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أستاذ المادة : م.د. آلاء شلال فرحان

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اسم المحاضرة التاسعة والعشرون باللغة الإنكليزية: Pelvic inflammatory disease:

محتوى المحاضرة التاسعة والعشرون
Pelvic inflammatory disease

Pelvic inflammatory disease is characterized by inflammation and infection leading to endometritis, salpingitis, oophoritis, pelvic peritonitis and subsequently formation of tubo-ovarian and pelvic abscesses.

Pelvic infection is common and usually results from sexually transmitted pathogens ascending from the lower to upper genital tract. Infection can also occur following pelvic surgery, in the puerperium and after instrumenting the uterus. Chlamydial and gonococcal infections are commonly implicated, however, other organisms may be identified.

Pelvic inflammatory disease (PID) is important because it can have serious long-term sequelae such as pelvic pain, ectopic pregnancy and infertility.

It is the result of post-infection scarring that is normally associated with healing. The virulence of the infection and the host-immune factors both determine the extent of the damage caused. There may be complete tubal closure, extensive peritubal adhesions, intratubal adhesions and mucosal and ciliary damage, all of which can cause ectopic pregnancy and infertility (including interference with ovum transport and sperm migration).

Epidemiology and risk factors

The incidence of PID is unknown, as many cases go unnoticed until investigations for infertility are performed. Approximately 1 in 60 consultations in general practice is for women less than 45 years for suspected PID.

Pelvic inflammatory disease (PID) is a major cause of morbidity in young women, although its incidence in primary and secondary care has been falling for several years. About 2% of young women in the UK give a history of PID when asked, and about 1 in 50 consultations made by young women with general practitioners relate to PID.

The risk factors for PID strongly reflect those of any sexually transmitted infection (STI) – young age, lack of condom use, lower socioeconomic status and Black Caribbean/Black African ethnicity. Cervical mucus provides an important barrier to ascending infection. Young women with anovulatory cycles have thinner cervical mucus and this, combined with higher rates of cervical ectopy may account for their high rates of PID. The ability of the immune response to control and contain infection will also determine the risk of upper genital tract involvement.

Differences in behaviour have been linked to the risk of PID. A clear association can be seen between vaginal douching and PID but more recent longitudinal studies suggest that douching does not cause PID; rather, it would appear that the vaginal discharge and menstrual irregularities associated with PID may themselves lead to more douching. Women who smoke are at higher risk of PID but it is unclear whether this is a marker for high-risk sexual behaviour or a direct effect of smoking itself on immune surveillance.

Many women with PID also have bacterial vaginosis with overgrowth of the normal commensal bacteria in the vagina and loss of vaginal lactobacilli. These same vaginal commensal bacteria are often isolated from the upper genital tract, raising the possibility that bacterial vaginosis may lead to PID. Longitudinal studies do not support a direct causal association, although women who contract gonorrhoea or chlamydia are at higher risk of PID if they also have pre-existing bacterial vaginosis, suggesting some synergy between the different infections.

Aetiology

Pelvic inflammatory disease is a polymicrobial infection. *Neisseria gonorrhoeae* and *Chlamydia trachomatis* are the most frequently recognized pathogens but a wide variety of other bacteria and viruses can also be isolated from the fallopian tubes of women with PID.

Other factors associated with PID include:

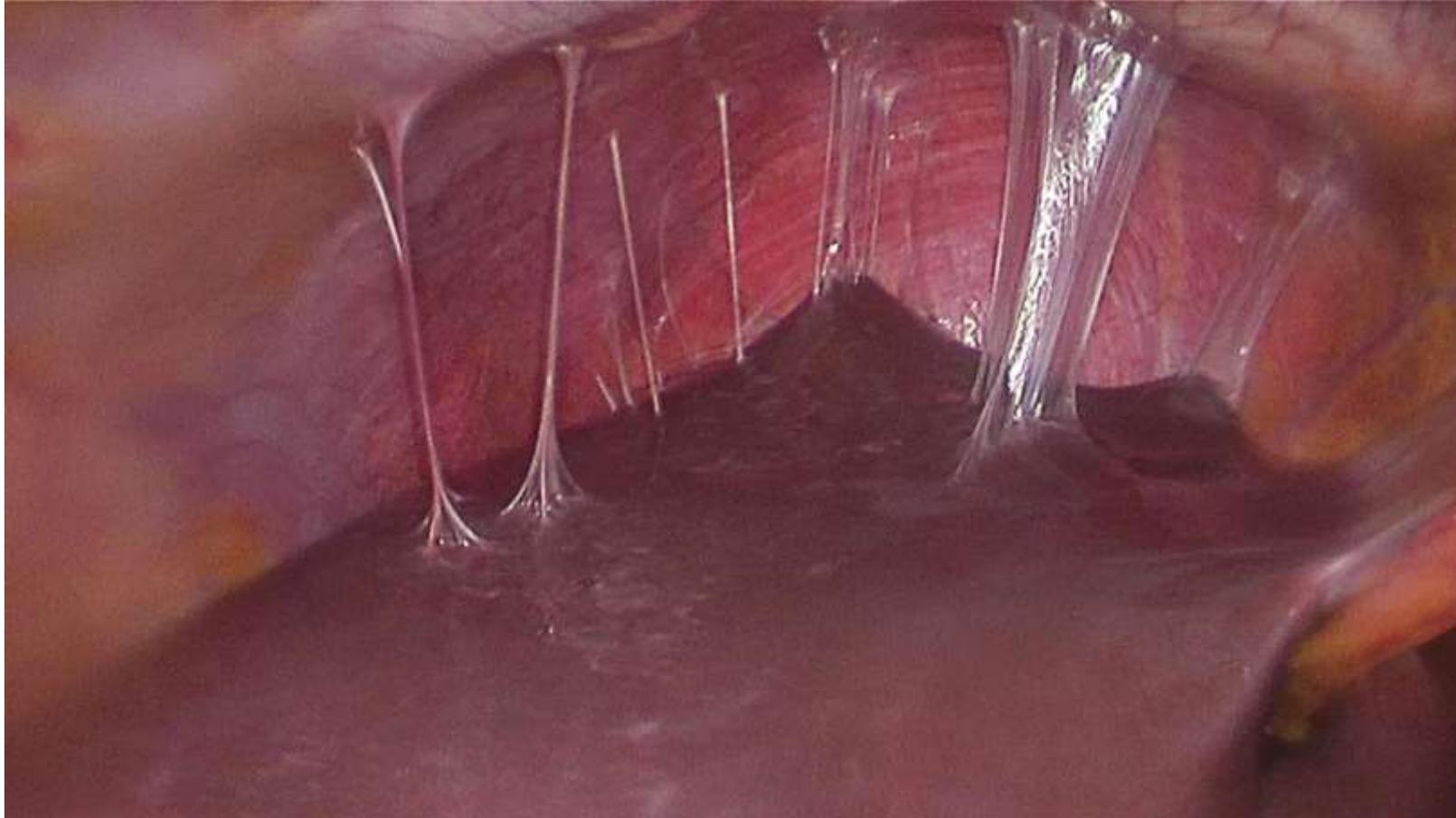
- 1.Young age (<25 years).
- 2.Past history of STI.
- 3.Termination of pregnancy.
- 4.Insertion of an IUD in the previous six weeks.
- 5.Hysterosalpingography.
- 6.IVF procedure.
- 7.Postpartum endometritis.
- 8.Bacterial vaginosis.

Pathophysiology

Once the infection has ascended to the upper genital tract, the Fallopian tubes are commonly damaged. There is inflammation of the mucosal lining which, if progressive, will destroy the cilia within the Fallopian tube followed by scarring in the tubal lumen. This can cause pocketing within the lumen with partial obstruction and thus predispose to ectopic pregnancy. In severe infection, mucopurulent discharge exudes through the fimbrial end of the Fallopian tube causing peritoneal inflammation.

This can lead to scarring and adhesion formation between the pelvic structures. It can affect the ovary and form a tubo-ovarian abscess with distortion of the anatomy. Infections are usually contained by the omentum and frequently omental adhesions are seen in the areas affected. Chlamydia and gonorrhoea can also cause perihepatitis leading to adhesions between the liver and the peritoneal surface. This gives a typical violin string appearance at laparoscopy and is known as the Fitz–Hugh–Curtis syndrome. Fitz–Hugh–Curtis syndrome comprises right upper quadrant pain associated with perihepatitis, which occurs in up to 10–20 per cent of women with PID and may be the most obvious symptom. There is insufficient evidence to recommend laparoscopic adhesiolysis in this situation.

Fitz–Hugh–Curtis syndrome (Perihepatic adhesions)



Diagnosis

The clinical diagnosis of PID is based on the presence of lower abdominal pain, usually bilateral, combined with either adnexal tenderness or cervical excitation on vaginal examination.

A comprehensive medical history and examination including an accurate gynecological history may help to reach a diagnosis. A pelvic examination is essential and a speculum examination is useful for identifying lower genital tract inflammation and excluding foreign bodies in the vagina such as retained tampons. The poor specificity and associated low positive predictive value of this approach (65–90%) is justified because a delay in antibiotic therapy of even a few days may increase the risk of impaired fertility. The risks of giving antibiotics to a woman who turns out not to have PID are low, although important differential diagnoses first need to be excluded.

Other clinical features can support a diagnosis of PID but are not essential before starting empirical therapy:

1. Intermenstrual or post-coital bleeding, resulting from endometritis and cervicitis.
2. Deep dyspareunia..
3. Abnormal vaginal discharge, indicating lower genital tract infection.
4. Fever is non-specific and usually only present in moderate to severe PID.
5. Nausea/vomiting may occur in severe PID but is more commonly associated with appendicitis.
6. Tender adnexal or palpable pelvic mass, Generalized sepsis in severe and systemic infection.

PID caused by gonorrhoea presents more acutely and is more severe compared with chlamydial PID. Worth remembering that for every woman presenting with clinical features of PID there are two others who are asymptomatic.

Differential diagnosis

The features that classically lead towards a diagnosis of PID are the typical lower abdominal pain and bilateral tenderness on pelvic examination. In bowel-related disorders the pain tends to be higher in the abdomen and more central or to the left. Other conditions tend to give unilateral pain, at least at their onset. The main diagnoses to exclude are ectopic pregnancy and causes of an acute abdomen, which may require surgical intervention, such as appendicitis and ovarian 'accident' (e.g. torsion or persistent bleeding from a ruptured cyst).

If the diagnosis is not clear, then empirical treatment with antibiotics should be commenced, but the patient kept under close observation to ensure that an alternative diagnosis has not been missed. Rather like signs and symptoms, the investigations available to diagnose acute PID lack accuracy.

Investigation of suspected PID

Blood tests:

Such as a white cell count, erythrocyte sedimentation rate and C-reactive protein are all relatively non-specific. They may be elevated in PID but in mild cases can be normal. In particular, a leucocytosis is often not seen in non-pyogenic infections.

Note:

Raised white cell count (neutrophilia suggestive of acute inflammatory process)

Reduced white cell count (neutropenia in severe infections)

Raised C reactive protein and ESR (erythrocyte sedimentation rate) can support the diagnosis.

A urinary pregnancy test is mandatory to exclude an ectopic pregnancy. Ideally this should be performed before commencing empirical antibiotic treatment.

Microbiological tests :

Testing for gonorrhoea and chlamydia in the lower genital tract is recommended, as positive results support a diagnosis. However, the absence of infection at this site does not exclude PID. Absence of cultured organisms may be due to poor sampling technique, inadequate storage and/or transportation of swabs or the presence of organisms that cannot easily be cultured in the laboratory, such as mycoplasmas.

All women presenting with possible PID should be offered an NAAT to check for the presence of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* on a vulvo-vaginal swab. The alternative enzyme-linked immunosorbent assays lack sensitivity.

Testing for *Mycoplasma genitalium* is advisable and should be performed when available since it may alter the choice of therapy. The detection of gonorrhoea, chlamydia or mycoplasma in the lower genital tract greatly increases the likelihood of PID as the cause of lower abdominal pain, but many women with PID also have a negative infection screen from the lower genital tract.

A lack of polymorphs on a Gram-stained smear of cervical discharge makes PID unlikely but their presence is non-specific, i.e. the absence of polymorphs has good negative predictive value but their presence has poor positive predictive value for PID. Screening for other STIs should be offered to women who test positive for gonorrhoea or chlamydia, and to those who are at higher risk of infection (e.g. lack of condom use or previous history of an STI).

An appropriate screen would include:

1. NAAT for *Trichomonas vaginalis* from a vulvo-vaginal sample;
2. Endocervical swab for *N. gonorrhoeae* culture, which should be placed in transport medium (either Stuart or Amies) and arrive at the laboratory preferably within 6 hours but certainly within 24 hours, otherwise viability is rapidly lost;
3. HIV antibody test; and
4. syphilis serology.

Radiology investigations

Transvaginal ultrasound of the pelvis may be useful where there is diagnostic difficulty. However, there are no features that are pathognomonic of acute PID. Free fluid in the pouch of Douglas is a common normal finding and is therefore not helpful. The value of ultrasonography generally lies in helping to exclude other pathology such as ectopic pregnancy, ovarian cysts or appendicitis, although it can also identify dilated fallopian tubes or a tubal abscess. However, this investigation may not be readily available in an emergency setting.

MRI can assist in making the diagnosis where there is difficulty, but it is also not widely available and has not entered routine management. CT scanning in acute PID may show obscuring of the pelvic fascial planes, thickening of the uterosacral ligaments and accumulation of fluid in the tubes and endometrial canal. In the upper abdomen it can provide evidence of perihepatitis. Enhancement of the hepatic and splenic capsules on abdominal CT scan has been suggested as characteristic of Fitz-Hugh–Curtis syndrome but it is of little value as a routine investigation.

Surgical investigation

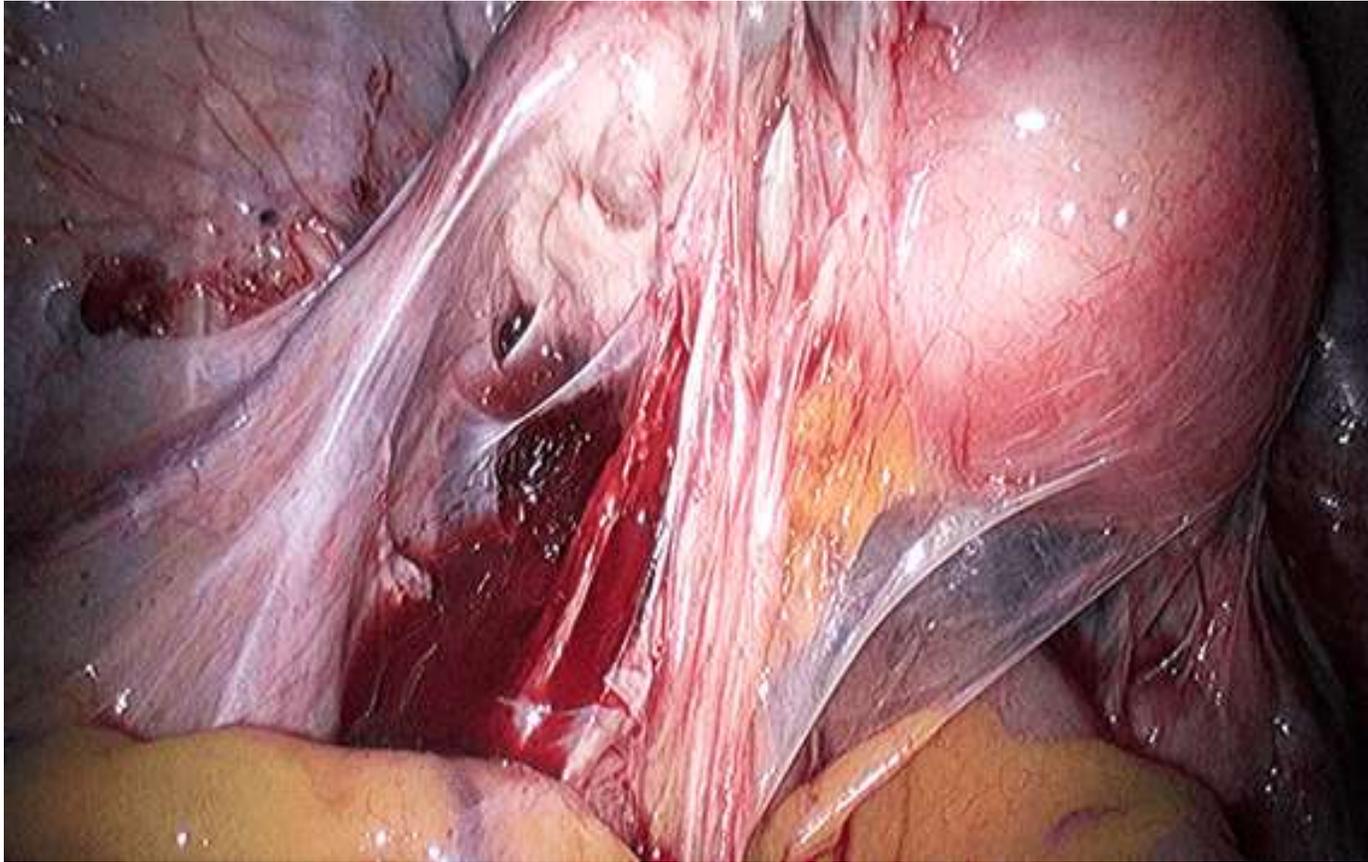
For many years the definitive diagnostic procedure for PID was considered to be laparoscopy and it probably remains more sensitive than any other investigation currently available. In many cases there will be clear evidence of dilated hyperaemic tubes with an inflammatory fibrinous exudate covering the tubes and the fundus of the uterus. In mild cases, however, intraluminal inflammation of the tubes may be missed and significant inter- and intra-observer variation in interpreting the appearance of salpingitis at laparoscopy has been reported. It does enable swabs to be taken from the fimbrial ends of the tubes, which may be more accurate than endocervical swabs, but the principal benefit of laparoscopy is to exclude other diagnoses.

As an invasive procedure it should be reserved for those cases where there is an element of doubt as to the diagnosis of acute PID or in cases where the patient fails to respond to antibiotics within 48–72 hours.

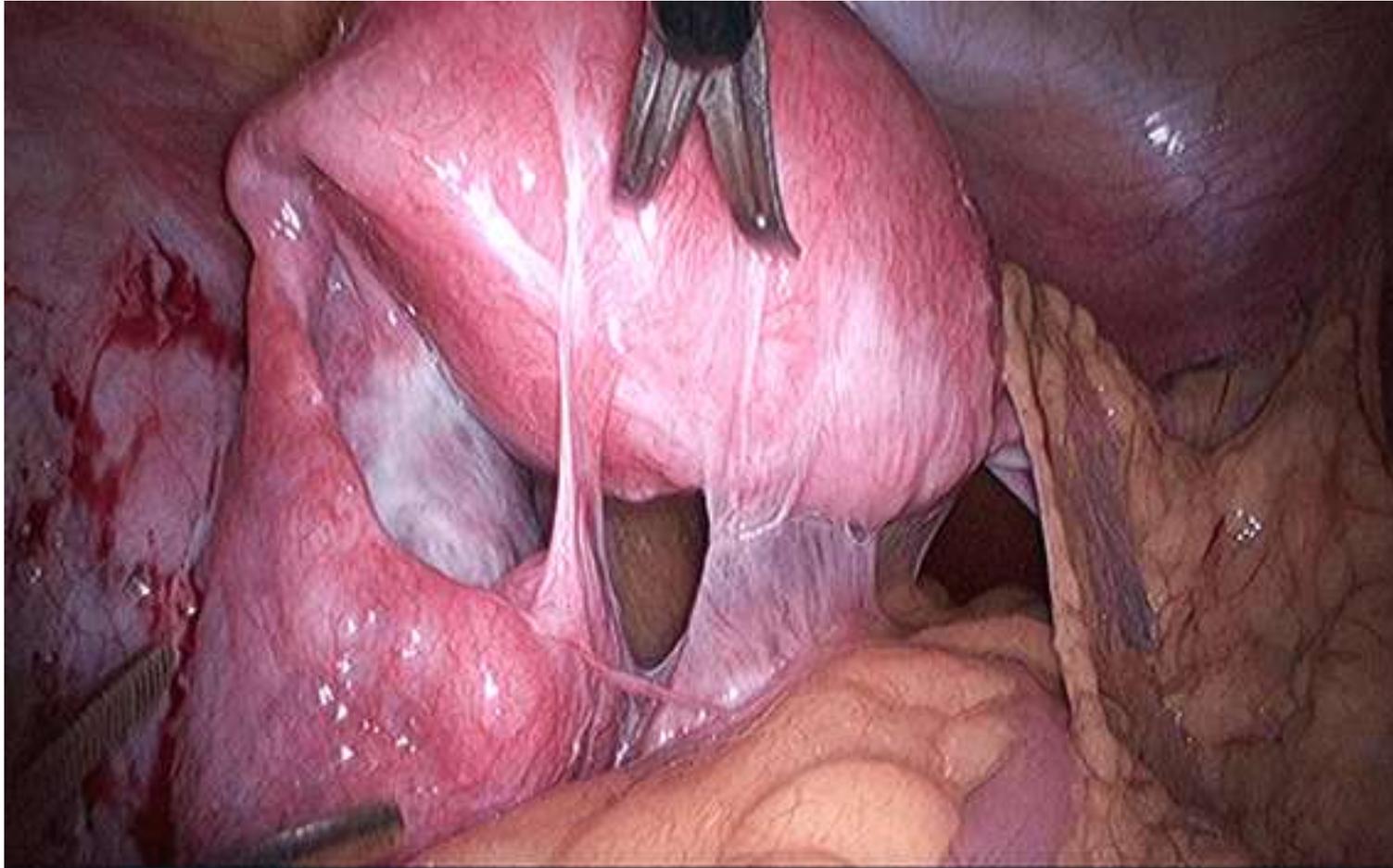
There is no evidence to support the routine use of hysteroscopy or endometrial biopsy in the diagnosis of acute PID. More invasive endoscopic techniques, such as fallaposcopy, may be potentially dangerous and have no place in management.

Laparoscopy may strongly support the diagnosis of PID, but is not justified routinely on the basis of cost and invasiveness. Furthermore, even laparoscopy lacks the sensitivity to identify mild intratubal inflammation or endometritis reliably. Endometrial biopsy and ultrasound scanning may also be helpful when there is diagnostic difficulty, but there is insufficient evidence to support their routine use at present.

Laproscopy show uterus, left tube and ovary buried in adhesions



Laparoscopy show adhesions between the uterus tubes and the intestine



Management

It is likely that delay in treatment increases the risk of the development of long-term sequelae of PID, such as ectopic pregnancy, pelvic pain and infertility. Owing to this, and to the lack of definitive diagnostic criteria, it is recommended that clinicians have a low threshold for treating empirically. It is also important that women are not labelled with the wrong diagnosis just because they appear to be in a high-risk group for having PID. Effort must be made to confirm the correct diagnosis, particularly in difficult or recurrent episodes of lower abdominal pain. It is also important in the gynaecological setting not to forget to investigate and treat the husband, in order to prevent reinfection.

General measures

Rest is advised for severe disease (preferably as an in-patient for observation to check that there is resolution of symptoms and signs).

A pregnancy test should be performed.

Appropriate analgesia is advised.

Parenteral therapy as an inpatient is advised for those with severe disease.

Patients should avoid sexual intercourse until they and their husbands have been fully treated and contact traced.

A full explanation should be given to the patient regarding the short- and long-term issues associated with PID. Leaflets to clarify and back up verbal explanation should be given to the client and her husband, if present.

All patients should be offered full STI screening and HIV testing at some point in the management. Good links with local GUM clinics are essential.

If no improvement is observed after 3 days of antibiotic therapy, then alternative diagnoses should be considered.

Antibiotic treatment

Broad-spectrum antibiotics are needed that will cover gonorrhoea and chlamydia. This treatment should be commenced as soon as possible. Information on recent and current medications should be obtained and appropriate advice given regarding any interactions. Latest evidence is that antibiotics (unless liver enzyme inducing e.g. rifampicin) do not affect the efficacy of hormonal contraception. There is a lack of evidence regarding antibiotic use and the prevention of long-term complications and fewer data on oral than parenteral regimens. There are important factors to be considered when choosing a regimen:

1. local antimicrobial sensitivities (especially gonorrhoea).
2. local epidemiology of infections (knowing where there are high-prevalence areas for gonorrhoea).
3. cost.
4. patient preference and likelihood of compliance.
5. severity of disease.

Depending on the severity of the infection, patients with mild/moderate disease can be managed on an outpatient basis with easy access to hospital admission if indicated.

When considering selection for inpatient treatment, the uncertainty of the diagnosis and severity of the disease will usually be sufficient to identify those who require inpatient observation. Other cases for which inpatient supervision is advised include women who have failed to respond to orally administered outpatient therapy, those who are suspected of having a tubo-ovarian mass and those who are unable to tolerate oral therapy. Two special subgroups might also be considered for inpatient treatment: those known to have an immunodeficiency problem (where a much more severe disease situation can develop quickly) and those who are pregnant – PID can occur up to about 12 weeks of pregnancy.

Recommended regimens

Outpatient antibiotic regimens:

Regimen 1

Ofloxacin 400 mg b.d. plus metronidazole 400 mg b.d. To complete 14 days of therapy.

Regimen 2

Moxifloxacin 400 mg once daily To complete 14 days of therapy.

Regimen 3

Ceftriaxone 500 mg i.m. immediately plus doxycycline 100 mg b.d. plus metronidazole 400 mg b.d. To complete 14 days of therapy.

Inpatient antibiotic regimens.

Regimen 1

Ceftriaxone 2: g i.v. daily plus i.v. or oral doxycycline 100 mg b.d. followed by* oral doxycycline 100 mg b.d. plus metronidazole 400 mg b.d.

Regimen 2:

Clindamycin 900 mg i.v. t.i.d. plus i.v. gentamicin 2 mg/kg loading dose followed by 1.5 mg/kg t.i.d. (a single daily dose may also be used) followed by oral doxycycline 100 mg b.d. plus metronidazole 400 mg b.d.

Regimen 3:

Ofloxacin 400 mg i.v. b.d. plus metronidazole 500 mg i.v. t.i.d. followed by oral ofloxacin 400 mg b.d. plus oral metronidazole 400 mg b.d.

Parenteral therapy should be continued until 24 hours after clinical improvement. Oral therapy to continue to complete 14 days of antibiotics in total.

Women with *M. genitalium*-associated PID should be treated with moxifloxacin. Quinolone resistance in gonorrhoea is common in many areas of the world and is rising in the UK. Ofloxacin or moxifloxacin should therefore be avoided if there is clinical suspicion of gonococcal PID as a result of, for example, clinically severe disease, a history of a partner with gonorrhoea, or sexual contact abroad. Oral metronidazole can be discontinued in those with mild to moderate PID if the patient is unable to tolerate it. If parenteral gentamicin is used, then serum drug levels and renal function should be monitored. A 'test of cure' to ensure resolution of the infection is required for women infected with *N. gonorrhoeae* (2 weeks after treatment) or *M. genitalium* (4 weeks after treatment).

Other important situations

Women with PID who are also infected with HIV should be treated with the same antibiotic regimens as women who are HIV-negative. Hospital admission and parenteral treatment is only required for those with clinically severe disease. Potential interactions between antibiotics and antiretroviral drugs should be considered.

The risk of giving any of the recommended antibiotic regimens in very early pregnancy (before a positive pregnancy test) is low, since significant drug toxicity results in failed implantation. Pregnant women should ideally receive IV therapy, as PID is associated with higher maternal and fetal morbidity. (However, PID in pregnancy is rare except for septic abortion.) None of the regimens above is of proven safety in this group. There is insufficient evidence in pregnant women to suggest one treatment over another as long as the appropriate organisms are covered for 14 days' treatment and this is parenteral, if possible.

Consideration should be given to removing an IUD in women presenting with PID, if symptoms have not resolved within 72 hours of starting antibiotics. The evidence for whether an IUD should be left in place or removed in women presenting with PID is limited. Removal of the IUD should be considered and may be associated with better short-term clinical outcomes, but the decision to remove it needs to be balanced against the risk of pregnancy in those who have had unprotected intercourse in the preceding seven days.

Emergency hormonal contraception may be appropriate for some women in this situation. Management of husbands should be by testing and treatment, ideally in a GUM clinic. Empirical treatment should be given. Broad-spectrum antibiotic treatment should be offered to husbands e.g. azithromycin 1 g single dose. They should avoid sexual intercourse until they have completed the treatment course.

Surgical treatment

Surgical intervention is rarely required as a treatment for acute PID. Most patients present at an early enough stage of the disease for antibiotic treatment to be fully effective. However, there may be an indication for laparoscopy or laparotomy to drain a pelvic abscess if this is diagnosed on ultrasonography and does not appear to be resolving with conservative antibiotic treatment. This may also exclude other causes of pain, such as appendicitis, endometriosis or ovarian pathology. The usual treatment would involve drainage of the abscess and sometimes the affected tube/ovary may have to be removed.

On the rare occasion when pelvic actinomyces is suspected, surgery should be avoided. The history is likely to be more chronic than in acute PID and there is usually clear clinical evidence of a pelvic mass which does not appear to be an abscess on ultrasound scanning. There is also usually a history of recent use of an IUCD. If surgery is performed, then there is a significant risk of bowel damage.

Management of Husbands

PID is usually secondary to a sexually acquired infection, so unless the husband either screened for infection or treated empirically, the woman with PID is at high risk of recurrence. Husbands should be offered screening for gonorrhoea and chlamydia. If screening for sexually acquired infections is not possible, then antibiotic therapy effective against gonorrhoea and chlamydia should be given empirically to the husbands.

The patients should be advised to avoid intercourse until both have either completed the treatment course or tested negative for STIs.

Follow-up

All patients should be followed up at three days to check improvement and exclude the need for parenteral or surgical treatment. Further review at four weeks is recommended to check resolution of symptoms, pregnancy test where appropriate and to discuss long-term issues. It is also an ideal time to check up on husband treatment.

Patient counselling

- Husband should be screened.
- There is a risk of reinfection if the husband is not treated.
- Use of barrier contraception will reduce the risk of further recurrences.
- Risks of tubal damage leading to subfertility, ectopic pregnancy and chronic pelvic pain which increases with further episodes of infection.
- Prompt and early treatment will reduce the risk of subfertility.
- Seek early medical advice if pregnant, due to the risk of an ectopic pregnancy.

Thank you