

Setting standards to improve women's health

# MANAGEMENT OF ACUTE PELVIC INFLAMMATORY DISEASE

# 1. Purpose and scope

Pelvic inflammatory disease (PID) is a common cause of morbidity and accounts for 1 in 60 GP consultations by women under the age of 45.¹ Delays of only a few days in receiving appropriate treatment markedly increase the risk of sequelae, which include infertility, ectopic pregnancy and chronic pelvic pain.² This guideline applies to women requiring treatment for confirmed or suspected acute PID being treated in an outpatient or inpatient setting by primary and secondary care practitioners.

PID is usually the result of infection ascending from the endocervix causing endometritis, salpingitis, parametritis, oophoritis, tuboovarian abscess and/or pelvic peritonitis. While sexually transmitted infections such as *Chlamydia trachomatis* and *Neisseria gonorrhoeae* have been identified as causative agents,<sup>3,4</sup> *Mycoplasma genitalium*, anaerobes and other organisms may also be implicated.<sup>3,5</sup>

There are currently marked variations in the antimicrobial regimens used in the treatment of PID, reflecting uncertainty in the optimal treatment schedule.<sup>6</sup> The guideline contains recommendations for treatment and graded evidence to support their use.

#### 2. Identification and assessment of evidence

A Medline search was carried out from January 1963 to April 2002, looking for the following terms in the title or abstract: 'pelvic inflammatory disease,' 'adnexitis,' 'oophoritis,' 'parametritis,' 'salpingitis' or 'adnexal disease' (the dataset for 1963–86 was limited to Argonne Information Management journals and human subjects); 2959 citations were identified. A search of the Cochrane database revealed no directly relevant systematic reviews. A search of the Cochrane controlled trials register using a search strategy of 'pelvic inflammatory disease,' 'adnexitis,' 'oophoritis,' 'parametritis,' 'salpingitis' or 'adnexal disease' identified 312 citations. The following guidelines and reports were also reviewed: Centers for Disease Control and Prevention Sexually Transmitted Diseases Treatment Guidelines (2002),<sup>7</sup> Recommendations from the 31st Royal College of Obstetrics and Gynaecology Study Group on Pelvic Inflammatory Disease (1996),<sup>4</sup> UK National Guidelines on Sexually Transmitted Diseases (2002)<sup>8</sup> and the European Guidelines for the Management of Pelvic Inflammatory Disease (2001).<sup>9</sup>

The recommendations given in this guideline have been graded according to the guidance for the development of RCOG green-top guidelines.

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# 3. Making a diagnosis of acute PID

#### 3.1 Clinical

Because of the lack of definitive clinical diagnostic criteria, a low threshold for empirical treatment of PID is recommended. Where there is diagnostic doubt or in clinically severe cases, admission to hospital for treatment and further investigation is advisable.

The following clinical features are suggestive of a diagnosis of PID:

- lower abdominal pain and tenderness
- deep dyspareunia
- abnormal vaginal or cervical discharge
- cervical excitation and adnexal tenderness motion
- fever (> 38°C).

Clinical symptoms and signs, however, lack sensitivity and specificity (the positive predictive value of a clinical diagnosis is 65–90% compared with laparoscopic diagnosis).<sup>3,6,10</sup> The presence of excess leucocytes on a wet mount vaginal smear is associated with PID<sup>11,12</sup> but is also found in women with isolated lower genital tract infection. Laparoscopy enables specimens to be taken from the fallopian tubes and the pouch of Douglas and can provide information on the severity of the condition.<sup>3,13</sup> Although it has been considered the gold standard in many studies of treatment regimens, 15–30% of suspected cases may have no laparoscopic evidence of acute infection despite organisms being isolated from the fallopian tubes.<sup>3,10,14</sup> When there is diagnostic doubt, however, laparoscopy may be useful to exclude alternative pathologies.<sup>3,14</sup>

Evidence level III

Transvaginal ultrasound scanning may be helpful where there is diagnostic difficulty. When supported by power Doppler it can identify inflamed and dilated tubes and tubo-ovarian masses, but there is insufficient evidence to support its routine use. 15,16 Magnetic resonance imaging can assist in making a diagnosis 17 but the evidence is limited and it is not widely available. A peripheral blood leucocytosis, elevated erythrocyte sedimentation rate or C-reactive protein also support the diagnosis 18 but are non-specific findings. There is insufficient evidence to support endometrial biopsy as a routine diagnostic test. 19

# 3.2 Microbiological

# Women wit

Women with suspected PID should be screened for gonorrhoea and chlamydia.

Testing for gonorrhoea and chlamydia in the lower genital tract is recommended, since a positive result strongly supports the diagnosis of PID, but the absence of infection at this site does not exclude PID.<sup>3,7,10</sup> Testing for gonorrhoea should be with an endocervical specimen and tested via culture (direct inoculation on to a culture plate or transport of the swab to the laboratory within 24 hours) or using a nucleic acid amplification test (NAAT). Screening for chlamydia should also be from the endocervix, preferably using a NAAT (e.g. polymerase chain reaction, strand displacement amplification). Taking an additional sample from the urethra increases the diagnostic yield for gonorrhoea and chlamydia. A first-catch urine sample provides an alternative sample for some NAATs.

Evidence level IV

Other organisms, including M. genitalium, have been associated with  $PID^{20,21}$  but routine screening is not yet justified.

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#### 4. Treatment for acute PID

# 4.1 Outpatient treatment

Α

Outpatient antibiotic treatment should be commenced as soon as the diagnosis is suspected.

In mild or moderate PID (in the absence of a tubo-ovarian abcess), there is no difference in outcome when patients are treated as outpatients or admitted to hospital.<sup>22</sup> It is likely that delaying treatment, especially in chlamydial infections, increases the severity of the condition and the risk of long-term sequelae such as ectopic pregnancy, subfertility and pelvic pain.<sup>2,23</sup>

Evidence level Ib

В

Outpatient antibiotic treatment should be based on one of the following regimens:

• oral ofloxacin 400 mg twice a day plus oral metronidazole 400 mg twice a day for 14 days<sup>24-27</sup>

OR

• intramuscular ceftriaxone 250 mg immediately or intramuscular cefoxitin 2 g immediately with oral probenecid 1 g, followed by oral doxycycline 100 mg twice a day plus metronidazole 400 mg twice a day for 14 days.<sup>7,24,25,28-30</sup>

Evidence level Ib

Broad-spectrum antibiotic therapy is required to cover N. gonorrhoeae, C. trachomatis and anaerobic infection.<sup>3,4,7</sup> The recommendation to cover N. gonorrhoeae in patients presenting with suspected PID in the UK is based on the following facts:

- the most recent British study found gonococcal infection in 14% of PID patients<sup>3</sup>
- the absence of endocervical gonorrhoea does not exclude gonococcal PID
- at present, there are no large controlled trials from the UK which support the use of regimens that do not cover *N. gonorrhoeae*
- the increasing incidence of gonorrhoea in the UK.<sup>31</sup>

Although the combination of oral doxycycline and metronidazole is in common use in the UK, there are no clinical trials assessing its effectiveness.<sup>6</sup>

use

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Patients should be provided with a detailed explanation of their condition, with particular emphasis on the long-term implications for the health of themselves and their partner(s), reinforced with clear and accurate written information.

# 4.2 Inpatient treatment

Admission to hospital would be appropriate in the following circumstances:7

- surgical emergency cannot be excluded
- clinically severe disease
- tuboovarian abscess
- PID in pregnancy
- lack of response to oral therapy
- intolerance to oral therapy.

In more severe cases inpatient antibiotic treatment should be based on intravenous therapy, which should be continued until 24 hours after clinical improvement and followed by oral therapy.

Evidence level Ib

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Evidence level IV

# **B** Recommended regimens are:

• intravenous cefoxitin 2 g three times a day plus intravenous doxycycline 100 mg twice a day (oral doxycycline may be used if tolerated), followed by oral doxycycline 100 mg twice a day plus oral metronidazole 400 mg twice a day for a total of 14 days<sup>7,24,25,29,30</sup>

OR

- intravenous clindamycin 900 mg three times a day plus intravenous gentamicin: 2 mg/kg loading dose followed by 1.5 mg/kg three times a day (a single daily dose of 7 mg/kg may be substituted), followed by either:
  - $\Diamond$  oral clindamycin 450 mg four times a day to complete 14 days OR

OR

• intravenous ofloxacin 400 mg twice a day plus intravenous metronidazole 500 mg three times a day for 14 days. 24,25,32

Intravenous doxycycline is available from IDIS World Medicines (+44 [0]208 410 0700). If parenteral gentamicin is used then serum drug levels and renal function should be monitored.

The choice of an appropriate treatment regimen will be influenced by robust evidence on local antimicrobial sensitivity patterns, robust evidence on the local epidemiology of specific infections in this setting, cost, patient preference and compliance, and severity of disease.

Evidence of the efficacy of antibiotic therapy in preventing the long-term complications of PID is currently limited.

## 4.3 Treatment in pregnancy

A pregnancy test should be performed in all women suspected of having PID to help exclude an ectopic pregnancy. The risk of giving any of the recommended antibiotic regimens in very early pregnancy (prior to a positive pregnancy test) is low, with any significant drug toxicity resulting in failed implantation (personal communication, UK National Teratology Information Service).

In an 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. 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.

# 4.4 Treatment in young women

Ofloxacin should be avoided in young women when bone development is still occurring, based on data from animal studies. No problems have been reported in human subjects and the *British National Formulary* currently recommends that ofloxacin can be used in children where other options are limited. Doxycycline can be safely used in children over the age of 12 years.

4.5 Treatment in a woman with an intrauterine contraceptive device

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.

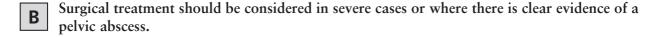
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Evidence level Ib

An IUCD only increases the risk of developing PID in the first few weeks after insertion.<sup>33</sup> A single small randomised controlled trial suggests that removing an IUCD does not affect the response to treatment but the study has suboptimal outcome measures.<sup>34</sup> An observational study also showed no benefit in removing an IUCD in this situation.<sup>35</sup>

Evidence level IIb

# 5. Other modes of treatment



Laparotomy/laparoscopy may help early resolution of the disease by division of adhesions and drainage of pelvic abscesses.<sup>36</sup> Ultrasound-guided aspiration of pelvic fluid collections is less invasive and may be equally effective.<sup>37,38</sup> It is also possible to perform adhesiolysis in cases of perihepatitis although there is no evidence as to whether this is superior to antibiotic therapy alone.

Evidence level III

# 6. Management of sexual partners of women with PID, which may be sexually acquired

B Current sexual partners of women with PID should be contacted and offered health advice and screening for gonorrhoea and chlamydia.

Other recent sexual partners may also be offered screening; tracing of contacts within a six-month period of onset of symptoms is recommended but this time period may be influenced by the sexual history. Patients should be advised to avoid intercourse until they and their partner have completed the treatment course. Gonorrhoea diagnosed in the sexual partner should be treated appropriately and concurrently with the index patient. Concurrent empirical treatment for chlamydia is recommended for all sexual contacts due to the variable sensitivity of currently available diagnostic tests. If adequate screening for gonorrhoea and chlamydia in the sexual partner(s) is not possible, empirical therapy for both gonorrhoea and chlamydia should be given. 39,40

Evidence level III

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Referral of the index patient and her partner to a genitourinary medicine clinic is recommended, to facilitate contact tracing and infection screening.

## 7. Review of patients with PID

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 investigation, 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.

Repeat testing for gonorrhoea after treatment is recommended in those initially found to be infected. Repeat testing for chlamydia may be appropriate in those in whom persisting symptoms, compliance with antibiotics and/or tracing of sexual contacts indicate the possibility of persistent or recurrent infection.

Evidence level III

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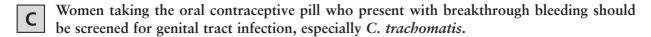
#### 8. Women who are infected with HIV

**B** Women with PID who are also infected with HIV should be treated with the same antibiotic regimens as women who are HIV negative.

Women who are HIV infected were previously thought to get clinically more severe PID but recent studies suggest that the differences may be minor and that they respond as well to treatment as patients who are not HIV infected.<sup>20,41,42</sup> Standard antibiotic treatment as outlined above is therefore appropriate and admission is only required for those with clinically severe disease. Potential interactions between antibiotics and anti-retroviral medication need to be considered on an individual basis.

Evidence level III

# 9. The oral contraceptive pill and PID



The use of the combined oral contraceptive pill has usually been regarded as protective against symptomatic PID.<sup>43</sup> Retrospective case–control and prospective studies have, however, shown an association with an increased incidence of asymptomatic cervical infection with *C. trachomatis*.<sup>44</sup> This has led to the suggestion that the oral contraception may mask endometritis.<sup>45</sup> Women using the oral contraceptive pill should be warned that its effectiveness may be reduced when taking antibiotic therapy.

### 10. Auditable outcomes

Little is known about the long-term outcomes, in relation to future fertility, ectopic pregnancy and chronic pelvic pain, following the treatment of PID. Appropriate short-term audit outcomes include:<sup>8</sup>

- the proportion of women in whom microbiological investigations have been undertaken
- the proportion of women having an adequately documented sexual history
- the proportion of women receiving treatment with a recommended regimen
- the proportion of women referred for the tracing of sexual contacts
- the proportion of named male contacts of women who have PID associated with sexually transmitted infection who are confirmed to have been screened for infection and/or treated.

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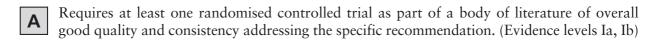
Clinical guidelines are: 'systematically developed statements which assist clinicians and patients in making decisions about appropriate treatment for specific conditions'. Each guideline is systematically developed using a standardised methodology. Exact details of this process can be found in *Clinical Governance Advice No. 1: Guidance for the Development of RCOG Green-top Guidelines* (available on the RCOG website at <a href="www.rcog.org.uk/clingov1">www.rcog.org.uk/clingov1</a>). These recommendations are not intended to dictate an exclusive course of management or treatment. They must be evaluated with reference to individual patient needs, resources and limitations unique to the institution and variations in local populations. It is hoped that this process of local ownership will help to incorporate these guidelines into routine practice. Attention is drawn to areas of clinical uncertainty where further research may be indicated.

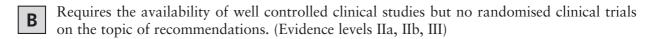
The evidence used in this guideline was graded using the scheme below and the recommendations formulated in a similar fashion with a standardised grading scheme.

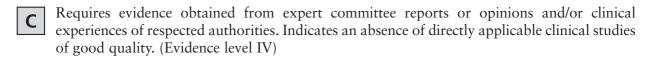
## Classification of evidence levels

- Ia Evidence obtained from meta-analysis of randomised controlled trials.
- Ib Evidence obtained from at least one randomised controlled trial.
- IIa Evidence obtained from at least one well-designed controlled study without randomisation.
- IIb Evidence obtained from at least one other type of well-designed quasi-experimental study.
- III Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.
- IV Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities.

## **Grades of recommendations**







# Good practice point

Recommended best practice based on the clinical experience of the guideline development group.

This Guideline was produced on behalf of the Royal College of Obstetricians and Gynaecologists, and the Association of Genitourinary Medicine and Medical Society for the Study of Venereal Diseases (AGM/MSSVD) by:

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The final version is the responsibility of the Guidelines and Audit Committee of the RCOG

Valid until May 2006 unless otherwise indicated

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