Brighton and Sussex University Hospitals NHS Trust

Pelvic Inflammatory Disease

Protocol: GP003

Date Agreed: May 2017

Manager responsible:	VuiVun Wong
Author:	Rebecca Tidswell
Protocol Title:	Pelvic Inflammatory Disease (PID)
Protocol Number:	GP003
Version number:	3
Approving Committee:	Women's Quality and Safety Committee
Date agreed:	May 2017
Amended Date:	March 2017, September 2017
Review Date:	March 2020

Contents

KEY PRINCIPLES

These guidelines and algorithms are aimed to assist in decision making. They are not designed to be prescriptive and you are not expected to use them in exclusion of discussions with senior colleagues.

Evidence used to inform these guidelines had been drawn from RCOG, BASHH or NICE guidelines. Where applicable other references are quoted.

SCOPE

This guideline applies to women attending with suspected pelvic inflammatory disease, which may be managed as an inpatient or outpatient. It covers recommendations on diagnosis, treatment, and health promotion principles required for effective management.

RESPONSIBILITIES

Gynaecologists, Nurses & Midwives:

- To access, read, understand and follow this guidance
- To use their professional judgement in application of this guidance

Management:

- To ensure the guideline is reviewed as required in line with Trust and national recommendations
- To ensure the guideline is accessible to all relevant staff

1.0 Objective Standards

1.1 Definition

The clinical syndrome associated with ascending infection from the endocervix, causing endometritis, parametritis, oophoritis, tubo-ovarian abscess, and/or pelvic peritonitis.

1.2 Epidemiology

The incidence of PID is unknown and probably grossly underestimated as figures are either based on inpatient episodes or cases treated in GUM outpatients. Many cases are treated in primary care and ~50% women have sub-clinical or unrecognised disease. It is estimated to account for 1:60 GP visits by females under 45 years.

Rates are probably increasing, reflecting increasing incidence of sexually transmitted diseases, particularly Chlamydia. Behavioural factors that increase the risk of sexually transmitted infections (STIs), such as younger age at first sexual intercourse, multiple sexual partners, and frequency of partner change, are all associated with increased risk of PID.

1.3 Pathogenesis

PID is commonly initiated by an STI, which predisposes to further colonisation by organisms that would normally be non-pathogenic. The isolation of anaerobes tends to be associated with more severe disease and anaerobes are invariably present in tubo-ovarian abscesses. The risk of PID is also increased by other factors that breech cervical host defences, such as IUCD insertion, childbirth, miscarriage, surgical procedures, and TOP.

2.0 Isolation Rates

- **Chlamydia trachomatis:** 40% (14-65%) using EIA, DIF & culture (higher with NAATs)
- **Neisseria gonorrhoea:** 14%
- **Anaerobes:** 60%

- **Mycoplasma:** 10-15%
- **No organisms isolated**: 25-50%

Complications

- **Infertility** (risk after 1 episode 8%, 2 episodes
- 9.5%, 3 episodes 40%),
- **Ectopic pregnancy** (9.5 times more likely)
- **Chronic pelvic pain** (9.8 times more likely)

With each infection, host defences become increasingly damaged and the risk of complications rises with each subsequent insult.

3.0 Diagnosis

PID may be symptomatic or asymptomatic. Even when present, clinical symptoms and signs lack sensitivity or specificity (positive predictive value of a clinical diagnosis is 65-90% compared to laparoscopic diagnosis).

Testing for gonorrhoea and chlamydia in the lower genital tract is recommended since a positive result support diagnosis. The absence of infection at this site does not exclude PID however.

An elevated ESR or CRP also supports diagnosis but is non-specific
The absence of endocervical or vaginal pus cells has a good negative predictive value (95%) for a diagnosis of PID but their presence is non-specific (poor positive predictive value - 17%)

3.1 Sexual History

- The number of sexual partners within the last 3 months
- The duration of each relationship
- The date of last sexual intercourse with each partner
- Whether barrier contraception used within each relationship

4.0 Clinical Features

The following features are suggestive of a diagnosis of PID

4.1 Symptoms

- Lower abdominal pain, usually bilateral
- Deep dyspareunia
- Abnormal vaginal bleeding, including post coital, inter-menstrual and menorrhagia
- Abnormal vaginal or cervical discharge, which is often purulent

4.2 Signs

- Lower abdominal tenderness, which is usually bilateral
- Adnexal tenderness on bimanual vaginal examination
- Cervical motion tenderness on bimanual vaginal examination
- Fever >38°C

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

4.2.1 Complicating **Factors**

- **IUCD** - Removal of IUCD should be considered and may be associated with better short term clinical outcomes. The decision to remove the IUCD should be balanced against the risk of pregnancy in those who have had otherwise unprotected intercourse in the preceding seven days. Hormonal emergency contraception may be appropriate for some women in this situation
- **HIV** - women with HIV may have more severe symptoms associated with PID, but respond well to standard antibiotic therapy. No change in treatment regime is required.
- **Fitz-Hugh-Curtis Syndrome** - this comprises right upper quadrant pain associated with perihepatitis. Although laparoscopic division of hepatic adhesions has been performed, there is insufficient clinical trial evidence to make specific recommendations for treatment beyond those for uncomplicated PID

5.0 Investigations

- Urinalysis, including pregnancy test
- Bloods, including FBC and CRP
- Observations, temperature
- Routine swabs
    - Endocervical Chlamydia & gonorrhoea
    - High vaginal swab (black charcoal)
- Pelvic Ultrasound, particularly if symptoms/signs of moderate/severe disease

6.0 Management

It is likely that delaying treatment increases the long term sequelae, such as ectopic pregnancy, infertility and chronic pelvic pain. Therefore, a low threshold for empiric treatment is recommended. Broad spectrum antibiotics are required to cover N. gonorrhoeae, C. trachomatis and a variety of anaerobic and aerobic bacteria commonly found in the upper genital tract in women with PID.
Treatment must be effective (>95% cure rate), easy to take, have low side effects, and be given promptly.

If gonococcus diagnosed on NAATs the patient should be reviewed by genitourinary medicine so cultures can be taken for gonorrhoea & contact tracing carried out. Please contact the liaison Health Advisor on 07789 995086 or ext. 4716

6.1 Outpatient Management

Patients seen in A&E and treated as outpatient must be provided with emergency drug packs.

6.2 Inpatient Management

If any of the following features are present, consider admission, IV antibiotics and/or laparoscopy:

- Severe or atypical disease
- Temp> 38^{O}C
- Nausea & vomiting,
- Peritonism
- WBC >15

- Pregnant or adolescent patient
- If the diagnosis is uncertain, pelvic abscess suspected or there is a possibility of a surgical emergency
- If the patient has not responded to out-patient therapy, or is intolerant to oral therapy

6.3 General Advice

- Rest advised for those with severe disease.
- Both patient and partner should abstain from sexual contact until completion of treatment and review
- Explanation of the treatment and its possible adverse effects
- Patient must avoid alcohol if being treated with metronidazole
- Potential OCP interactions with antibiotics (advise to abstain from sexual contact whilst on antibiotics)
- Importance of compliance to treatment
- Importance of follow up
- All patients must be asked to give consent for follow up for themselves and sexual contacts.
- It is essential that sexual partners also receive treatment, whether or not an organism is identified on tests (they should contact CNC for treatment)

7.0 Patient information

Ensure patients receive patient information leaflet - click here for RCOG leaflet (https://www.rcog.org.uk/globalassets/documents/patients/patient-information-leaflets/gynaecology/pi-acute-pid.pdf).

We should discuss long term sequelae of PID with the patient, including the following:

- Following treatment, fertility is usually maintained but there remains a risk of future infertility, chronic pelvic pain or ectopic pregnancy
- Clinically more severe disease is associated with a greater risk of sequelae
- Repeated episodes of PID are associated with an exponential increase in the risk of infertility
- The earlier treatment is given, the lower the risk of future fertility problems
- Future use of barrier contraception will significantly reduce risk of PID
- The need to screen/treat her sexual contacts for infection to prevent her becoming re-infected

8.0 Analgesia

All patients should be offered adequate analgesia and anti-emetics eg:

- Metoclopramide oral / IM 10mg TDS or cyclizine 50mg IM/PO TDS
- Ibuprofen 400mg TDS
- Paracetamol oral / IV 1g QDs

9.0 Antibiotic Treatment Regimens

9.1 Antibiotic guidance

1st Line	Penicillin Allergy
Outpatient	
Non-pregnant	Ofloxacin oral 400mg bd for 14 days + Metronidazole oral 400mg bd for 5 days
Pregnant Or Ofloxacin Contraindicated	Ceftriaxone 500mg IM stat (omit if penicillin allergy, IgE mediated e.g anaphylaxis, if gonococcus diagnosed on NAAT, discuss with GUM) + Clarithromycin oral 500mg bd for 14 days + Metronidazole oral 400mg bd for 5 days
Inpatient	
Non-Pregnant	Ceftriaxone IV 2g od for 14 days (omit if penicillin allergy, IgE mediated e.g anaphylaxis, if gonococcus diagnosed on NAAT, discuss with GUM) + Ofloxacin IV 400mg bd for 14 days + Metronidazole IV 500mg tds for 14 days
Pregnant Or Ofloxacin Contraindicated	Ceftriaxone IV 2g od for 14 days (omit if penicillin allergy, IgE mediated e.g anaphylaxis, if gonococcus diagnosed on NAAT, discuss with GUM) + Clarithromycin IV 500mg bd for 14 days + Metronidazole IV 500mg tds for 14 days

*UK gonorrhoea resistance to quinolones in heterosexual women is about 15% therefore if patient is high risk for gonorrhoea (patient's partner has gonorrhoea, clinically severe disease, following sexual contact abroad), discuss alternative regimens with genitourinary medicine.

9.2 Penicillin Allergy

Reaction	Which antibiotic can be given		
	Penicillin	Cephalosporin	Other beta-lactams
Anaphylaxis	No	No	No
Urticaria	No	No	No
Pruritic rash (immediate)	No	No	No
Laryngeal oedema/ angioedema/bronchospasm	No	No	No
Minor rash (non- confluent, non-pruritic, restricted to small area of the body)	With caution in serious infection	Yes	Yes
Rash occurring > 72 hours post penicillin exposure	With caution in serious infection	Yes	Yes
Nausea, vomiting, diarrhoaea	Yes	Yes	Yes

9.3 IV TO ORAL SWITCH

IV antibiotics should be switched to oral equivalents and complete 14 days after 48 hours if:-

- Temperature < 38℃ for at least 24 hours
- Clinical improvement observed
- WCC & CRP improving
- Haemodynamically stable
- Oral route viable (no evidence of malabsorption, vomiting or unsafe swallow)

10.0 NICE guidance on drug choice during very early pregnancy (before a positive pregnancy test)

- **PARACETAMOL**: experience suggests this can be used at any time during pregnancy or breastfeeding [NTIS, 2004; Schaefer et al, 2007].
- **NSAIDS:** The UK Teratology Information Service (UKTIS, formerly the National Teratology Information Service [NTIS]), reviewed safety data of NSAIDs from

published research and post marketing surveillance systems. They concluded that 'the available data do not indicate that exposure to ibuprofen before 30 weeks of pregnancy is associated with an increased risk of congenital defects or spontaneous abortions' [NTIS, 2004].

- **ANTIBIOTICS**: The RCOG recommends that the risk of giving any of their recommended antibiotic regimens in very early pregnancy (before a positive pregnancy test) is low, since significant drug toxicity results in failed implantation [RCOG, 2009], and BASHH states that the risk of giving any of the recommended antibiotic regimens in very early pregnancy (prior to a pregnancy test becoming positive) is justified by the need to provide effective therapy and the low risk to the fetus [BASHH, 2011a].
- **CEFTRIAXONE** has not specifically been studied during pregnancy. However, the risk associated with use of cephalosporins during pregnancy is thought to be low and, although data are limited for individual agents such as ceftriaxone, the cephalosporins as a class are considered to be an appropriate choice during pregnancy [NTIS, 2008b]. Although ceftriaxone crosses the placental barrier, it has not been associated with adverse events on fetal development in laboratory animals [ABPI Medicines Compendium, 2009].
- **DOXYCYCLINE** is contraindicated beyond the 15th week of gestation because, from the 16th week of pregnancy it causes tooth and bone discolouration and inhibits bone growth. However, it can be used in the first trimester. Inadvertent first-trimester use of tetracyclines occurs frequently and has not been associated with an increased risk of congenital malformations [Schaefer et al, 2007].
- **METRONIDAZOLE** has been in clinical use for a long time, and experience suggests that it is not teratogenic in humans [Schaefer et al, 2007]. A recent prospective controlled study in 228 women exposed to metronidazole in pregnancy, 86% of whom had first trimester exposure, confirms these findings [Schaefer et al, 2007].
- **OFLOXACIN** has only limited pregnancy-exposure data. Quinolones have caused arthropathy in animal studies. However, a recent study (most of the data are on ciprofloxacin and norfloxacin, but some are on ofloxacin) did not find that quinolone use in the first trimester of pregnancy was associated with an increased risk of malformations or other adverse effects on pregnancy outcome [Schaefer et al, 2007].
- There are fewer published data on the use of **AZITHROMYCIN** rather than **ERYTHROMYCIN** during pregnancy and breastfeeding. The limited published data and follow-up data collected by the UK Teratology Information Service (UKTIS, formerly the National Teratology Information Service [NTIS]), do not

demonstrate an increased risk of congenital malformations following exposure to azithromycin in human pregnancy [NTIS, 2008a].

11.0 IUCD and PID

Removal of IUCD should be considered and may be associated with better short term clinical outcomes. The decision to remove the IUCD should be balanced against the risk of pregnancy in those who have had otherwise unprotected intercourse in the preceding seven days. Hormonal emergency contraception may be appropriate for some women in this situation (BASHH).

11.1 NICE guidance on IUCD and PID:

Evidence on whether or not to remove intrauterine contraception in a woman who has pelvic inflammatory disease (PID) is limited and conflicting. There are no long term data on the effects on fertility.

Expert opinion differs regarding the management of women with PID who have intrauterine contraception:

- **The Faculty of Sexual and Reproductive Healthcare** (FSRH), does not routinely recommend the removal of intrauterine contraception. The Faculty's Clinical Effectiveness Unit supports the continued use of intrauterine contraception and appropriate antibiotic treatment if PID is suspected; there is no need to remove the device unless symptoms fail to resolve within 72 hours, or the woman wants it removed [FFPRHC, 2006; FSRH, 2007].
- **The Royal College of Obstetricians and Gynaecologists** [RCOG, 2009] advises that consideration should be given to removing the device, especially if symptoms have not resolved within 72 hours.
- **The British Association for Sexual Health and HIV** recommends considering removing the device if the woman develops PID. They advise balancing the decision to remove the device against the risk of pregnancy if the woman has had sexual intercourse in the preceding 7 days [BASHH, 2011a].
- **The World Health Organisation** - selected practice recommendations for contraceptive use state that [WHO, 2004]:
    - There is no need for removal of the intrauterine contraception if the woman wishes to continue its use.
    - If the woman wishes removal, it should be removed after antibiotic treatment has been started.
    - If the infection does not improve, generally the course would be to remove the device and continue antibiotic treatment. If the device is not removed, the antibiotic should also be continued. In both cases the woman should be monitored closely.

12.0 Follow Up

All patients with a suspected diagnosis of PID should be referred to the liaison health advisors at the Claude Nicole Centre (CNC) (This involves faxing the PID proforma to 01273 664720).

For moderate to severe disease treated as an outpatient, patients should be re-assessed at 48h and be investigated further if not responding to treatment. This should be undertaken by the gynaecology team.

For patients who require prolonged inpatient stays or with severe disease, review by the health advisors may be possible on the ward.

All patients will be reviewed at two weeks, by CNC, to assess:

- Treatment compliance for both her and current sexual partner
- Clinical progress
- Whether patient has had sexual intercourse before review
- Whether partner(s) have received treatment
- To address any concerns the patient may have
- To re-iterate safer sex messages

13.0 Training

Please refer to the Training Needs Analysis document for details on staff training in relation to this protocol.

14.0 Monitoring Compliance

Please refer to the Monitoring and Auditing document for details on monitoring compliance for this protocol

15.0 References

The guidance in this document is based on best practice and current RCOG clinical guidelines

http://www.rcog.org.uk/files/rcog-corp/uploaded-files/T32PelvicInflamatoryDisease2008MinorRevision.pdf.
http://www.bashh.org/documents/3205
http://www.ffprhc.org.uk/admin/uploads/CEUGuidanceDrugInteractionsHormonal.pdf

National Teratology Information Service – personal communication 7th August & 7th September 2009

In addition some primary research has been used

1. Weström L, Joesoef R, Reynolds G, Hagdu A, Thompson SE. Pelvic inflammatory disease and fertility. A cohort study of 1,844 women with laparoscopically verified disease and 657 control women with normal laparoscopic results. *Sex Transm Dis.* 1992; **19**(4): 185-92
2. Westrom L. Effect of pelvic inflammatory disease on fertility. *Venereology.* 1995; **8**(4): 219-22
3. Adler MW, Belsey EH, O'Connor BH. Morbidity associated with pelvic inflammatory disease. *Br J Vener Dis.* 1982;**58**(3):151-7
4. Management of PID (2011) British association for sexual health and HIV. http://www.bashh.org/guidelines