling? BMJ, 348, g1538. Ross JDC, et al. (2018). UK National Guideline for the Management of PID. <http://www.bashh.org/guidelines>: 2018 Scholes D, et al. (1996). Prevention of pelvic inflammatory disease by screening for cervical chlamydial infection. N Engl J Med, 334, 1362-6. 50% 45% 50% 35% 30% 25% 20% 15% 10% Percentage 5% 0% 1st episode 3 or more episodes 2nd episode Risk of infertility Fig. 9.8.2 Risk of infertility following repeated episodes of pelvic infection.

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