Pelvic inflammatory disease

Management of new-onset low abdominal pain in young women

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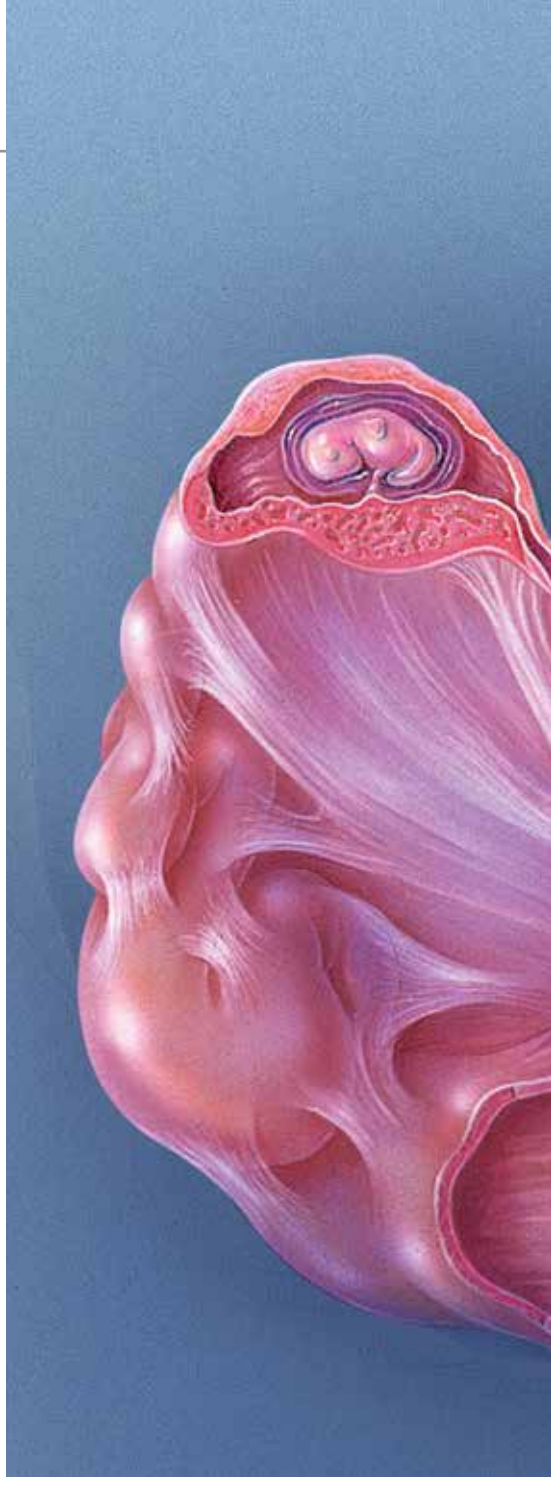
Pelvic inflammatory disease (PID) is a highly variable syndrome that should be considered in all young women presenting with new-onset low abdominal pain. Prompt antibiotic treatment is essential to prevent potentially serious complications. Tests are often negative for sexually transmitted infection but rapid clinical improvement with treatment supports the diagnosis of PID.



Pelvic inflammatory disease (PID) is an upper genital tract inflammatory syndrome of great variability, which presents with symptoms that range from mild and manageable in primary care to severe, requiring inpatient management. The diagnosis should be considered in all young women who present with new-onset low abdominal pain. Untreated PID can lead to serious sequelae, including tubal infertility, ectopic pregnancy and chronic pain, with the risk increasing significantly with repeat infections. Updated national management guidelines emphasise the clinical nature of the diagnosis and advise prompt initiation of treatment to prevent long-term damage to the fallopian tubes.[1]

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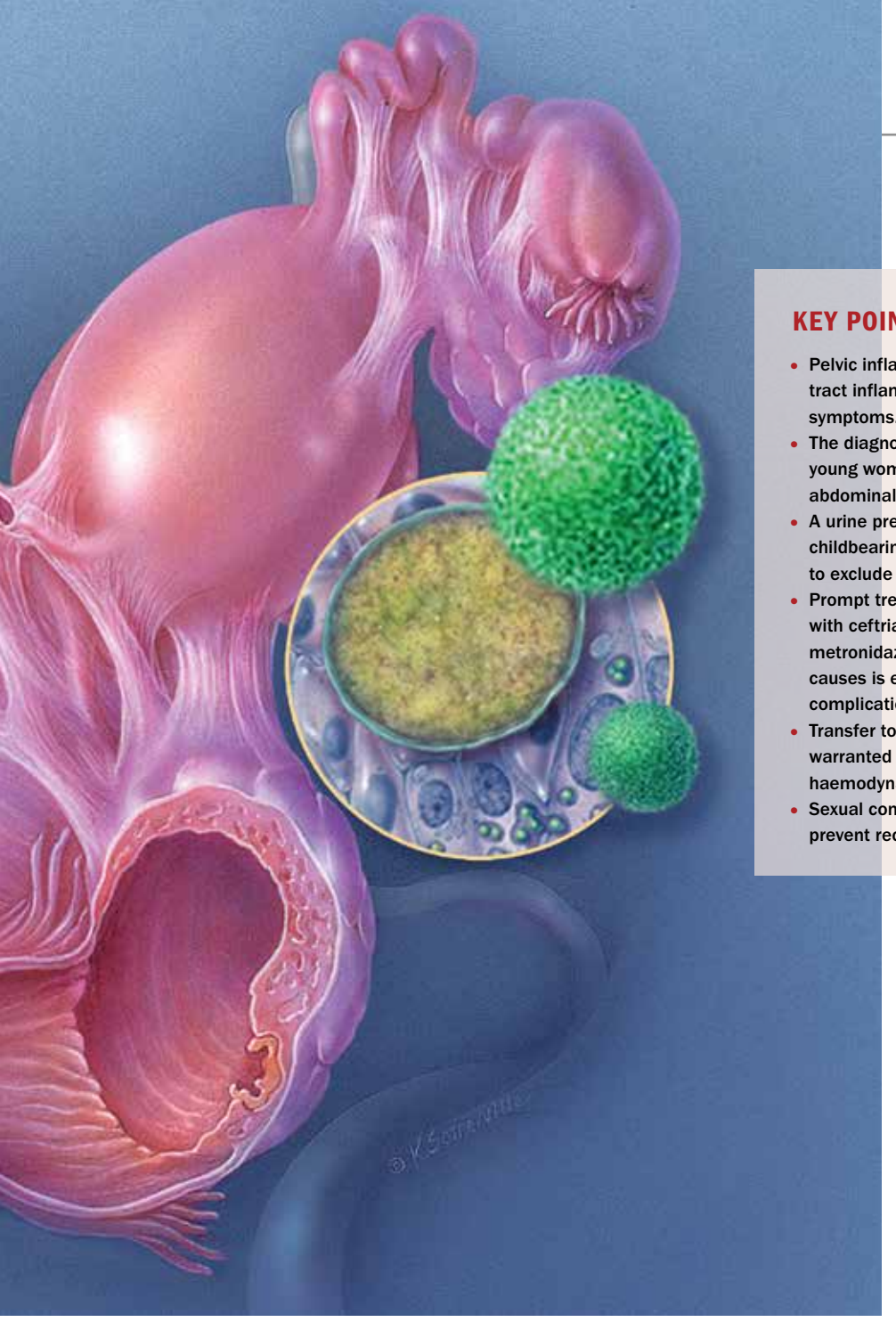
What is pelvic inflammatory disease?

PID is a syndrome comprising a spectrum of inflammatory disorders caused by infection ascending from the vagina or cervix to the pelvis. These disorders include endometritis, salpingitis, tubo-ovarian abscess and pelvic peritonitis. These disorders can vary in their severity from mild disease, which may go undiagnosed, to pelvic sepsis.[2] Generally, women with more severe symptoms tend to have more serious disease and an increased risk of long-term sequelae.[3] The long-term effects of PID include tubal infertility, ectopic pregnancy and chronic pelvic pain.[3-5]

Evidence suggests that up to 17% of women experience enough tubal damage from one episode of PID to become infertile and that the risk increases with each episode.[3-5] The risk of chronic pelvic pain



KEY POINTS

- Pelvic inflammatory disease (PID) is an upper genital tract inflammatory syndrome with highly variable symptoms.
- The diagnosis of PID should be considered in all young women who present with new-onset low abdominal pain.
- A urine pregnancy test is essential in all women of childbearing age with new-onset low abdominal pain to exclude ectopic pregnancy.
- Prompt treatment of women with suspected PID with ceftriaxone, azithromycin, doxycycline and metronidazole to cover the potential polymicrobial causes is essential to prevent long-term complications.
- Transfer to the nearest emergency department is warranted for women with severe symptoms or haemodynamic instability.
- Sexual contacts should be tested and treated to prevent recurrence of PID.

is increased fourfold by a recurrent episode of PID.[4] Delay in initiation of treatment is associated with increased rates of infertility and chronic pelvic pain.[5,6]

The incidence of PID is difficult to determine as the vast majority of women with PID are managed in outpatient ambulatory care, where data collection is more difficult.[7] The threshold for making a presumptive diagnosis of PID may vary between practitioners, and in some settings, such as among adolescents and in remote Australian communities, PID may be underdiagnosed.[8-10] PID accounted for approximately 0.05% of hospital admissions in NSW from 2001 to 2010, and the rate of hospitalisation for PID decreased over this period.[11] Likewise, the number of general practice encounters for PID has shown a decreasing trend among young women.[7]

Risk factors for pelvic inflammatory disease

The strongest risk factor for PID is young age.[12,13] Other risk factors for PID include a recent change of partner or having a partner with a sexually transmitted infection (STI) or symptoms suggestive of an STI. More rarely, PID can follow uterine instrumentation, such as a hysteroscopy or insertion of an intrauterine device (IUD). Note that the risk of infection is increased only in the first 20 days after an IUD is inserted, after which it returns to the woman's baseline risk of acquiring PID through sexual transmission.[14] It is important to be aware that PID can occur during pregnancy and although this is rare, it requires urgent attention to prevent serious outcomes for the woman and the pregnancy.

PID occurs almost exclusively in women who are sexually active. The upper genital tract infection is polymicrobial; disruption of the cervical mucous barrier allows vaginal or cervical organisms to ascend to the uterus and fallopian tubes. Organisms detected in cases of PID include anaerobes and other bacteria that are frequently present in the vagina. Organisms associated with bacterial vaginosis are particularly common, and bacterial vaginosis may have a role in the pathogenesis of PID.[15] *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and *Mycoplasma genitalium* are all

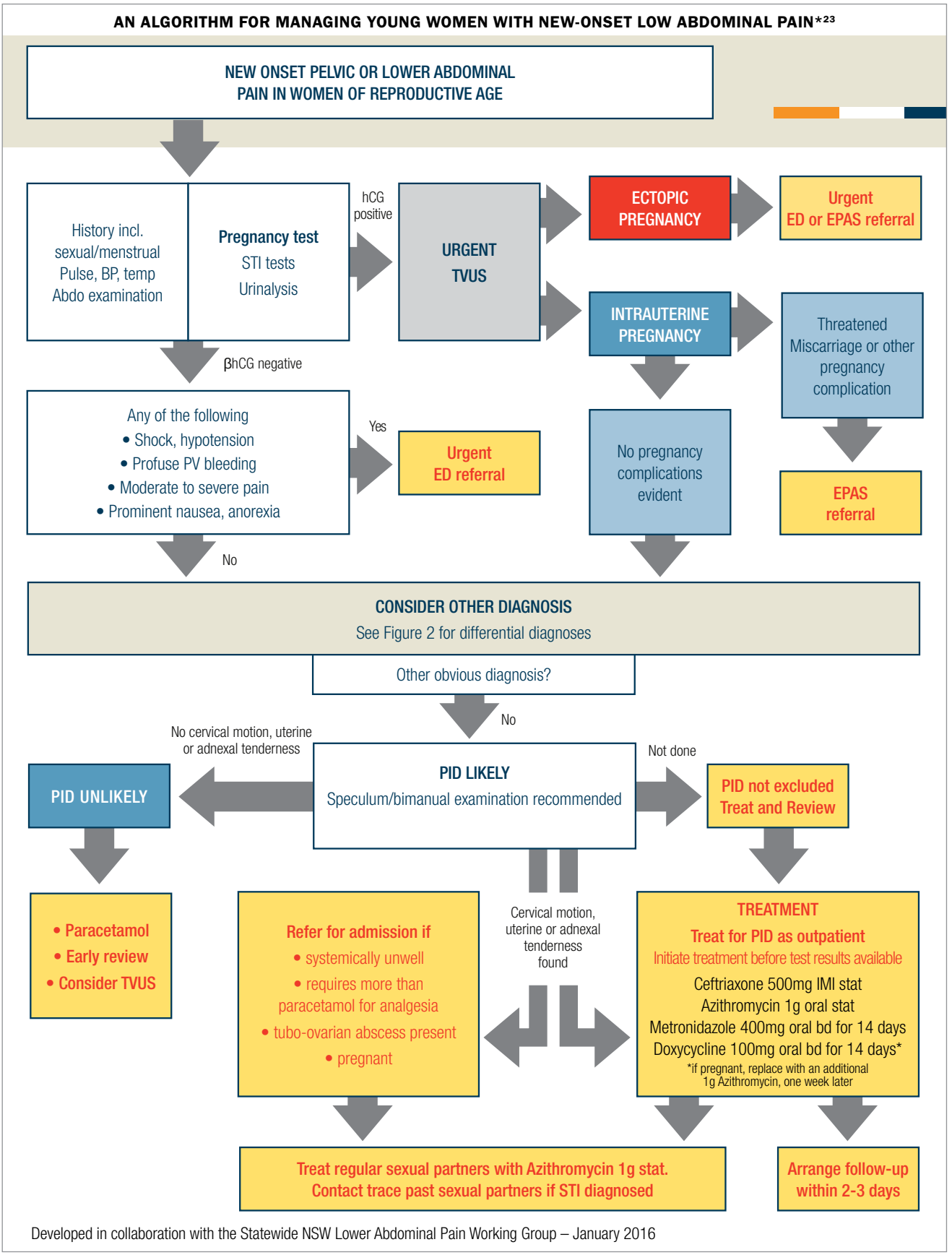


Figure 1. An algorithm for the management of new-onset low abdominal pain in young women*[23]

Abbreviations: Abdo = abdominal; bd = twice daily; BP = blood pressure; ED = emergency department; EPAS = early pregnancy assessment unit; hCG = human chorionic gonadotropin; IMI = intramuscular injection; PID = pelvic inflammatory disease; PV = per vagina; stat = immediately; STI = sexually transmitted infection; TVUS = transvaginal ultrasound.

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Common causes of low abdominal (pelvic) pain in women of reproductive age

This table is intended as a guide to assist with the diagnosis of a new onset of low abdominal (pelvic) pain among women of reproductive age but is not an exhaustive list. Note that concurrent diagnoses are common and may result in mixed signs and symptoms. Fever and raised WCC may be present among women presenting with acute pelvic pain from any cause, however these signs are non-specific and their presence or absence does not necessarily support or exclude a specific diagnosis.

DIFFERENTIAL DIAGNOSIS	TYPICAL PRESENTATION	FINDINGS THAT SUPPORT THE DIAGNOSIS	DEFINITIVE DIAGNOSTIC FINDINGS
MEDICAL EMERGENCIES			
Ectopic Pregnancy	• Pelvic pain and/or bleeding in the first trimester (typically 6 to 8 weeks) • Pain may localize to one side	• Positive pregnancy test • Empty uterus on ultrasound	Ectopic pregnancy identified on imaging and/or laparoscopy
Appendicitis	• Acute onset (hours to days) • Migration of pain from peri umbilicus to RIF • Systemic symptoms present: anorexia, nausea, vomiting	• Migration of pain from umbilicus to right iliac fossa • Onset of pain not associated with menses • McBurney's point site of maximal tenderness	Appendicitis confirmed on imaging, laparoscopic and/or histological findings
Ovarian cyst complications (rupture /torsion)	• Sudden onset of unilateral pelvic pain, more common in the right iliac fossa • May be associated with vaginal bleeding	• Adnexal mass felt on bimanual examination	Ruptured ovarian cyst identified on imaging and/or laparoscopy
OTHER CAUSES			
PID [1]	Typical pain: • Onset days to weeks and typically starts at the time of disruption of blood vessels [2] • Similar to period pain in character and distribution – initially bilateral but may localise to right or left iliac fossa • Deep dyspareunia • Pain may refer to RUQ [3] • Abnormal or inter-menstrual bleeding and/or vaginal discharge may be present	• Age 15 to 30 • Onset of pain typically occurs at the time of disruption of blood vessels [2] • No migration of pain from periumbilicus • Pain on moving the cervix • Rapid response to appropriate antibiotic treatment (within 7 days) Other findings that support the diagnosis but their absence does not exclude PID • *Chlamydia trachomatis, Neisseria gonorrhoeae* or *Mycoplasma genitalium* detected [4] • Muco-purulent cervical discharge on examination • Recent diagnosis of chlamydia, gonorrhoea or urethritis in the woman or a sexual partner • New partner in the last 6 months	Endometritis/Salpingitis and/or tubo-ovarian abscess identified at laparoscopy and/or on histology Causative organism(s) identified from pelvic fluid or endometrial samples
UTI	• Dysuria, frequency +/- suprapubic pain	• Dysuria, frequency and /or positive nitrites on urinalysis (Beware not to overdiagnose UTI based on urinary dip as this may be positive in the presence of PID)	Causative organism identified on urine culture
Pyelonephritis	• Pain ascends unilaterally from the suprapubic area through the iliac fossa to the renal angle • Systemic symptoms may be present	• Renal angle tenderness	
OTHER COMMON CAUSES OF PHYSIOLOGICAL OR CHRONIC PELVIC PAIN THAT MAY BE CONCURRENT OR NEED TO BE EXCLUDED			
Endometriosis	• Dysmenorrhoea • Pelvic pain similar in character and distribution to period pain but not confined to the first few days of menses • Deep dyspareunia • Bowel symptoms may be present • Typical chronic rather than an acute onset • Cyclical nature	• Pain does not respond to PID antibiotic treatment	Endometriosis identified by laparoscopic and/or histological findings
Mittleschmerz /Mid Cycle/ Ovulation pain	• Typically mild unilateral iliac fossa pain last a few hours to a few days	• Mid cycle of a regular menstrual cycle	
Physiological period pain	• Typically bilateral pelvic pain, onset with menstruation • Pain may refer to lower back /upper thighs	• Onset at the time of menstruation, last 1-2 days only	

FOOTNOTES [1] Pelvic Inflammatory Disease (PID) encompasses endometritis, salpingitis, tubo-ovarian abscess. Among pregnant women PID may present as pain and /or bleeding in 1st trimester (threatened or complete miscarriage) or post-partum (endometritis). [2] Menstruation, following rupture of membranes or instrumentation of the genital tract (e.g. TOP/ IUCD insertion). [3] Fitz Hugh Curtis syndrome. [4] It is a sexually transmitted condition although for various reasons no causative organism is detected in up to 70% of cases of PID

Figure 2. Differential diagnosis of low abdominal (pelvic) pain in women of reproductive age*[24]

Abbreviations: IUCD = intrauterine contraceptive device; PID = pelvic inflammatory disease; RIF = right iliac fossa; RUQ = right upper quadrant; TOP = termination of pregnancy; UTI = urinary tract infection; WCC = white cell count.

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associated with a diagnosis of PID.[16-18] The risk of PID in untreated chlamydial infection is approximately 9%, dropping to 1 to 2% when timely treatment of chlamydia is initiated.[16,19] It is important to note that in up to 70% of women with PID, a causal organism is not identified.[13,17]

How is pelvic inflammatory disease diagnosed?

Diagnosis of PID in general practice relies on history taking and physical examination, with secondary support from specific investigations. The gold standard for diagnosing PID involves laparoscopy, but this is reserved for complicated infections that fail to respond to standard management. Besides laparoscopy, there is no diagnostic test or algorithm that has both high specificity and sensitivity.[20,21] However, early treatment and clinical review for PID is important to avoid long-term sequelae and rarely delays an alternative significant diagnosis. Therefore, after exclusion of emergency differential diagnoses, GPs should be prepared to overdiagnose PID and to reconsider the diagnosis if the patient fails to respond to treatment.[21]

Treatment guidelines from the US Centers for Disease Control and Prevention recommend presumptive treatment for PID for sexually active young women and other women at risk of STIs if:[22]

- they are experiencing pelvic or lower abdominal pain and
- no cause for the illness other than PID can be identified and
- minimum clinical criteria are met (the presence on pelvic examination of any one of cervical motion tenderness or uterine tenderness or adnexal tenderness).

To aid prompt treatment of possible PID, an algorithm for the management of new-onset low abdominal pain in young women has been developed by the NSW PID Working Group in conjunction with the NSW STI Programs Unit (Figure 1).[23]

Given the potential seriousness of a diagnosis of ectopic pregnancy, it is essential that a urine pregnancy test is performed in all women of reproductive age who present with new-onset low abdominal pain. Women with a positive test in this context should be referred for immediate assessment of the location of the pregnancy, usually by transvaginal ultrasound examination. In most cases, this referral will be to the nearest emergency department.

Other emergency presentations include acute appendicitis and ovarian cyst complications. If a woman has hypotension, profuse vaginal bleeding, severe pain or prominent symptoms of nausea and vomiting, she should be immediately referred to an emergency department.

In a woman without symptoms of severe disease, GPs are able to consider the possible differential diagnosis of new-onset low abdominal pain aside from ectopic pregnancy. The main diagnoses can be differentiated by considering the history and examination findings. The differential diagnoses include:

- ovarian pathology – cyst rupture or torsion
- acute appendicitis
- urinary tract infection and pyelonephritis
- chronic conditions that may be concurrent or should be excluded – endometriosis, mid-cycle ovulation pain and dysmenorrhoea.

The main features of these differential diagnoses are shown in the table in Figure 2.[24]

History taking

It is important to take a comprehensive general medical history, as well as a menstrual and sexual history in women with new-onset low abdominal pain.

The pain of PID is generally mild to moderate and has usually been present for days to weeks before the woman presents to medical care. The pain is usually described as being like period pain and can radiate to the thighs. Pain may also be present in the right upper quadrant, indicating Fitz-Hugh-Curtis syndrome (inflammation of the perihepatic structures), which can be misdiagnosed as cholecystitis. Direct questioning may be required to elicit a history of deep dyspareunia, which is highly suggestive of pelvic inflammation. In contrast, the pain of appendicitis and ectopic pregnancy is usually more acute and radiates to the right iliac fossa (in appendicitis) or to one side (in ectopic pregnancy). Pyelonephritis generally presents with pain ascending to one flank and may be associated with symptoms of cystitis, frequency and dysuria.

A contraception, sexual and menstrual history are useful to determine whether pregnancy is likely. A recent change of sexual partner is a risk factor for PID. Symptoms of PID often begin after menstruation. Postcoital bleeding and a change in vaginal discharge are both features that may indicate cervicitis, which is highly supportive of the diagnosis of PID. Barrier contraception reduces the risk of PID and PID sequelae.[25] The recent insertion of an IUD may be associated with an increased risk.

Physical examination

After the woman's blood pressure and pulse rate are checked, the abdomen should be palpated to assess for tenderness, an enlarged uterus or any masses. It should be explained to the patient that a bimanual pelvic examination as well as a speculum examination are important to help determine the cause of the symptoms. Verbal consent to examination should be obtained, and male practitioners might consider the presence of a chaperone.

If speculum and bimanual pelvic examinations are not performed then treatment for PID should be commenced if the diagnosis of PID is considered highly likely based on history, risk factors and abdominal palpation or if no other diagnosis is obvious. Improvement in symptoms after the patient commences treatment supports a diagnosis of PID.

Bimanual pelvic examination

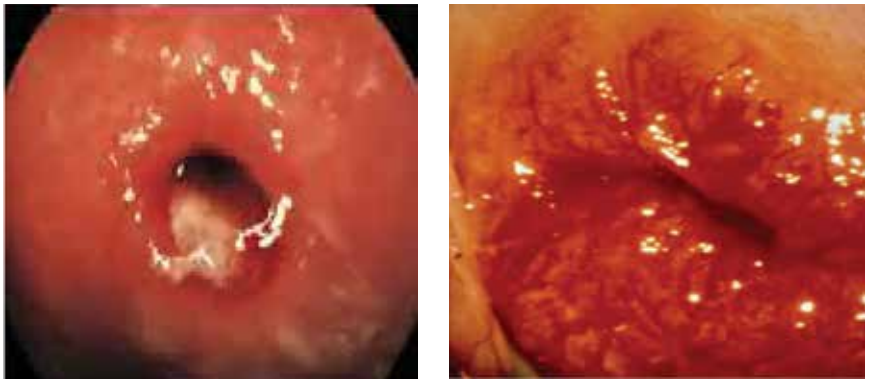
Bimanual pelvic examination is used to detect the presence of an enlarged uterus

or adnexal masses and to assess the location and severity of tenderness. It is especially important for eliciting cervical motion tenderness (sometimes termed cervical excitation) on rocking the cervix from side to side with two gloved fingers. Cervical motion tenderness indicates inflammation within the pelvis. In the absence of cervical motion, uterine or adnexal tenderness, the diagnosis of PID should be reconsidered.

Speculum examination

Insertion of a bivalve speculum allows visual assessment of the cervix and identification of any bleeding from the cervical os or a mucopurulent cervical discharge. A cervix that is inflamed, erythematous and friable to the touch is consistent with a diagnosis of cervicitis, the presence of which supports the diagnosis of PID (Figures 3a and b). For women with an IUD in situ, the presence and length of the IUD threads is important to note and, rarely, a partially expelled IUD stem may be visible and be the cause of the woman's pain.

Vaginal discharge may also be noted. A thin white discharge with a pH more than 4.5 and an amine odour is consistent with bacterial vaginosis, which may contribute to the development of PID.



Figures 3a and b. Signs of cervicitis that support the diagnosis of pelvic inflammatory disease. a (left). Mucopurulent discharge. b (right). Prominent ectropion and friability.

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Investigations

All young women with new-onset low abdominal pain should undergo a pregnancy test and STI tests.

Endocervical swabs can be taken at the time of the speculum examination; one swab is taken for *C. trachomatis* and *N. gonorrhoeae* nucleic acid amplification testing (NAAT; e.g. by polymerase chain reaction [PCR]) and an additional swab is recommended for a *M. genitalium* PCR test.[1] If a mucopurulent discharge is present then culture with antibiotic sensitivity testing can be considered for *N. gonorrhoeae*. In situations where a speculum examination is not performed, NAAT should be performed on a self- or clinician-collected vaginal swab or a first-pass urine specimen.

An additional high vaginal swab should be taken for microscopy, culture and sensitivity testing. The absence of leucocytes on a high vaginal swab makes the diagnosis of PID unlikely. A high vaginal swab may indicate the presence of bacterial vaginosis.

If urinary or renal symptoms are present then a clean catch midstream urine sample should be collected. The sample can be sent for microscopy and culture if leucocytes or nitrites are found on urinalysis. However, it is important to be aware of the potential for overdiagnosis of urinary tract infections based on the finding of leucocytes in the urine that are a contaminant from the genital tract.

Depending on the severity of symptoms and context of the consultation, blood tests (full blood count and electrolytes, urea and creatinine levels) may be clinically useful.

How is pelvic inflammatory disease treated?

If PID is clinically suspected then treatment should be initiated promptly, without waiting for test results.

New Australian STI management guidelines from the Australasian Sexual Health Alliance (ASHA) for the management of women with PID advise the use of a regimen that covers potential infection with *C. trachomatis* and *N. gonorrhoeae*, as well as polymicrobial vaginal flora.[1]

The antibiotic regimen for suspected PID comprises:

- ceftriaxone 500 mg in 2 mL of 1% lignocaine by intramuscular injection plus
- azithromycin 1 g orally immediately plus
- metronidazole 400 mg orally twice daily for 14 days plus
- doxycycline 100 mg orally twice daily for 14 days.

For women who are pregnant or breastfeeding, doxycycline can be replaced with a dose of azithromycin 1 g orally one week after the initial dose. This alternative regimen can also be used if noncompliance with the 14-day doxycycline course is likely. Treatment advice for women with drug allergies is available in the STI management guidelines.[1] For women with PID following a gynaecological or obstetric procedure, specialist advice is advised.

It is important to be aware of the potential for azithromycin resistance when *M. genitalium* is identified in women with PID. In proven *M. genitalium*-associated PID that does not respond to first-line treatment, a 14-day course of a fourth-generation non-PBS listed quinolone, moxifloxacin, is advised in consultation with the laboratory or the local sexual health clinic. If symptoms still fail to respond then referral to a sexual health physician is advised.

When symptoms are severe or fail to respond to treatment

Most women with PID can be successfully treated as outpatients.[26] Referral to the local emergency department for consideration of inpatient treatment is warranted if:

- symptoms are severe with systemic features
- tubo-ovarian abscess is suspected
- the woman is pregnant and has possible PID.

Inpatient care is also appropriate if there is a lack of response or intolerance to ambulatory treatment. As prompt resolution of symptoms with treatment is highly suggestive of a diagnosis of PID, referral for consideration of other causes is advised if symptoms persist despite adequate treatment.

If the symptoms of presumed PID fail to respond to first-line treatment then referral for a transvaginal ultrasound can be helpful.[27] Although features of PID on ultrasound examination are generally nonspecific, this investigation can be useful to exclude other diagnoses, such as ovarian cyst complications, and also to diagnose serious features, including a tubo-ovarian abscess. Ultrasound is the imaging technique of choice for young women presenting with low abdominal pain.[27]

Possible features of PID on ultrasound examination include:

- normal ultrasound appearance
- fluid in the pouch of Douglas
- thickening or increased vascularity of the fallopian tubes
- presence of a tubo-ovarian abscess.

General management strategies for suspected PID

It is essential to schedule a follow-up consultation two to three days after initiation of treatment for PID to ensure that the woman's condition is improving. Review on completion of the antibiotic course should also be organised to confirm the absence of any residual symptoms or signs of PID.

Avoidance of intercourse is advised during treatment and for an additional seven days, as well as rest and simple analgesia.

As PID is sexually transmitted in most cases, management of sexual contacts is essential to prevent recurrence, even when STI test results are negative. Current contacts should be tested and receive immediate treatment with azithromycin 1 g orally (with the addition of ceftriaxone if *N. gonorrhoeae* is likely), regardless of test results. If chlamydial infection or gonorrhoea is diagnosed then sexual contacts from the preceding six or two months, respectively, should be advised and offered treatment and testing.[28] Advice about the future use of condoms with new sexual partners is essential to prevent repeat episodes, which are associated with an increased risk of long-term complications, including infertility.[25]

For women with an IUD in situ, if symptoms and signs are improving at the scheduled review two to three days after treatment initiation then the IUD may be kept in place. Removal should be considered if no improvement is seen, provided the benefits of removal outweigh the risk of pregnancy. Another IUD may be inserted after treatment has been completed.

Given the complex nature of PID and the multitude of questions and concerns it may raise during the consultation, provision of information in the form of factsheets or credible websites can be helpful. Patient information on PID is available from organisations such as Family Planning NSW (https://www.fpnsw.org.au/health-information/stis/pelvic-inflammatory-disease-pid) and the NSW STI Programs Unit (http://stipu.nsw.gov.au/wp-content/uploads/PID.pdf).

Conclusion

It is essential to perform a urine pregnancy test for all women of reproductive age presenting with new-onset low abdominal pain, as the differential diagnoses include a potentially life-threatening ectopic pregnancy. Transfer to the nearest emergency department is warranted for women with severe symptoms or haemodynamic instability. A high index of suspicion is required for PID, especially in young women. Negative STI test results are the rule rather than the exception and do not exclude the diagnosis of PID. The symptoms and signs of PID can vary from mild to severe, reflecting the spectrum of disease within the syndrome.

Prompt treatment with ceftriaxone, azithromycin, doxycycline and metronidazole to cover the potential polymicrobial causes is essential to prevent long-term complications. Sexual contacts should also be tested and treated to prevent recurrence of PID, with advice about minimising the risk of future episodes by using condoms with new partners. Multiple resources are available to support practitioners as well as women diagnosed with this condition. MT

References

A list of references is included in the website version of this article (www.medicinetoday.com.au).

COMPETING INTERESTS: None.

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