Diagnosis and treatment of pelvic inflammatory disease

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Pelvic inflammatory disease (PID) can be difficult to diagnose, but delaying treatment increases the risk of both acute and long-term complications. This article provides a guide to the assessment and recommended management of PID.

Pelvic inflammatory disease (PID) is a condition that affects sexually active women of reproductive age. It comprises a range of upper genital tract inflammatory disorders that result from the spread of micro-organisms from the lower to the upper genital tract. The ensuing pathology can include any combination of endometritis, salpingitis, parametritis, oophoritis, tubo-ovarian abscess and pelvic peritonitis.1

Prevalence
While PID diagnosis rates are declining in the UK2 and the USA,3 it remains a common diagnosis in primary care and in hospital settings. The most recent data for the UK (2011) showed that the overall rate of definite/probable PID diagnoses among women aged 15 to 44 years was 176 per 100,000 person-years in GP settings and 241 per 100,000 population in hospital settings. There was wide local variation, and rates for definite/probable PID diagnoses in GP settings ranged from 125 (London) to 274 (East Midlands) per 100,000 person years. Rates of PID diagnoses in hospital inpatient settings ranged from 204 (East of England) to 284 (South West England) per 100,000 population. As there are approximately six to eight GPs per 100,000 population in UK,4 each GP can expect to make in the region of 30 PID diagnoses per year.

Epidemiology
PID is caused by the spread of bacteria from the female nonsterile lower genital tract to the upper genital tract and peritoneal cavity. The most common causative organisms isolated are Chlamydia trachomatis and Neisseria gonorrhoeae, although they account for only 25 per cent of the cases in the UK.5 Other organisms in the vaginal flora implicated in PID are those associated with bacterial vaginosis (BV) including Gardnerella vaginalis, Haemophilus influenzae, enteric Gram-negative rods and Streptococcus agalac-

Neisseria gonorrhoeae: one of the most common causes of pelvic inflammatory disease in UK, each GP can expect to make in the region of 30 PID diagnoses per year.
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tiae. In addition, cytomegalovirus (CMV), *Mycoplasma hominis*, *Ureaplasma urealyticum* and *Mycoplasma genitalium* are associated with the pathogenesis of PID in some cases. Anaerobic bacteria such as *Prevotella*, *Atopobium* and *Leptotrichia* may also be implicated.

Several demographic, behavioural and contraceptive factors have been identified as risk factors for PID acquisition. Young age (<25 years), multiple sexual partners, a prior history of PID, sexually transmitted infections (STIs) and nonuse of barrier contraceptives have all been recognised as risk factors.

### Diagnosis

The clinical diagnosis of PID is difficult because no single symptom, physical finding, imaging technique, investigation or serological marker is specific and sensitive for the diagnosis of PID. Furthermore, many women are asymptomatic or have subtle nonspecific symptoms, so many episodes go undetected.

Because of the difficulty in diagnosis, and as PID can cause acute complications such as tubo-ovarian abscess, Fitz-Hugh Curtis syndrome (perihepatitis) and long-term complications, including tubal factor infertility, ectopic pregnancy and chronic pelvic pain, guidelines recommend a low threshold for the initiation of PID treatment (see Figure 1).

The UK National Guideline for the Management of PID (2011) states that:

“A diagnosis of PID, and empirical antibiotic treatment, should be considered and usually offered in any young (under 25 years) sexually active woman who has recent-onset, bilateral lower abdominal pain associated with local tenderness on bimanual examination, in whom pregnancy has been excluded.”

More recently, the US Centers for Disease Control and Prevention (CDC) offer a similar recommendation:

“Presumptive treatment for PID should be initiated in sexually active young women and other women at risk for STDs if they are experiencing pelvic or lower abdominal pain, if no cause for the illness other than PID can be identified, and if one or more of the following minimum clinical criteria are present on pelvic examination:

• cervical motion tenderness or
• uterine tenderness or
• adnexal tenderness.”

Other additional criteria can be used to support a diagnosis of PID, including deep dyspareunia, abnormal vaginal bleeding such as postcoital and intermenstrual bleeding, abnormal purulent discharge or cervical friability, and a fever over 38°C.

Clinical diagnosis competes with diagnosis using laparoscopy, endometrial biopsy or ultrasound scanning:

• Laparoscopy is considered the ‘gold standard’ for the diagnosis of PID. While it can give immediate and accurate results, it is more expensive, more difficult to access, more painful and has inherent surgical risks compared with a treatment based on a clinical diagnosis.

• Endometrial biopsy to detect histopathologic evidence of endometritis is helpful for making a diagnosis of PID, has a high sensitivity and specificity and can safely be performed in an outpatient setting. However, it has limited use in a

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*Figure 1. The diagnosis and management of pelvic inflammatory disease (PID)*
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Case study

Jane is 18 years old and presents to the surgery with lower abdominal pain, gradual in onset and dysuria for three days; she has also been feeling feverish in the evenings. Her last menstrual period (LMP) was two weeks ago. She denies any gastrointestinal symptoms and has no vaginal discharge or abnormal bleeding. She says she is in a new relationship and has been together with her boyfriend for two months. She has a contraceptive implant in situ and does not use condoms. About two years ago, she had a positive test for C. trachomatis and was treated with antibiotics at a local GUM clinic.

On examination, vital signs are within normal limits. Abdominal examination reveals tenderness in the lower quadrants. No flank pain. Normal external genitalia. Speculum examination reveals a minimal purulent discharge from the cervix. Bimanual examination reveals uterine and adnexal tenderness as well as cervical motion tenderness. A low vaginal swab (LVS) for C. trachomatis and N. gonorrhoeae is obtained. Urine dipstick is positive for leukocytes; the pregnancy test is negative.

Based on the history and examination, she is commenced on empirical treatment for pelvic inflammatory disease (PID) and her partner is advised to come in for testing and treatment.

Clinical setting because of the delay in histological processing and the associated delay in treatment.9

• In a recent review, Romosan and Valentin concluded that “transvaginal ultrasound has limited ability to diagnose acute PID.”10

However, empirical management based on clinical indication leads to overtreatment, which is not without risks. The treatment might be biomedically low risk and the number of people overtreated may be low enough to be acceptable with regard to antimicrobial stewardship, but a PID diagnosis can be very stressful for the patient.

Differential diagnosis

There are several conditions that need to be investigated and excluded in patients presenting with symptoms of PID:

• An ectopic pregnancy should be excluded if a pregnancy test is positive.
• Acute appendicitis; in this case, nausea and vomiting is more common and cervical excitation and adnexal tenderness are less likely.
• Ovarian and adnexal pathology such as a torsion, haemorrhage, abscess or cyst rupture.
• Gastrointestinal and urological causes of acute pelvic pain.

Management

Following a diagnosis of PID, the following general advice should be followed:

• Sexually active patients should be offered a pregnancy test as well as a screen for STIs, including HIV.
• Male partners over the last three months should be evaluated, tested for STIs and treated accordingly. Empirical treatment with appropriate antibiotic therapy should be offered to all male partners. Sexual intercourse should be avoided until the patient and her partner(s) have completed the treatment course and symptoms have resolved.
• For clinically mild and moderate disease, outpatient therapy is effective.
• Admission and parenteral treatment should be considered if there is clinically severe disease, an inability to exclude a surgical emergency, no significant improvement in signs and symptoms after 72 hours in moderate and severe disease, intolerance to oral treatment, complications or pregnancy.
• Provide appropriate analgesia as required.
• The risk of PID associated with IUDs is mostly restricted to the first three weeks after insertion. An IUD does not need to be removed when a diagnosis of PID is made but PID should be treated according to the guidelines. If no clinical improvement occurs after 72 hours of treatment, removal of the IUD should be considered but weighed up against the risk of pregnancy.6
• Arrange follow-up at 72 hours for patients with moderate or severe disease to assess symptoms and signs.

Treatments

The objective of PID treatment includes not only improving the acute inflammatory symptoms but also preventing long-term sequelae. Treatment regimens must provide broad-spectrum coverage for likely pathogens including N. gonorrhoeae and C. trachomatis, as well as a variety of aerobic and anaerobic bacteria that are commonly isolated from the upper genital tract in women with PID.

The PID Evaluation and Clinical Health (PEACH) study has provided some of the best evidence for the effectiveness of antibiotic treatment to prevent long-term complications such as tubal infertility and ectopic pregnancy. A follow-up of PEACH patients showed that women with symptoms of mild to moderate PID who received a third-generation cephalosporin in addition to doxycycline 100mg twice daily for two weeks had similar reproductive outcomes to women in the population at large, and women should be reassured that their fertility is unlikely to be affected.11

Choosing an appropriate antimicrobial regimen is influenced by local antibiotic sensitivity patterns, the local epidemiology and the severity of the disease, as well as patient acceptance, compliance and cost. Treatment should be started as soon as a presumptive diagnosis has been made to prevent long-term sequelae. As there are no definitive diagnostic criteria, a low threshold is recommended for empirical treatment.

Recommended outpatient regimens for PID are shown in Table 1.5

To improve coverage for anaerobic bacteria, metronidazole is included in some of the regimens; this is, however, of greater importance in severe disease. If the disease is mild or moderate, or if metronidazole is not tolerated, it may be discontinued. The addition of metronidazole will also treat bacterial vaginosis, which has been implicated in PID.

There has been increasing resistance to quinolones in the treatment of N. gonorrhoeae infections in the UK. If
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Patients are at high risk of gonococcal PID, ofloxacin and moxifloxacin monotherapy should be avoided or ceftriaxone should be added. There is no clinical evidence for using an oral cephalosporin, e.g. cefixime, and therefore is not recommended. In addition, there is decreasing susceptibility to cephalosporins with N. gonorrhoeae infections. Using azithromycin as an alternative treatment option may be considered if allergy or intolerance is an issue. However, there is limited clinical trial evidence to support this and multiple-dose therapy is needed. Moxifloxacin has been associated with serious adverse effects such as cardiac events and hepatic failure. Although some randomised controlled trials support its use, it should not be used as a first-line treatment option.

Conclusion
PID remains common in community and hospital settings. Practitioners need to be vigilant, especially in at-risk groups, and have a low threshold for commenced treatment for PID. Signs, symptoms and investigations alone cannot be relied upon for diagnosis as not one marker is specific and sensitive enough for a definite diagnosis. Prompt diagnosis and management is, however, essential to prevent acute complications as well as long-term morbidity.

References

Declaration of interests
None to declare.

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Recommended regimens
(all offer a comparable efficacy)

- IM ceftriaxone 500mg as a single dose followed by oral doxycycline 100mg twice daily plus oral metronidazole 400mg twice daily for 14 days
- Oral ofloxacin 400mg twice daily plus metronidazole 400mg twice daily for 14 days

Alternative regimens in case of allergy, intolerance or adverse reactions

- IM ceftriaxone 500mg as a single dose followed by oral azithromycin 1g weekly for 2 weeks
- Oral moxifloxacin 400mg once daily for 14 days

Table 1. Outpatient regimens for treatment of pelvic inflammatory disease

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