# Dysmenorrhoea

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## Abstract

Dysmenorrhoea is a medical condition characterised by severe uterine pain during menstruation manifesting as cyclical lower abdominal pain. It is commonly classified into primary dysmenorrhoea in the absence of co-existent pathology and secondary dysmenorrhoea when there is an identifiable pathological condition. About 40–70% of women of reproductive age suffer with dysmenorrhoea along with its associated psychological, physical, behavioural and social distress. The exact pathophysiological processes are not fully understood but it probably reflects increased myometrial activity induced by an excessive production of prostaglandin causing ischaemia (uterine 'angina'). History is critical in establishing the diagnosis of dysmenorrhoea and also in differentiating between primary and secondary dysmenorrhoea. Mainstay treatment is generally supportive providing symptomatic relief and more directive surgical treatment is reserved for specific secondary causes of dysmenorrhoea or for refractory cases. Therefore, patients with primary dysmenorrhoea may simply need reassurance and simple analgesics, while those with secondary dysmenorrhoea require investigation and treatment of the underlying organic problem. We present an overview of managing this condition.

**Keywords** dysmenorrhoea; menstrual disorders; primary; secondary

## Background

Dysmenorrhoea is a very common gynaecological condition affecting anywhere from 45 to 95% of women with one in five cases being severe. Dysmenorrhoea is a medical condition characterised by severe uterine pain during menstruation manifesting as cyclical lower abdominal or pelvic pain, which may also radiate to the back and thighs. The term dysmenorrhoea is derived from the Greek words 'dys' meaning difficult, painful or abnormal, 'meno' meaning month and 'rrhea' meaning flow.

It is commonly divided into primary dysmenorrhoea, where there is no co-existent pathology, and secondary dysmenorrhoea where there is an identifiable pathological condition known to contribute to painful menstruation. Symptoms of primary dysmenorrhoea begin a few hours before the start of menstruation and are often relieved during the first few days of bleeding. The initial onset of primary dysmenorrhoea is usually shortly after menarche (6–12 months), when ovulatory cycles are established. Secondary dysmenorrhoea can also occur at any time after menarche but is most commonly observed in women in their third and fourth decade of life in association with an existing condition.

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## Risk factors

Risk factors for primary dysmenorrhea include earlier age at menarche, heavy menstrual flow, nulliparity, family history of dysmenorrhoea, and stress.

According to NICE *Clinical Knowledge Summary on Dysmenorrhoea* (November 2018).

- Primary dysmenorrhoea improves with increased age, parity, and use of oral contraceptives.
- There is inconsistent and conflicting evidence on the association between primary dysmenorrhoea and modifiable factors, such as cigarette smoking, diet, obesity, depression, and abuse.

## Pathophysiology

The most important physiological event reported with dysmenorrhoea is increased myometrial activity with accompanying uterine ischemia (uterine 'angina'), which stimulates the type C afferent pain neurones.

In a normal menstrual cycle, at the end of the luteal phase as the corpus luteum regresses after non-fertilisation of an ovum, there is a decline in progesterone levels. It is this withdrawal of progesterone that leads to the shedding of endometrium and, during its destruction, an increase in inflammatory cytokines, vascular endothelial growth factors and matrix metalloproteinases (MMPs). This leads to a degradation and loss of integrity of blood vessels and destruction of endometrial interstitial matrix and hence the bleeding of menstruation. Uterine contraction and vasoconstriction is caused by the disintegrating endometrial cells releasing $PGF_{2á}$ which is a myometrial stimulant and vasoconstrictor. The uterine contractions and ischaemia that results from decreased blood flow results in uterine pain.

### Primary dysmenorrhoea

In women with primary dysmenorrhoea there are increased levels of inflammatory markers such as vasopressin, prostaglandins $PGE_2$ and $PGF_{2á}$ and leukotrienes in endometrial fluid. PGF2á is a potent myometrial stimulant and vasoconstrictor. Leukotrienes increase myometrial stimulation and vasoconstriction as well as increasing the sensitivity of pain fibres. Vasopressin stimulates uterine activity, decreased uterine blood flow and, in vitro, constricts uterine arteries. The primary stimulus for these increased levels is unknown but it is thought that this myometrial activity is modulated and augmented by prostaglandin synthesis. In addition to stimulating uterine contractions, $PGF_2$ and $PGE_2$ can cause contraction of bronchial, bowel, and vascular smooth muscle resulting in bronchoconstriction, nausea, vomiting, diarrhoea and hypertension. Diarrhoea and nausea are commonly associated with primary dysmenorrhoea.

Compared with controls, women with primary dysmenorrhoea have increased uterine pressures from increased uterine muscle activity and frequency of contractions (frequently more than 150 mmHg). Doppler flow studies have supported this by showing higher uterine and arcuate artery resistance on the first day of menses in women with primary dysmenorrhoea than in

controls. Pain fibres are also stimulated from ischaemia caused by vasoconstriction and anaerobic metabolites produced by an ischaemic endometrium which stimulate type C pain neurons.

Added to this is the possible effect of psychological and behavioural factors which can act centrally and contribute to pain perception. There is an increased prevalence of dysmenorrhoea in women with a history of sexual abuse but there is little research into this compared to other chronic pelvic pain syndromes.

### Secondary dysmenorrhoea

Secondary dysmenorrhoea is caused by an underlying pelvic pathology. Endometriosis is the most common cause. However, there is no correlation between the severity of the disease and extent of pain. Pelvic Inflammatory Disease causes both increased inflammatory mediators and scar tissue. Adenomyosis causes tonic contractions through endometrial gland infiltration and polyps, submucous fibroids and IUDs cause increased uterine contractions in order to expel them. All of the less common causes of dysmenorrhoea are due to abnormal uterine contractions. See Table 1 for a comparison of primary and secondary dysmenorrhoea.

### Evaluation of dysmenorrhoea

Secondary dysmenorrhoea must be excluded before considering a diagnosis of primary dysmenorrhoea.

- History and clinical assessment:
  - Relation of pain to menarche.
  - Characteristics of the pain, including type of pain, timing and duration, severity, and exacerbating and alleviating factors.
  - Any associated symptoms, including other gynaecological symptoms and non-gynaecological symptoms.
  - Menstrual history, including length of menstrual cycle, regularity, and duration, and the volume of menstrual flow.
  - Risk factors for primary dysmenorrhoea, such as family history of dysmenorrhoea.
  - Medical history. Several conditions (for example, irritable bowel syndrome and lactose intolerance) can mimic pain similar to dysmenorrhoea.
  - Obstetric history, including plans for pregnancy.
  - Drug history, including prior treatment and effect.
- Examination:
  - Perform an abdominal examination in all women — to assess for large fibroids and other masses.
  - Perform a pelvic examination (including a speculum examination of the cervix), except in young women who are not sexually active if the symptoms are suggestive of primary dysmenorrhoea.
- Consider the following investigations:
  - An ultrasound scan — to rule out fibroids, adnexal pathology, and endometriosis.
  - High vaginal and endocervical swabs — if the woman is at risk of a sexually transmitted infection, especially if pain is associated with vaginal discharge and abnormal vaginal bleeding.
  - Pregnancy test — to exclude an ectopic pregnancy.

- **Primary dysmenorrhoea is the most likely diagnosis when:**
  - Menstrual pain starts 6–12 months after the menarche, once cycles are regular.
  - Pain, usually cramping in nature, occurs in the lower abdomen but may radiate to the back and inner thigh.
  - Pain starts shortly before the onset of menstruation and lasts for up to 72 h, improving as the menses progresses.
  - Non-gynaecological symptoms, such as nausea, vomiting, diarrhoea, fatigue, irritability, dizziness, bloating, headache, lower back pain, and emotional symptoms, are present.
  - Other gynaecological symptoms are *not* present.
  - Pelvic examination is normal.
- **Secondary dysmenorrhoea is the most likely diagnosis when:**
  - Pain starts after several years of painless periods.
  - Pain is not consistently related to menstruation alone and may persist after menstruation finishes or may be present throughout the menstrual cycle but is exacerbated by menstruation.
  - Other symptoms are present, including:
    - Other gynaecological symptoms, such as dyspareunia, vaginal discharge, menorrhagia, intermenstrual bleeding, and postcoital bleeding.

**Differential characteristics of primary and secondary dysmenorrhoea**

| | Primary | Secondary |
|---|---|---|
| Age (years) | 16–25 | 30–45 |
| Onset of pain | Just prior to menstruation (spasmodic). | Pain often progresses through late luteal (congestive). |
| Pathophysiology | Excess prostaglandins and leukotrienes. | Underlying disorder. |
| Symptoms | Usually self-limiting, lasts for first 1–3 days menstruation.<br>Responds to COCP and NSAIDs, Periods normal or light. | Associated with other features related to underlying disease.<br>Resistant to COCP and NSAIDs.<br>Periods often heavy. |
| Signs | Unremarkable | Dependent on cause but may include a tender, enlarged, fixed, retroverted uterus with adnexal tenderness and a mass |

**Table 1**

### Major causes of secondary dysmenorrhoea

**Gynaecologic disorders:**

- Endometriosis
- Adenomyosis
- Pelvic inflammatory disease
- Fibroids
- Endometrial polyps
- Ovarian cysts
- Intrauterine contraceptive device
- Intrauterine adhesions (Asherman's syndrome)
- Congenital obstructive mullerian malformations
- Pelvic congestion syndrome
- Cervical stenosis

**Non-gynaecologic disorders:**

- Inflammatory bowel disease
- Irritable bowel syndrome
- Urogenital disease
- Psychogenic disorders

**Table 2**

- Non-gynaecological symptoms, such as rectal pain and bleeding (which may be associated with endometriosis).
  - o Pelvic examination is abnormal, although the absence of abnormal findings does not exclude secondary dysmenorrhoea

For primary dysmenorrhoea, history and examination should suffice and further investigation is rarely necessary. If there are atypical symptoms or a trial of non-steroidal anti-inflammatory medication or combined oral contraceptive is unsuccessful then pelvic ultrasound scan should be considered. For secondary dysmenorrhoea pelvic USS should be considered. Hysteroscopy and laparoscopy have a role in confirming a suspected diagnosis and treating the underlying pathology (See Tables 2 and 3).

## Management

For primary dysmenorrhoea, treatment is based on tackling the aetiology with cyclo-oxygenase inhibitors and inhibiting ovulation. Treatment of secondary dysmenorrhoea targets the cause. One must treat women individually taking account of their age, desire for fertility and concurrent symptoms.

Many studies have employed patient self-reporting using a visual analogue or other pain scale, quality of life scales, or other similar measures such as the Menstrual Distress or Menstrual Symptom Questionnaires. Additional measures include analysis of the proportion of women requiring analgesics in addition to their assigned treatment and recording the percentage of women reporting restriction of social activities or absence from work or school. Whichever system is used, grading dysmenorrhoea according to severity of pain and limitation of daily activity will help guide the treatment strategy and catalogue the response to treatment.

### Clinical features and evaluation of some common causes of secondary dysmenorrhoea

| Condition | Clinical features | Evaluation |
|---|---|---|
| Endometriosis (most common cause of secondary dysmenorrhoea) | Cyclical or chronic pelvic pain frequently occurring prior to menstruation and accompanied by heavy menstrual bleeding and deep dyspareunia. | Transvaginal pelvic ultrasound is highly accurate for ovarian endometrioma.<br>MRI may be indicated for deep infiltrating endometriomas.<br>Laparoscopy allows confirmation of diagnosis and treatment |
| Adenomyosis | Usually associated with menorrhagia and intermenstrual bleeding.<br>Enlarged, tender, boggy uterus on examination. | Transvaginal ultrasound or MRI. |
| Fibroids | Lower abdominal pain, frequently accompanied by menorrhagia; a pelvic mass may be identified on examination | Transvaginal/transabdominal ultrasound |
| PID | Lower abdominal pain and tenderness that may be accompanied by dyspareunia, abnormal vaginal bleeding, and abnormal vaginal discharge. In acute infection, fever may be present. | Cervical infection with *Chlamydia trachomatis* or *Neisseria gonorrhoeae* is confirmatory.<br>May have elevated C-reactive protein.<br>Transvaginal ultrasound useful in detecting tubo-ovarian masses. |
| Endometrial polyps | Menorrhagia, congestive and spasmodic dysmenorrhoea and intermenstrual bleeding | Transvaginal USG, saline infusion sonography, hysteroscopy. |
| Pelvic congestion syndrome | Chronic pelvic pain that increases premenstrually; with prolonged standing, postural changes, walking, or activities that increase intra-abdominal pressure; and after intercourse (postcoital ache). | Radiological imaging is frequently used to confirm the clinical suspicion of this condition.<br>Gold standard is selective venography. |

**Table 3**

According to NICE *Clinical Knowledge Summary for Managing Dysmenorrhoea* (Nov 2018):

1. **First-line treatment for women with primary dysmenorrhoea should be a non-steroidal anti-inflammatory drug (NSAID), unless contraindicated.** (Figures 1 and 2)

Women with dysmenorrhoea have high levels of prostaglandins (hormones known to cause cramping abdominal pain). NSAIDs act by blocking prostaglandin production by inhibiting the action of cyclo-oxygenase (COX, an enzyme responsible for the formation of prostaglandins).

The COX enzyme exists in two forms: COX-1 and COX-2. Standard NSAIDs (such as ibuprofen, naproxen, and mefenamic acid) are considered 'non-selective' because they inhibit both COX-1 and COX-2 enzymes. Coxibs (such as celecoxib and etoricoxib) are highly selective for COX-2 but can interact with COX-1 in certain circumstances.

A Cochrane systematic review compared 20 different NSAIDs (18 non-selective and two COX-2-specific) with placebo, paracetamol, or each other in 5820 women with dysmenorrhoea and found that:

- NSAIDs were more effective for pain relief than placebo but were associated with more adverse effects.
- NSAIDs appeared to be more effective for pain relief than paracetamol. There was no evidence of a difference with regard to adverse effects, although data was very scanty.

### Choice of NSAIDs

Options include ibuprofen, naproxen, mefenamic acid, flurbiprofen, or tiaprofenic acid.

The Cochrane systematic review found little evidence of the superiority of any individual NSAID for either pain relief or safety, but the available evidence had little power to detect such differences as most individual comparisons were based on very few small trials. There was no evidence that COX-2-specific inhibitors were more effective or tolerable for the treatment of dysmenorrhoea than standard NSAIDs, although data was very scanty.

### Licensed indications

- Ibuprofen, naproxen, and flurbiprofen are licensed for the treatment of dysmenorrhoea.
- Mefenamic acid is also licensed for the treatment of dysmenorrhoea; however, there are concerns that it is more likely to cause seizures in overdose than other NSAIDs. It has a narrow therapeutic window, which increases the risk of accidental overdose. The National Poisons Information Service considers an ingestion of 40 mg/kg or more to be potentially toxic. This means that a woman who weighs 50 kg would only need to ingest one extra dose of 500 mg of mefenamic acid in 24 hours (total of 2000 mg) to be considered to be at risk of toxicity.

2. **Offer paracetamol if NSAIDs are contraindicated or not tolerated, or in addition to an NSAID if the response is insufficient.**

Evidence from the Cochrane systematic review showed that NSAIDs appeared to be more effective than paracetamol in the treatment of primary dysmenorrhoea. However, paracetamol is a well-tolerated analgesic and is a widely used alternative to NSAIDs for musculoskeletal pain.

**If the woman does not wish to conceive,** consider prescribing a 3–6 month trial of a hormonal contraceptive as an alternative first-line treatment.

Combined hormonal contraceptives, including combined oral contraceptives, the contraceptive ring, and the transdermal patch, all work to decrease the endometrial lining, which

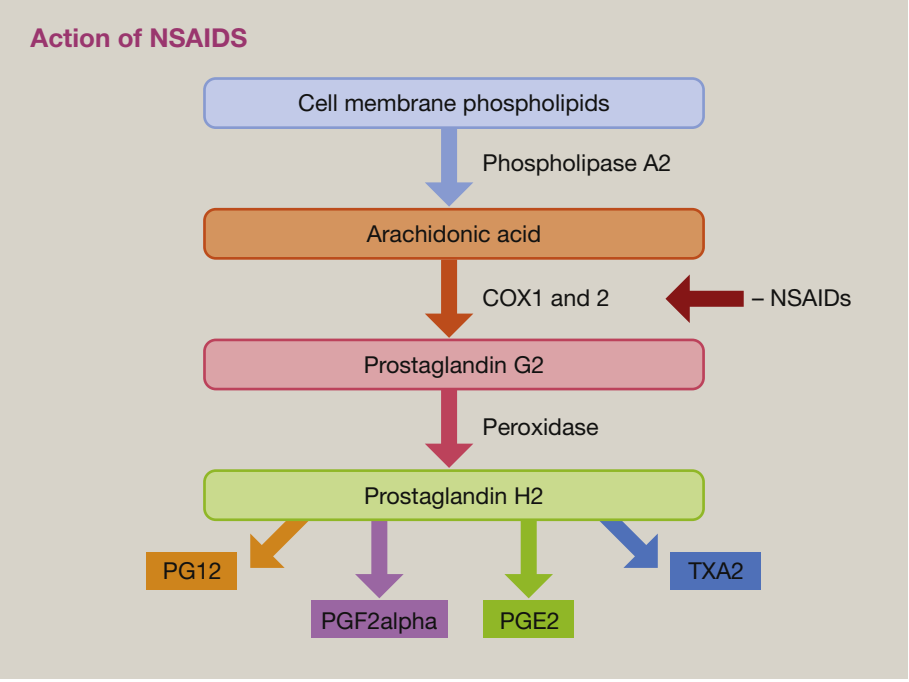


**Figure 1**

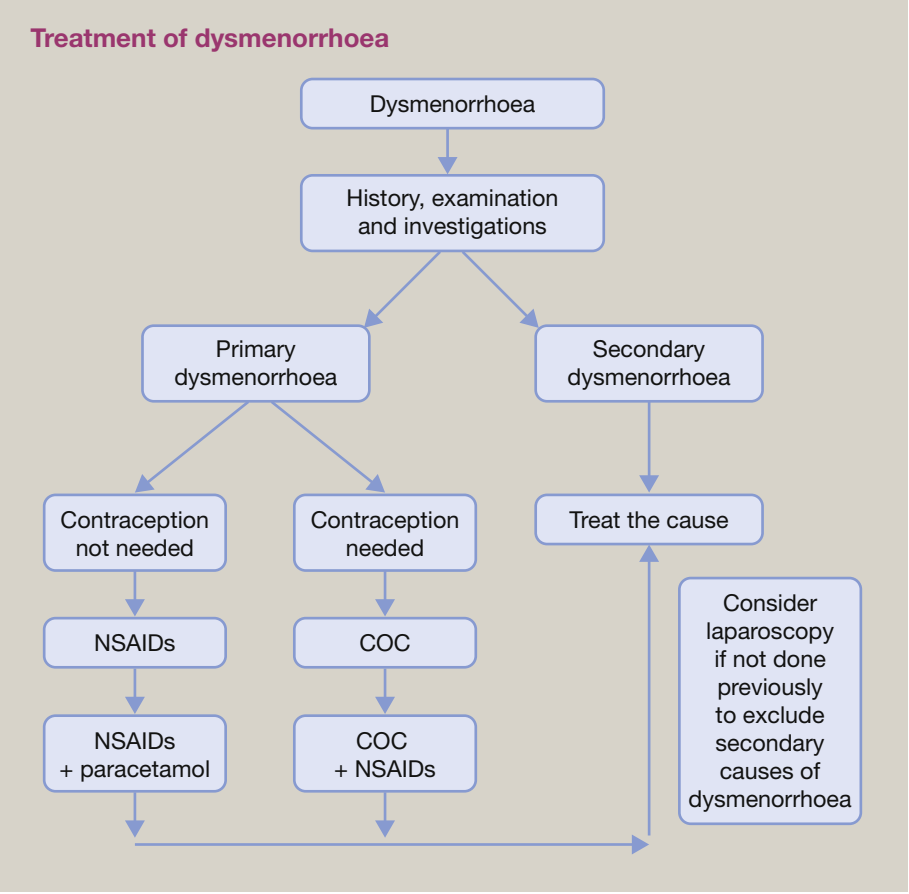


**Figure 2**

produces prostaglandins and leukotrienes that contribute to the menstrual pain. In addition, their role in inhibiting ovulation and subsequent progesterone production also decreases the formation of prostaglandins and leukotrienes. Thus, these products have been prescribed for primary dysmenorrhea, as well as some causes of secondary dysmenorrhea, particularly endometriosis.

a. Monophasic combined oral contraceptive (COC) preparations containing 30–35 μg of ethinylestradiol and norethisterone, norgestimate, or levonorgestrel are usually first choice.
   i. A Cochrane systematic review found limited evidence that COCs are effective for relieving pain associated with primary dysmenorrhoea. However, the overall quality of the trials was poor, some trials were over 25 years old, and some used COCs with higher doses of oestrogen than is present in currently available products.
   ii. Despite the limited trial evidence, COCs are widely recommended by experts for this indication, and the added contraceptive advantages make them a suitable first-line option for some women.
   iii. COCs containing 20 μg of ethinylestradiol are less preferred because they are more likely to cause unscheduled bleeding.

b. Oral (desogestrel 75 μg), parenteral (Depo-Provera or Sayana Press, and Nexplanon), and intrauterine progestogen-only (Mirena) contraceptives may also be considered after a full discussion of the advantages and disadvantages.

**Oral progestogen-only contraceptives**

iv. An observational study assessed the effects of desogestrel 75 μg (Cerazette) in women with dysmenorrhoea and found that dysmenorrhoea resolved or considerably improved in 93% of the study population.

**Parenteral progestogens**

v. A review of open-label, non-comparative and comparative studies assessed the effects of etonogestrel subdermal implant (Implanon, which is bioequivalent to Nexplanon) on menstrual bleeding patterns and found that it reduced both the incidence and severity of dysmenorrhoea. Most women (77%) who had baseline dysmenorrhoea experienced complete resolution of symptoms.

vi. Some experts recommend that parenteral progestogens (such as depot medroxyprogesterone acetate) may be considered in the treatment of dysmenorrhoea. Depot medroxyprogesterone acetate works primarily by suppressing ovulation; it can also induce endometrial atrophy. One of its benefits is amenorrhea with a resultant reduction in the incidence of dysmenorrhea.

b. **Intrauterine contraception**
   i. A longitudinal population study assessed the prevalence and severity of dysmenorrhea in women using an

intrauterine contraception and found that the levonorgestrel-releasing intrauterine system (LNG-IUS, Mirena) was associated with reduced dysmenorrhea severity compared with other methods of contraception (barrier methods, natural family planning, coitus interruptus, and sterilization) or no method of contraception. The copper intrauterine device (Cu-IUD) did not reduce the severity of dysmenorrhea when compared with other methods of contraception.

ii. The RCOG guideline states that non endometriosis-related cyclical pain also appears to be well controlled by the LNG-IUS. It is also an option for those who do not require contraception, particularly older women who have had children and women with heavy menstrual bleeding.

3. **If the response to individual treatments is insufficient,** a combination of an NSAID (or paracetamol) and hormonal contraception may be considered.
4. **Consider recommending the following non-drug measures (in addition to drug treatments) to help reduce pain:**
   c. Local application of heat (e.g. a hot water bottle or heat patch).
   d. Transcutaneous electrical nerve stimulation (TENS) — set to a high frequency.

**Heat therapy and transcutaneous electrical nerve stimulation (TENS)**

A systematic review assessed the effectiveness of heat therapy and TENS interventions for pain relief and quality of life improvement in women with primary dysmenorrhea.

i. Evidence from trials on heat therapy showed individual improvement in pain levels.

ii. Evidence from trials on TENS showed relatively positive effects in pain reduction. Overall, the evidence suggested that conventional TENS is better option in dysmenorrhoeal pain relief than other forms of TENS (such as acupuncture-like TENS, and OVA TENS) and that high-frequency TENS is more effective for pain relief, although there was insufficient to determine the effectiveness of low frequency TENS in reducing dysmenorrhea.

5. **Other non-drug measures**
   e. There is a lack of good-quality evidence to support the use of herbal remedies, dietary supplements, acupuncture, acupressure, spinal manipulation, behavioural therapy, and exercise to treat dysmenorrhoea. In addition, herbal remedies have the potential to cause adverse effects and may interact with other medicines.

## Prognosis

There are very few longitudinal studies examining the progression and eventual outcome of primary or secondary dysmenorrhoea. Primary dysmenorrhoea often improves in the third decade of a woman's reproductive life and appears to be reduced after childbirth. The prognosis of secondary dysmenorrhoea is not known as its severity, progression and eventual outcome depend on the underlying pathology.

## Conclusions

Dysmenorrhoea has a significant physical, behavioural, psychological and social impact, affecting a large proportion of women of reproductive age. The exact pathophysiological processes are not fully understood but it probably reflects increased myometrial activity induced by an excessive production of prostaglandin causing ischaemia. Mainstay of treatment is generally supportive providing symptomatic relief with NSAIDs or COCP and more directive surgical treatment should be reserved for specific secondary causes of dysmenorrhoea or for refractory cases. ◆

## Practice points

- Around 45–95% of menstruating women suffer with dysmenorrhoea
- Increased myometrial activity induced by an excessive production of prostaglandin causing uterine ischaemia is the most accepted pathophysiological mechanism
- Primary dysmenorrhoea is seen in young women with ovulatory cycles and is characterised by spasmodic menstrual pain starting just before menstruation lasting for 24–48 h. There is no coexisting pathology
- Secondary dysmenorrhoea is always associated with an underlying pathology and is characterised by congestive menstrual pain, which increases progressively through the late luteal phase, peaking with onset of menstruation
- History is critical in establishing the diagnosis of dysmenorrhoea
- Treatment is aimed at symptomatic relief with analgesics — especially NSAIDs — and at treating the underlying pathology.

## FURTHER READING

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