

CLINICAL PRACTICE GUIDELINE

Gynaecology (Non-oncological)

This document should be read in conjunction with the **Disclaimer**

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Acute pelvic inflammatory disease

Background

Pelvic Inflammatory Disease (PID) constitutes a general term for a spectrum of genital tract infection. The disease lacks a precise definition and not all patients complain of symptoms.

It is usually the result of infection ascending from the endocervix causing endometritis, salpingitis, parametritis, oophritis, tubo-ovarian abscess and / or pelvic peritonitis. While sexually transmitted infections such as *Chlamydia trachomatis* and *Neisseria gonorrhoea* have been identified as causative agents, additional STIs including *Mycoplasma genitalium*, anaerobes and other organisms may also be implicated.^{1,2} Bacterial vaginosis is a recognised association. Other organisms may be implicated in acute PID infection including (*Haemophilus influenzae*, *Streptococcus pneumoniae*, group A streptococcus and *S. aureus*). Sexually active young women are particularly at risk of PID.A high index of suspicion and a low threshold for empiric treatment of PID is recommended since the potential consequences of not treating PID are significant, resulting in infertility, ectopic pregnancy and chronic pelvic pain.^{3,4} The risk of complications increases with delayed diagnosis or repeated episodes.

Chronic PID (> 1 month duration) may result from infection with *Mycobacterium tuberculosis* or *Actinomyces* spp. These infections are not discussed in detail in this guideline.

Diagnosis

There is no single pathognomonic sign, symptom or investigation in the diagnosis of PID. The approach to the diagnosis should be multifaceted.

Clinical

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

- Bilateral lower abdominal tenderness (sometimes radiating to the legs)
- Abnormal vaginal or cervical discharge
- Fever > 38° C (not always present)
- Abnormal vaginal bleeding- including intermenstrual, postcoital or 'breakthrough' bleeding
- Deep dyspareunia
- Cervical motion tenderness on bimanual examination (with or without palpable mass), uterine and adnexal tenderness
- Dysuria
- Right upper quadrant pain (Fitz Hugh Curtis syndrome)

Recommended investigations

- Full blood picture
- C reactive protein

- Mid-stream urine (MC&S)
- Urine HCG to exclude complications of pregnancy e.g. ectopic pregnancy, miscarriage
- Endocervical and low vaginal dry swabs (either self-obtained by patient or during a physical examination) for *Chlamydia trachomatis* and *Neisseria gonorrhoea* PCR. First void urine can also be used for *C. trachomatis* and *N. gonorrhoeae* PCR. Endocervical or high vaginal or low vaginal swab for culture and sensitivity (gel swab). For complex or recalcitrant disease, consider adding *M.genitalium* PCR (dry swabs or first void urine).
- Serology for potentially sexually transmitted diseases where an extended STD workup appropriate (HIV infection is associated with increased risk of tuboovarian abscess) i.e. HIV, syphilis, HCV serology, HBV surface antigen, antibody
- Imaging if uncertain clinical diagnosis, severe illness or if unresponsive to the initial therapy.
 - Transvaginal ultrasound scanning may be helpful when there is diagnostic difficulty but is frequently normal in early or uncomplicated disease. When supported by power Doppler, it can identify inflamed and dilated tubes and tubo-ovarian masses / abscesses. It may differentiate in some cases from appendicitis, ectopic pregnancy or ovarian cyst complications, but there is insufficient evidence to support its routine use.^{5,6,8}
 - CT may be indicated in patients with diffuse pelvic pain, peritonitis or equivocal ultrasound.¹⁵
 - MRI has shown to be superior to TVUS in the diagnosis of PID but cost and availability are prohibitive^{16.} There is potential for use in selected cases where further investigation is required or theatre is contraindicated

When there is diagnostic doubt, laparoscopy may be useful to exclude other pathologies. It also enables specimens to be taken from the fallopian tubes and the Pouch of Douglas, and can provide information on the severity of the condition.^{7,8} However it is invasive, pelvic organs may appear normal in mild disease(lower sensitivity) and it plays a limited role in the treatment of acute PID.¹⁷

Differential diagnosis

The differential diagnosis of lower abdominal pain in a young woman includes:

- Ectopic pregnancy
- Acute appendicitis
- Endometriosis
- Irritable bowel syndrome (and less commonly, other gastrointestinal disorders)
- Complications of an ovarian cyst such as rupture or torsion
- Urinary tract infection
- Functional pain (pain of unknown physical origin)

Treatment of acute PID in sexually active women with no predisposing factors

Mild – Moderate PID: suitable for outpatient management

- PID suspected clinically or confirmed microbiologically
- Clinically well no evidence of sepsis, haemodynamically stable, pain controlled with simple analgesia
- No evidence of TOA on TVUS
- Compliant with oral treatment and follow-up

In mild or moderate PID (in the absence of a tubo-ovarian abscess), there is no difference in outcome when women are treated as outpatients or admitted to hospital. It is likely that delaying treatment, especially in Chlamydia infections, increases the severity of the condition and the risk of long-term sequelae such as ectopic pregnancy, subfertility and pelvic pain.¹¹

Outpatient treatment of mild – moderate STI related PID

The response to treatment is often a good indicator of whether PID is likely.

- Ceftriaxone 500mg in 2mL 1% lignocaine IM, or 500mg IV as a single dose. **plus**
 - lo 400mg orolly, 12 hourly fo
 - Metronidazole 400mg orally, 12 hourly for 14 days

plus

• Azithromycin 1g orally as a single dose for women who are pregnant or suspected to be non- adherent to doxycycline, then Azithromycin 1g orally as a single dose 1 week later

plus

- Doxycycline 100mg orally, 12 hourly for 14 days or
 - for women who are pregnant or suspected to be non-adherent to doxycycline:
- Azithromycin 1g orally as a single dose 1 week later

Women should be reviewed in 72 hours from initial presentation by their General Practitioner or in the Emergency Centre. Failure to clinically improve may indicate the need for further investigation or to consider other diagnoses or alternative management such as inpatient treatment. Further review in 4-6 weeks after treatment by a GP should be performed.

Admission to hospital is appropriate in the following:

- PID in pregnancy
- Lack of response to oral therapy
- Non adherence or intolerance to oral therapy
- Clinically severe disease (haemodynamically unstable, pain, nausea and vomiting, pyrexia, acute abdomen)
- Tubo-ovarian abscess
- Unable to exclude surgical emergency

Most admissions can be managed at secondary gynaecological services. Transfer to the tertiary centre may be required if there are no gynaecological services available, if specialist ultrasonography services are required or if considering surgical intervention and the gynae-oncology / endoscopy team needs to be consulted.

Inpatient treatment of severe STI related PID

- ceftriaxone 2g IV daily
 - plus
- metronidazole 500mg IV 12 hourly plus
- azithromycin 500mg IV daily

Until the patient is afebrile and improved, then

 doxycycline 100mg 12 hourly orally for a minimum of two weeks and up to four weeks in complicated cases (slow clinical resolution; pelvic collections) or Azithromycin if pregnant :see above

plus

 amoxicillin plus clavulanate 875mg/125mg, orally, 12 hourly for a minimum of 2 weeks and up to 4 weeks

Alternative IV regimen, especially for patients with immediate hypersensitivity to penicillin

 gentamicin IV (usual dose 5 mg/kg ideal body weight see <u>gentamicin</u> guidelines)

Plus

• Azithromycin 500mg IV daily

Plus

• clindamycin 600mg IV, 8 hourly.(Microbiology approval required for IV clindamycin within 24 hours of starting therapy).

Until the patient is afebrile and improved then,

- metronidazole 400mg orally, 12 hourly for a minimum of 2 weeks plus
- doxycycline 100mg 12 hourly orally for a minimum of 2 weeks or Azithromycin if pregnant : see above).

Outpatient treatment of mild – moderate procedure related PID (nonpregnant)

For patients who develop PID after a recent pregnancy, termination or gynaecological procedure (including IUCD insertion or removal) and those with a prior history of PID, *Chlamydia trachomatis, Neisseria gonorrhoea* and *Mycoplasma*

hominis may be implicated, together with mixed anaerobic and aerobic bacteria such as *Bacteroides spp*, anaerobic cocci, *Streptococcus spp* and enteric bacteria.

- Doxycycline 100mg orally 12 hourly for 2 to 4 weeks plus
- Amoxicillin plus Clavulanate 875mg/125mg orally, 12 hourly for 2 to 4 weeks

For patients with an immediate hypersensitivity to penicillin

- Doxycycline 100mg orally, 12 hourly for 2 to 4 weeks or if non STI related: ciprofloxacin 500mg orally, 12 hourly
 Plus
- Metronidazole 400mg orally, 12 hourly for 2 to 4 weeks

Inpatient treatment of severe procedure related PID

For **severe infection** related to pregnancy or surgery that is unlikely to be sexually acquired:

- Amoxicillin 2g IV 6 hourly *Plus*
 Gentamicin IV (usual dose 5mg/ kg ideal body weight. See <u>gentamicin</u> <u>guideline</u>)

 Plus
 - Metronidazole 500mg IV 12 hourly

Alternative Regimen

• Clindamycin 600 mg IV TDS (microbiology approval required within 24 hours of starting therapy).

Plus

• Ceftriaxone* 2g IV daily

Plus

• Azithromycin 500 mg IV daily

*If the patient is allergic to cephalosporin agents or has a type 1 hypersensitivity reaction to penicillin, replace ceftriaxone with gentamicin

For mild to moderate infection, or "step down" oral therapy

• amoxicillin+clavulanate 875+125 mg orally, 12-hourly for 14 days

plus

• doxycycline 100 mg orally, 12-hourly for 14 days or Azithromycin : see above

For non- pregnant patients with hypersensitivity to penicillins (see <u>Therapeutic</u> <u>Guidelines</u> (external website)), use:

- Doxycycline 100mg orally, 12 hourly for 2 weeks or Ciprofoxacin 500mg BD
 Plus
- Metronidazole 400mg orally, 12 hourly for 2 weeks

Other Regimens

There are many potential antimicrobial options to treat PID.¹⁸ There is also increasing antimicrobial resistance among some of the organisms which may be causative e.g. Enterobacteriacae to cephalosporins and Group B Streptococcus to clindamycin . Discuss with microbiology if above regimens are unsuitable due to allergy, other medical conditions, severe disease, unusual organism, lack of clinical response or potential need for hospital in the Home (HITH) treatment.

Mycoplasma genitalium

There is increasing awareness of this organism as a potential pathogen in PID and other genital infections. The above treatment regimens may be ineffective for PID when *M. genitalium* is a causative organism. Azithromycin is often recommended as first line therapy (http://ww2.health.wa.gov.au/Silver-book/Non-notifiable-infections/Mycoplasma-genitalium) but resistance is common.¹⁹Moxifloxacin may be an effective treatment option although clinical failure in *M. genitalium* infections has been described in some cases.²⁰ Please seek advice from the on call microbiologist for treatment and testing of partners and test of cure advice if this organism is identified

Follow up

- Follow up is important to ensure symptoms have resolved, that the patient was compliant with medication and that partners have been treated if *Chlamydia trachomatis* and / or *Neisseria gonorrhoea* have been detected. If any of these factors remain unresolved, a test of cure may be required.
- The patient should be reviewed within 24-48 hours to ensure symptoms and signs respond to treatment.
- Ensure the woman understands the importance of compliance with medication
- Advise the woman to avoid sexual intercourse until both she and her partner are fully treated (i.e. have completed their respective antibiotic courses).
- If there is no improvement, therapy should be re-evaluated and alternative diagnoses considered.

Intrauterine contraceptive device

In the presence of an intrauterine contraceptive device (IUCD), consideration should be given to the removal of the device, particularly if there has been no resolution of symptoms within 72 hours or if inserted within the last 2-3 weeks. Current Australian Therapeutic Guidelines do not recommend routine removal of an IUD in the presence of PID especially if occurring 3 weeks after insertion. IDSA guidelines recommend close follow up however, if an IUD is left in place in a patient diagnosed with PID.

Tubo- ovarian abscess

- In the presence of Tubo-Ovarian abscess ultrasound or CT guided drainage should be considered following discussion involving the Gynaecology Consultant and the Consultant Sonologist.
- Surgical treatment is another alternative management strategy that needs to be considered in severe cases or when there is evidence of pelvic abscess.
- Antibiotic courses of longer length than those recommended above (ie > 4 weeks) may be required in patients with extensive disease. Specialist consultation with Clinical Microbiologists/Infectious Diseases is recommended.

Management of sexual partner(s) of women with PID

When a sexually transmitted infection is either proven or likely to be the cause of PID, the current sexual partner(s) should be offered health advice and screening for chlamydial and gonococcal infection through their GP. *Mycoplasma genitalium* also may infect partners see information in the HDWA "silver book"

(http://ww2.health.wa.gov.au/Silver-book/Non-notifiable-infections/Mycoplasmagenitalium)

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Ovarian cyst accidents

Background

Ovarian cyst accidents refer to any of the three complications of ovarian cysts¹.

- 1. Ovarian torsion
- 2. Ovarian cyst haemorrhage
- 3. Ovarian cyst rupture

Key points

- Other gynaecological complications can present similarly to an ovarian cyst event. On examination, consider conditions such as: ectopic pregnancy, pelvic inflammatory disease, tubo-ovarian abscess, or non-gynaecological issues e.g. appendicitis¹.
- Ovarian cyst accidents will most commonly involve benign ovarian cysts.
- Immediate treatment should occur if ovarian torsion is suspected as this is a gynaecologicemergency².

Torsion

Ovarian torsion is partial or complete rotation of the ovarian vascular pedicle causing obstruction to venous outflow and later arterial inflow¹. Adnexal torsion refers to additional fallopian tube torsion. The incidence of ovarian torsion occurs mainly in women of childbearing age, it is rare and accounts for 3% of gynaecologic emergencies^{1, 3}. Thought to be primarily caused by a "bulky' ovary in conditions such as ovarian hyper stimulation or teratoma; right sided ovarian torsion is more common¹. 10-20% of ovarian torsion can occur during pregnancy; with infertility treatment being a possible risk factor³. Recurrence can occur in polycystic ovaries³. 15% of ovarian torsion can occur in children and adolescents ⁴. Prompt diagnosis is important for preservation of ovarian function. However, symptoms can be nonspecific and diagnosis can therefore be challenging. The primary risk factor for ovarian torsion is an ovarian mass greater than 5cm size.

Diagnosis: Is based on a high index of clinical suspicion³:

Signs of ovarian torsion include:

- Pelvic pain is present in up to 90%. This can be colicky pain in lower abdomen or pelvis, which becomes constant and can disappear if tissue is severely necrosed³.
- 50% of cases present with nausea and vomiting³.
- The presence of an adnexal mass on USS (present in up to 95%) raises the suspicion of a torted ovarian cyst. Doppler sonography can be useful in diagnosis but normal blood flow does not exclude torsion⁵.
- Fever (up to 20%)
- PV bleeding (up to 4%)⁷

Management of ovarian torsion

- Perform laparoscopy if suspicion of ovarian torsion as soon as possible to aid in preservation of ovarian tissue. Diagnosis can only be made at laparoscopy or laparotomy.
- During surgery attempted de-torsion and ovarian preservation is recommended as blood resupply in 91-100% of cases will be restored, even when the ovary initially appears necrosed⁸. Further surgery at a later stage should be considered for cysts deemed to be complex^{1, 3}.
- Ovarian conservation is especially recommended in paediatric and adolescent populations⁸
- In patients with a non-viable necrotic ovary or post-menopausal patients, salpingo-oophorectomy may be performed, following de-torsion and observation for a suitable period of time to confirm loss of ovarian viability.
- Oophoropexy may have a role in recurrent ovarian torsion

Rupture & haemorrhage

Rupture of an ovarian cyst is a common occurrence in women of reproductive age, and may occur in the context of follicular cysts, corpus luteal cysts, or pathologic cysts including endometrioma, dermoids and malignant neoplasms. Usually this is a physiological event during the ovarian cycle involving the follicle or corpus luteum. Complications can occur with women with a history of coagulopathy¹. If a benign teratoma/ endometriotic cyst is involved the ruptured cyst content can be extremely irritant for the peritoneum¹. Historically treatment for functional ovarian cysts has included the oral contraceptive pill; this has not been proven to be beneficial in most cases as functional ovarian cysts are likely to resolve within several months⁶. Other treatment such as repeated laparoscopic ovarian cystectomies for functional cysts has been shown to reduce fertility without any added benefit to the woman. An extremely rare cause of rupture is pseudomyxoma, (mucinous cyst)¹.

Signs of rupture / haemorrhage³:

- Characterised by a sudden onset of sharp then constant ache. Pain is at its worst at the time of onset, and is typically unilateral lower quadrant pain. Onset may occur during physical activity including exercise and sexual intercourse.
- Most women are systemically well; mild signs of peritonism may be present on examination, not associated with fevers, tachycardia or inflammatory markers.
- Free fluid may be seen on USS.
- If significant blood loss occurs the women could present with hypovolemic shock. This is a very late sign.

Investigation

• Ultrasound is the first line of investigation.

- FBC and group and hold
- Coagulopathy screen if clinically indicated
- Tests to exclude other causes of pain: BhCG, urinalysis, vaginal swabs etc

Management

- Management is usually conservative, with analgesia and observation.
- Address any predisposing cause such as Factor VIII deficiency causing haemorrhage¹.
- If pain does not improve within 48 hours consider an alternative diagnosis¹
- If the pain persists beyond a few days or the patient is unstable then laparoscopy should be considered.
- Follow up after 6 weeks with an ultrasound to confirm resolution is recommended when an ovarian haemorrhagic cyst has been identified¹.

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Vulvodynia

Aim

• To describe the <u>diagnosis</u> and <u>management</u> of vulvodynia.

Background

The 2003 ISSVD Terminology and Classification of Vulvodynia divided vulvar pain into 2 major groups⁸:

- 1. Vulvar pain related to a known disorder
 - a. Infectious
 - b. Inflammatory
 - c. Neoplastic
 - d. Neurologic
 - e. Trauma
 - f. latrogenic
 - g. Hormonal deficiencies
- 2. Vulvar pain in the absence of clinical findings or disease, known as vulvodynia
 - a. Localised (eg vestibulodynia, clitorodynia), Generalised, or Mixed
 - b. Provoked (eg insertional, contact), or Unprovoked or Mixed
 - c. Onset (primary or secondary)
 - d. Temporal pattern (intermittent, persistent, constant, immediate, delayed)

Vulvodynia is vulval pain, occurring in the absence of relevant visible findings or a specific, clinically identifiable, neurologic disorder. The term vestibulitis has been eliminated from this terminology because inflammation is absent. Vulvodynia is uncommon,¹ however is the most common cause of vulval pain seen in the sexual health clinic and an important cause of dyspareunia^{2, 3}. The characteristic features are of introital dyspareunia, vestibular erythema and localised tenderness confined to the vulvar vestibule.¹ To diagnose the condition, other causes of vulvodynia such as vulval dermatoses, herpes vulvitis, atrophic vaginitis,¹ cyclic vulvovaginitis and dysthetic vulvodynia need to be excluded. Candida has been reported in up to 43% of women with this condition.⁴

Diagnosis Medical history

Enquire about the following points in addition to a standard medical history:

- Presenting symptoms⁵- specifically pain, times the pain is experienced, location, duration, precipitating and alleviating factors
- Duration of symptoms
 - Primary: symptoms have always been present
 - Secondary: symptoms have developed after a period of normal function
- Sexual activity- record the frequency and severity of pain with sexual intercourse
- Severity of symptoms:
 - ➢ Grade 0 no pain with sexual intercourse.
 - > Grade 1 some pain with sexual intercourse.
 - > Grade 2 has to stop sexual intercourse because of pain.
 - Grade 4 avoiding sexual intercourse.
- Is the woman able to insert a tampon?
- Attend a personal / family history (e.g. autoimmune or atopic conditions, incontinence, smoking) and drug history.⁵

The following conditions should also be enquired about:

- Has the woman ever had pain free sexual intercourse?
- Candidiasis
- Skin disorders i.e. psoriasis, eczema, lichen sclerosus, lichen planus, dermatitis
- Other gynaecological conditions
- Medication which is associated with genital oestrogen deficiency Depo-Provera, implanon, conditions associated with a high prolactin levelprolonged breast feeding, phenothiazines.
- Current medications and known drug allergies
- Allergies, hay-fever, asthma
- Sexual assault
- Consider whether the pain might be referred- any history of back injury through sport or a motor vehicle injury or arthritis.

Medical assessment

- Perform a standard symptomatic STI screen⁵ (See Clinical Guideline, O&G, STI: Screening Tests for Symptomatic Females), including Cervical Screening Test and HSV2 serology.
- Exclude other conditions i.e. atrophic vaginitis, nonspecific vaginitis, cervicitis. Consider testing for other conditions e.g. thyroid disease, diabetes, iron deficiency⁵
- Look for dermatitis, and examine skin at other sites⁵
- Document clinical signs of vestibulitis:
 - Peri-vestibular erythema

- > Tenderness on touching the vestibular glands with a dry cotton bud.
- Document any tenderness in a clockwise manner at 7 points of the vestibule via a patient self-rating scale out of 10 for pain (0= no pain, 10 = severe pain).
 Both sides of urethra and at 0200, 0400, 0600, 0800, 1000 of vaginal orifice.

Management

- Lifestyle change to remove vulval irritation: discuss soothing products, wearing loose fitting clothing and perineal hygiene, keeping the area clean, dry and ventilated.^{1, 5}
- Diagnose and suppress vaginitis (candida, inflammatory vaginitis, trichomonas)
 - Prescribe Fluconazole 150mg per week for 6 weeks unless contraindicated, even if Candida is not isolated.
- Suppress herpes if active
- Provide local oestrogen: prescribe Ovestin cream topically (a tiny smear) to introitus bd for 6-9 months (If there is a history of breast cancer, consult with their oncologist, if there is a history of a thromboembolic condition, consult with their haematologist).
- Diagnose and treat dermatitis and dermatoses
- Consider seminal plasma allergy
- Provide medical counselling as appropriate.⁵ In particular provide information about the disease, and information on sexual activity.⁵
- Referral to women's health physiotherapy.
- Referral to psychologist
- Consult pain specialist, urologist prn
- Transcutaneous electrical nerve stimulation (TENS) may be effective for reducing pain associated with vestibulodynia.⁶
- Review in 6 weeks.

6 week review

- Provide the results from the first appointment.
- Assess clinical response.
- Discuss the condition and treatment and compliance to date.
- Assess sexual intercourse and pain levels.⁵
- If Candida is present, consider fluconazole prophylaxis 150mg/ week for 6 months.
- If the patient is not prescribed fluconazole
 - Explain the importance of diagnosis and treatment of candidiasis if recurrences occur.

- Inform the woman that she should present to the clinic for diagnostic testing if she develops symptoms of Candida or her vulval pain worsens.
- If HSV 2 serology is positive prescribe antiviral therapy for at least 12 months and then review.
- Ensure the patient has attended physiotherapy.

12 week review

- Repeat medical assessment.
- Exclude candidiasis.
- Encourage the physiotherapy programme and enquire about progress.
- If the woman is in a sexual relationship, enquire about her partner's response to the condition and treatment.
- Consider antihistamines for the atopic group.
- Consider vagifem for localised oestrogen deficiency in addition to topical ovestin (3-6 months supplemental course of 10mcg two times a week).

4 month review

- If there is no significant improvement, commence on analgesics i.e. Low dose <u>amitryptyline</u>.⁷ Commence at 10mg / day and increase by 10mg per fortnight until the pain is controlled or side effects up to a dose of 200mg/ day. Topical anaesthetics and antidepressants (amitriptyline hydrochloride) may be prescribed to reduce itch and discomfort.¹ NB: ideally the woman should have had approximately 3 months of physiotherapy before being commenced on analgesia. Women who gain weight on <u>amitryptyline</u> can be given roboxetine.
- For women unable to tolerate either of the above medications, <u>gabapentin</u>, pregabalin or nortryptiline can be given.
- Advise the woman that the treatment is usually given for over 12 months and is continued for 6 months after the pain levels have reduced or gone before the drug is discontinued. Surgical intervention can be considered if symptoms remain unrelieved after medical treatment.³
- Frequent follow-up is suggested to monitor progress.¹ Continue to review the woman at 6-8 week intervals to monitor progress, therapy compliance and provide support / encouragement.
- Consider assessing urine for evidence of oxalate crystalluria.
- Consider psychosexual counselling^{3, 5} with referral to a clinical psychologist. A clinical psychologist can assist with a number of concerns common to women with vulvodynia including current sexual functioning, self-esteem and the development of a graduated sexual reintroduction programme.

 Consider referral to the KEMH Chronic Pelvic Pain Clinic for ongoing multidisciplinary management

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Myomectomy: Strategies to reduce blood loss& anaemia

Aim

To minimise the need for blood transfusion and to decrease the impact of postoperative anaemia in women undergoing a Myomectomy.

Background/Rationale

Leiomyomas (fibroids) are benign lesions of the uterus which commonly cause menstrual disorders such as menorrhagia and can interfere with fertility. For women who wish to preserve fertility Myomectomy is the procedure of choice (vs hysterectomy). Myomectomy, especially open abdominal procedures, can be associated with a large degree of blood loss. Women with heavy menstrual bleeding may also be suffering from anaemia +/- iron deficiency prior to surgery, further increasing the likelihood that they may need a blood transfusion. A recent audit at King Edward Memorial Hospital for Women, Western Australia, identified a 15% transfusion rate of women undergoing open abdominal myomectomy.⁴ Although serious reactions are rare, transfusion is not without risks e.g. labelling errors, Transfusion Related Acute Lung Injury (TRALI) and Transfusion Associated Circulatory Overload (TACO). Perioperative transfusions and anaemia have both been associated with increased complications and length of stay in surgical patients.⁵ Since Myomectomy is an elective procedure, with careful planning and considered use of some of the interventions listed below, it should be possible in most cases to avoid the need for transfusion and minimise the impact of postoperative anaemia. Some of these techniques may be applicable for other types of surgery.

Disclaimer

This document is a written practical resource designed to be used specifically by clinical staff here at King Edward Memorial Hospital for Women (KEMH) - Western Australia (WA). The techniques/regimens that have been included are based on the opinion of experienced clinicians familiar with using these techniques. The decision to use any of these techniques is at the discretion of the treating clinician and should take into account their own personal experience, the literature and individual patient characteristics.

Pre-Operative

1 – Correction of preoperative anaemia and iron deficiency

Screening for anaemia and iron deficiency should be done as early as possible prior to surgery and should be corrected prior to an elective major surgical procedure. Elective surgery should be scheduled to allow anaemia correction to occur first ¹. If

anaemia is complex (e.g. Haemoglobinopathy or thalassaemia), consider early referral to haematology.

These patients often have heavy menstrual bleeding and iron deficiency anaemia due to the presence of fibroids. Treatment with intravenous iron is recommended if there is a short time to surgery, moderate to severe anaemia (e.g. Haemoglobin < 100), a history of intolerance to oral iron, or heavy ongoing menstrual bleeding (for which oral iron is mostly not suitable).¹

2 – Medical treatments for heavy menstrual bleeding

Medical treatments used for the management of heavy menstrual bleeding include, tranexamic acid, gonadotrophin releasing hormone antagonists, non-steroidal antiinflammatories, and other hormonal therapies. These may also be beneficial in decreasing preoperative blood loss and thus facilitating the correction of preoperative anaemia and iron deficiency. The decision to use any of these medical therapies is at the discretion of the treating clinician.

3 – Preoperative misoprostol

A recent systematic review demonstrated a decrease in average blood loss of 149mL, and a smaller reduction in post-operative Hb, in women given PV misoprostol.^{2,6} Dose recommended: Misoprostol 400 mcg intra-vaginally, one hour prior to surgery.

Intra operative Vasoconstrictor therapy

Vasopressin

A Cochrane review of two RCTs demonstrated a median decrease in blood loss of 299ml²

Contraindications:

- History of CVS disease, such as hypertension, ischaemic heart disease or other cardiac disease.
- Caution in smokers or those on nicotine replacement therapy.

Suggested vasopressin dilution

Add 20units of vasopressin (1 ampoule) into 200mL of saline = 0.1u/mL Max Dose for infiltration is 50mL (5 units) of this solution.

Recommendations:

- Surgeons should inform the anaesthetist when injecting.
- Inject into the base of myomas prior to incision.
- Aspirate regularly to avoid intravascular injection.
- Pneumoperitoneum may increase the risk of bradycardia.
- Vasopressin has a short half-life. A repeat injection in 45-60 minutes may be safe.

• Never exceed the maximum dose of 5 units.

Noradrenaline

There is no published literature but this is used in some centres including hospitals in WA, and is probably just as efficacious. The same precautions with regard to potential cardiovascular contraindications / precautions apply.

Suggested noradrenaline dilution

Add 2mg of Noradrenaline (1 ampoule) into 1 litre of dextrose 5% = 2mcg/mL Max Dose for infiltration is 100mL of this solution, although more than 60mL is rarely needed

Repeat dose in 45-60minutes (probably safe due to short half-life)

Surgical Techniques

Peri-cervical tourniquet

Two RCT's demonstrate a median decrease in blood loss of 289mL²

This can be achieved by passing and tying a Foley's catheter around the cervix and the infundibular pelvic ligaments as low as possible compressing the uterine and ovarian vessels.

The best way to achieve a tight seal is to throw one knot on the catheter and then use a clip to hold this tight. This technique may not be feasible if the location of the fibroids prevents the catheter from encircling the cervix.

Ovarian artery clamps

The addition of ovarian artery clamps to a peri-cervical tourniquet (the triple tourniquet technique) has shown the greatest benefit in decreasing overall blood loss. Specific ovarian artery clamps designed to avoid damage to the fallopian tubes are available for this purpose.³

Uterine artery clamps

This technique, as part of the triple tourniquet method, has been demonstrated to be of benefit, with a significant reduction in blood loss of 1870ml.⁷

Recommendations

- Myomectomies, laparoscopic or open, carry a high re-bleed risk. Consider insertion of an intra-peritoneal drain and measuring haemoglobin level at 6 hours post-op to allow early detection of intra-abdominal bleeding.
- Myomectomy sites also form adhesions frequently, consider overlaying the Myomectomy site with an adhesion barrier (e.g. Interceed or OxiPlex).

Anaesthesia techniques

Controlled hypotension / intra-operative blood pressure control

There is good evidence that there is a linear relationship between mean arterial blood pressure and blood loss. Most of the evidence for controlled hypotension/deliberate hypotension comes from spinal surgery, ENT/maxillofacial surgery, orthopaedic joint replacement surgery and some older papers in gynaeoncologic surgery showing benefit. The major risk is organ ischaemia or hypo-perfusion and caution should be exercised in patients with cardiovascular disease. It is probable that the risks of a MAP <65mmHg may outweigh any benefit, but it is recommended practice to avoid hypertension. Aiming for a MAP 65-70mmHg (e.g. low normal) seems reasonable in patients without pre-existing cardiovascular disease. Any method can be used e.g. thoracic epidural, Spinal + GA, Remifentanil, or deepening the volatile anaesthesia depth. If infusing vaso-active drugs (e.g. GTN or Phentolamine), the insertion of an arterial line is considered prudent.

It is not advisable to use deliberate hypotension if the patient has poorly controlled hypertension, cardiovascular or cerebrovascular disease. To ensure the surgeons have obtained good haemostasis before closing, the anaesthetist should allow the BP to return to normal levels first. This reveals any bleeding points which may not be obvious at the lower blood pressure but which may lead to concealed postoperative bleeding, if not dealt with prior to closure.

Regional anaesthesia

There is evidence that regional techniques decrease intra-operative blood loss, possibly through their ability to lower blood pressure and sympathetic responses. When discussing merits of thoracic epidural analgesia with patients, this additional benefit should be included in the discussion.

Another acceptable alternative for patients not keen on an epidural is a single shot spinal with intrathecal morphine in addition to general anaesthesia.

Avoidance of hypothermia

Aggressive intra-operative warming and avoidance of hypothermia will decrease blood loss. Consider the use of two full body bair huggers (top and bottom) and the inditherm heating mattress. Wrapping the patient's head and warming all irrigation and intravenous fluids also helps.

Intravenous fluid & coagulation management

Monitor coagulation with either traditional coagulation tests or Rotational Thrombo-Elastometry (ROTEM) when indicated and treat abnormalities accordingly. Colloid solutions (especially starches such as Voluven) can interfere with fibrinogen polymerisation, and potentially increase blood loss. Consider avoiding or minimising colloid use if possible.

Acute Normovolaemic Haemodilution (ANH)

There is limited evidence for the routine use of Acute Normovolaemic Haemodilution outside of cardiac surgery. It probably adds little benefit if intra-operative cell salvage is already planned. This technique could be considered in patients who refuse blood products (e.g. Jehovah's witnesses).

There are benefits to the clotting factors and platelets in autologous fresh blood, whereas cell salvage will provide only red cells. The equipment and training / experience required is not routinely available here at KEMH at present, hence prior planning would be required, and the involvement of an anaesthetist experienced in this technique would be desirable.

Tranexamic acid

One RCT has demonstrated a median decrease in blood loss of 243mL⁷

This treatment is contraindicated in women with a history of, or risk factors for, thromboembolic disease.

SUGGESTED TRANEXAMIC ACID REGIMEN Tranexamic acid 10mg/kg (maximum 1G) loading dose over 10min followed by infusion of 1mg/kg/min Cease at the end of surgery.

Intraoperative cell salvage

This should be used routinely with open abdominal myomectomy which at present has a very high incidence of >1000mL blood loss. Correct technique is very important, and much of the shed blood may end up in packs and swabs in the operating theatre. It is vital that these are carefully washed in saline then collected via the cell salvage suction apparatus.

Recommendation: For optimal success surgeons must be diligent with the use of suction and communication between the theatre scrub nurse, the surgical team member and the Anaesthetic Consultant/Registrar with expectations clearly outlined is of the utmost importance. (i.e. to collect all of the blood possible).

Postoperative

Anaemia correction

Women undergoing Myomectomy are usually relatively young and fit with minimal co-morbidities. They are likely to be able to tolerate lower levels of Haemoglobin (Hb) for short periods of time compared to other elderly patients or those with CVS / respiratory disease. Consider enhancing their own ability to replace the lost Hb with intravenous iron if there is significant post-operative anaemia (or oral iron if mild). This is important if they were iron deficient preoperatively and this hasn't been

corrected, as they will have no iron stores to help them correct their postoperative anaemia. In the stable non-bleeding patient, a reasonable aim should be to transfuse only if Hb < 60-70g/L and give only one unit at a time while assessing the patient's response.

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Care following a simple / radical vulvectomy

Aim

• The appropriate management and care of a woman following a simple / radical vulvectomy.

Post-operative care

- Nurse in the semi recumbent or Fowlers position, for the initial 24-48 hours post operatively, to decrease tension on the suture line and promote comfort. Use a bed cradle if required.¹
- Post-operative observations shall be performed and recorded as per Clinical Guideline, O&G: Surgical Patient: Management of: Care Following Major Gynaecology, Oncology or Urogynaecological Surgery
- 3. Encourage 2 hourly change of position. Ensure standard VTE prophylaxis^{1, 2} including Flowtron boots³, graduated compression stockings,⁴ heparin, early mobilisation and appropriate chest physiotherapy, and pressure ulcer prevention^{1, 5} particularly of the heels.
- 4. Ensure groin drains are secured appropriately to prevent dislodgement as extensive lymphatic drainage is usual. There may also be a Yates drain in the perineum (usually sutured) this drains into a gauze pad.
- 5. Ensure the in-dwelling catheter (IDC) is secured to promote drainage and comfort.
- 6. Drains and the IDC shall be removed as ordered.
- 7. Groin dressings are usually removed at 24 hours or as ordered. A dressing shall be reapplied as required.
- 8. Report any discolouration or induration of the suture line as it may indicate lymphoedema or lymphocyst formation. This can often present insidiously and be accompanied by low grade pyrexia.
- Perineal toilet is performed three times per day and following all bowel actions¹. The area is dried using a hairdryer set to 'cool'.¹ Paraffin gauze may be ordered for the perineal suture line. Use a combine as the perineal pad underwear is not normally worn at this stage.
- 10. Consider the need for aperients to prevent straining.¹
- 11. Voiding patterns are usually re-established without difficulty however some 'spraying' of urinary flow may be noticed post-operatively. Encourage perineal toilets after passing urine or faeces.¹
- 12. Assist with mobilisation to prevent over extension of the suture line (particularly when getting into / out of bed). Consider the use of a footstool.
- 13. Provide the woman with opportunities to express her feelings and concerns about the surgery, including the recommencement of sexual activity and body image concerns.¹ Women may have difficulty discussing personal problems

with family or friends.¹ Spending time counselling and providing advice helps reduce the negative impact from these concerns.¹

- 14. On discharge advise the woman to report any:
 - Unusual odour

- Fresh bleeding
- Breakdown on the incision
- Perineal pain.

- 15. Educate the woman about:
 - The possibility of developing lower limb lymphoedema², and the signs, symptoms and action to be taken,¹
 - Preventative measures including a meticulous skin regime, advice on appropriate rest, exercise and movement,² and the importance of maintaining a healthy body mass index.
 - Wearing elastic stockings for 12 months after surgery to assist development of collateral pathways for lymph drainage.⁶

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Obstetrics & Gynaecology

Goserelin prescribing protocol

Aim

• To provide guidance and structure regarding the prescribing of goserelin at KEMH in order to improve governance over prescribing high cost medications.

Background

In 2017, a medication usage review conducted by the pharmacy and gynaecology departments demonstrated that goserelin is frequently prescribed for various gynaecological conditions despite being a high cost medication.

In the literature and in the aforementioned audit, goserelin has been shown to be an effective treatment for conditions such as endometriosis, fibroids (symptom management and reduction in fibroid size pre-myomectomy), chronic pelvic pain and refractory heavy menstrual bleeding (HMB). The medication usage review discovered that goserelin is often prescribed before other, less costly, medications have been trialled and before standard surgical procedures have been performed. The duration of goserelin therapy is often limited due to cost to both the hospital and patient and adverse effects, most notably reduction in bone mineral density (BMD).

Goserelin prescribing principles

Goserelin is a gonadotrophin releasing hormone (GnRH) agonist with a longer halflife than the endogenous GnRH. Goserelin binds to receptors in the pituitary, inhibiting gonadotrophin production resulting in supressed ovarian steroidgenesis. Adverse effects are mostly due to the induced hypoestrogenic state and may include hot flushes, vaginal dryness, decreased libido, mood swings, breast tenderness, headaches and bone mineral depletion. Thus, regular bone mineral density (BMD) scans are recommended before and during treatment with goserelin. To minimise adverse effects, addback therapy is usually commenced. Options include tibolone or oral hormone replacement therapy (HRT) with or without vaginal estrogen. The amount of estrogen and progesterone necessary to prevent hot flushes and bone mineral loss is less than that which would stimulate endometriosis.

The recommended maximum duration of therapy is 24 months.

Prescribing restrictions

A number of restrictions exist surrounding the prescription of goserelin at KEMH and must be considered before deciding if a patient is eligible for goserelin treatment.

1. Pharmaceutical Benefits Scheme (PBS)

The goserelin 3.6mg implant (administered monthly) is PBS approved for:

- Carcinoma of the prostate (not applicable at KEMH)
- Breast cancer (not applicable at KEMH)
- Anticipated premature ovarian failure (not applicable at KEMH)
- Endometriosis (applicable at KEMH)

Must be visually proven and treatment can only be short-term (only 1 course of a maximum of 6 months duration will be authorised)

The <u>goserelin 10.8mg implant</u> (administered every three months) is PBS approved for:

• Carcinoma of the prostate (not applicable at KEMH)

At KEMH, the hospital will only receive a Medicare reimbursement for patients with endometriosis who are prescribed the 3.6mg implant for a maximum of 6 months.

2. Formulary 1 (F1)

The State-wide medicines formulary (SMF), F1, now governs what medications can be stocked at HDWA facilities and how they can be prescribed.

On F1, both strengths of goserelin implants are approved for:

- The aforementioned PBS indications
- Suppression of ovarian function during chemotherapy (not applicable at KEMH)
- Treatment of proven endometriosis following laparoscopy under direction of a gynaecologist (applicable at KEMH)
- Treatment of heavy uncontrolled bleeding from fibroids under direction of a gynaecologist (applicable at KEMH)
- Reduction in uterine fibroid size prior to surgical management under direction of a specialist obstetrician (applicable at KEMH)

At KEMH, goserelin may be prescribed for the above conditions without an individual patient application (IPA) if deemed clinically appropriate.

3. KEMH Medicines and Therapeutics Committee

For indications not approved by the PBS or F1, refer to the <u>Medicines Management</u> <u>Framework</u> (available to WA Health staff through HealthPoint).

Prescribing goserelin for individual conditions

Endometriosis

Eligibility criteria for goserelin therapy for endometriosis:

- First line medical therapy is not effective or appropriate
- Chronic pelvic pain unresponsive to surgery or first line medical treatments
- Gynaecological pathology has not been detected but the patient suffers from gynaecological chronic pelvic pain (cyclical exacerbation)

Refer to Endometriosis Quick Reference Guide in this document for further details.

Other indications

Goserelin may also be prescribed in the following situations. If the indication is not covered by the PBS or the SMF, an IPA is required (refer to Medicines Management Framework).

Indication	PBS	SMF	Comments
Chronic pelvic pain in the absence of pathology where standard treatments have been ineffective	×	×	IPA required
As a diagnostic/therapeutic option in premenopausal patients who are being considered for bilateral oophorectomies to establish that the source of their pain is ovarian	×	×	IPA required
Treatment of HMB from fibroids	×	√	
Preoperative shrinkage of fibroids to facilitate the laparoscopic approach or a smaller abdominal incision	×	√	
Patients who undergo surgical resection of endometriosis and require 'down- regulation' prior to commencement of Assisted Reproductive Technology (ART)	×	×	KEMH is not an approved ART practice site; IPA required

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Endometriosis quick reference guide (QRG): Goserelin prescribing protocol

Severity of Endometriosis

References

See guideline sections in chapters above

Related policies

• Australian Commission on Safety and Quality in Health Care.

- NSQHS Standards. Standard 5 Comprehensive Care: Minimising Patient Harm: <u>Preventing and managing pressure injuries (external website)</u> actions 5.21-5.23
- Australian Guidelines for Prevention and Control of Infection in Healthcare (external website). 2022.

Related WNHS policies, procedures and guidelines

WNHS Clinical Guidelines:

Anaesthetics: Intraoperative cell salvage Obstetrics and Gynaecology:

- Sexually Transmitted Infections
- Perioperative- Preparation and Management: Care Following Major Gynaecology, Oncology or Urogynaecological Surgery
- Venous Thromboembolism (VTE): Anti-embolic therapy; VTE: Risk Assessment and Recommended Venous Thromboembolic Prophylaxis in Patients Admitted for Gynaecological Conditions

WNHS Policy: <u>Pressure Injury Prevention and Management</u> (available to WA Health staff through HealthPoint)

Useful resources

- RANZCOG
 - > Patient information resource: Endometriosis (external website)
 - > Guideline: Endometriosis Clinical Practice Guideline (external website)
 - Guideline: <u>The Initial Management of Chronic Pelvic Pain</u> (external website)
- European Society of Human Reproduction and Embryology (ESHRE) <u>Guideline:</u> <u>Guideline on the management of women with endometriosis (external website)</u>
- WNHS Pharmacy Department Medication Usage Review: Goserelin (Zoladex®)

Keywords:	PID, pelvic inflammatory disease, genital tract infection, sexually acquired PID, non- sexually acquired PID, Mycoplasma genitalium, tubo-ovarian abscess, TOA, endometriosis, salpingitis, ovarian rupture, ovarian torsion, ovarian haemorrhage, ovarian cyst, dyspareunia, vaginitis, vulvodynia, vestibulitis, Myomectomy, postoperative anaemia, Leiomyomas, fibroids, peri-cervical tourniquet, Vulvectomy, simple vulvectomy, radical vulvectomy, vulval cancer, goserelin, zolodex, zoladex, endometriosis, Goserelin Prescribing Protocol					
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Endorsed by:	GSMSC GSMSC (Goserelin sections added only)		Date: Date:	April 2018 May 2018		
NSQHS Standards (v2) applicable:	 I: Clinical Governance 2: Partnering with Consumers 3: Preventing and Controlling Healthcare Associated Infection 4: Medication Safety 	 S: Comprehensive Care 6: Communicating for Safety 7: Blood Management 8: Recognising and Responding to Acute Deterioration 				
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