Chronic pelvic pain (CPP) is defined as noncyclic pain in the pelvis, anterior abdominal wall, back, or buttocks that has been present for at least 6 months and is severe enough to cause functional disability or require medical care. CPP is very common, with an estimated prevalence of 15% to 20%. It accounts for 20% of gynecology visits and 15% of hysterectomies in the United States, and it is believed to account for $2.8 billion in direct health care spending annually.2–5

Caring for patients with CPP can be very challenging. They often arrive at your office frustrated, having seen multiple providers or having undergone multiple surgeries. They may come to you whether you are a general ObGyn or subspecialize in maternal-fetal medicine, oncology, reproductive endocrinology, urogynecology, or adolescent gynecology. From interactions with other providers or their own family members, these patients may have received the message—either subtly or overtly—that their pain is “all in their head.” As such, some patients may resist any implication that their pain does not have an anatomic source. It is therefore critical to have appropriate tools for evaluating and managing the complex problem of CPP.

Perform a thorough and thoughtful assessment
Chronic pelvic pain often presents as a constellation of symptoms with contributions from multiple sources, as opposed to a single disease entity. Occasionally there is a single cause of pain, such as a large endometrioma or degenerating fibroid, where surgery can be curative. But more commonly the pain arises from multiple organ systems. In such cases, surgery may be unnecessary and, often, can worsen pain.

Thoughtful evaluation is critical in the CPP population. Take a thorough patient history to determine the characteristics of pain (cyclic or constant, widespread or localized), exacerbating factors, sleep disturbances,
Central pain amplification is characterized clinically by widespread pain, fatigue, sleep disturbances, memory difficulties, and somatic symptoms. Chronic pain does not behave like acute injury or postsurgical pain. Continuous peripheral pain signals for a prolonged period can lead to changes in how the brain processes pain; specifically, the brain can begin to amplify pain signals. This “central pain amplification” is characterized clinically by widespread pain, fatigue, sleep disturbances, memory difficulties, and somatic symptoms. Central pain amplification occurs in many chronic pain conditions, including fibromyalgia, interstitial cystitis, irritable bowel syndrome, low back pain, chronic headaches, and temporomandibular joint disorder. Recent clinical and functional magnetic resonance imaging (MRI) studies demonstrate central pain amplification in many patients with CPP. Notably, these findings are independent of the presence or severity of endometriosis.

In this article we discuss many therapies that have not been specifically studied in patients with CPP, and treatment efficacy is extrapolated from other conditions with chronic pain amplification, such as fibromyalgia or interstitial cystitis. Additionally, many treatments for conditions associated with central pain amplification are used off-label, that is, the US Food and Drug Administration (FDA) has not approved the medication for treatment of these specific conditions. This should be disclosed to patients during counseling.

Discuss treatment expectations with patients
Educating patients regarding the pathophysiology of chronic pain and setting reasonable expectations is the cornerstone of providing patient-centered care for this complex condition. We start most of our discussions about treatment options by telling patients that while we may not cure their pain, we will provide them with medical, surgical, and behavioral strategies that will reduce their pain, improve their function, and enhance their quality of life.

Surprisingly, most patients say that a cure is not their goal. They just want to feel better so they can return to work or activities, fully participate in family life, or not feel exhausted all the time. As such, a multimodal treatment plan is generally the best strategy for achieving a satisfactory improvement in symptoms.

Case 1
Patient’s pain continues after endometriosis excision
A 32-year-old woman (G1P1) reports having CPP for 8 years. She underwent excision of stage 1 endometriosis last year, which resulted in a modest improvement in pain for 6 months. Her pain is worse during menses, at the end of the day, and with vaginal intercourse (both during and lasting for 1 to 2 days after). On examination, you find diffuse pelvic floor tenderness but no adnexal masses or rectovaginal nodularity on palpation.

What treatment options would you consider for this patient?

Multimodal treatment often needed to manage CPP symptoms
The patient described in Case 1 may benefit from a combination of therapies that include analgesics, hormone suppression agents, and physical therapy (PT).

Analgesics
Nonsteroidal anti-inflammatory drugs (NSAIDs), including ibuprofen and naproxen, work by inhibiting cyclooxygenase enzyme, which decreases assembly of peripheral prostaglandins and thromboxane. In a large Cochrane review, NSAIDs were associated with moderate or excellent pain relief for approximately 50% of patients with dysmenorrhea, and they have been shown to reduce menstrual flow due to decreased production of uterine prostaglandins. There is little evidence for use of NSAIDs in chronic pain conditions.
No evidence supports opioid use in CPP or other chronic pain conditions. Long-term opioid use is associated with a multitude of adverse effects, risk for dependence, and the induction of opioid-induced hyperalgesia.

Acetaminophen’s mechanism of action is unclear, but the drug likely inhibits central prostaglandin synthesis, and it works synergistically with other analgesics.

Opioids act on μ and δ opioid receptors in the central and peripheral nervous systems as well as in the gastrointestinal system. No evidence supports opioid use in CPP or other chronic pain conditions. Long-term opioid use is associated with a multitude of adverse effects, risk for dependence, and the induction of opioid-induced hyperalgesia (in which patients develop greater sensitivity to pain stimuli).

Analgesics, specifically NSAIDs, can be considered for use in patients with dysmenorrhea, cyclic pain exacerbation, or a suspected inflammatory component of pain. Best practices include scheduling NSAID use before the onset of menses and continuing the drugs on a scheduled basis throughout. NSAIDs should be used for a brief period, and regular use on an empty stomach should be avoided.

Hormone suppression
Many types of hormone suppression therapy are available, including combined estrogen-progestin medications, progestin-only medications, and gonadotropin-releasing hormone (GnRH) agonists and antagonists.

Combined estrogen-progestin medications include oral contraceptive pills (OCPs), vaginal rings, and transdermal patches. Combined estrogen-progestin methods cause atrophy of eutopic and ectopic endometrium and suppress GnRH.

Progestin-only methods include oral formulations, the levonorgestrel intrauterine device, intramuscular and subcuticular injections, and subdermal implants. Progestin-only methods lead to atrophy of eutopic and ectopic endometrium.

A GnRH agonist, leuprolide depot works by downregulating luteinizing hormone and follicle stimulating hormone release from the pituitary, causing suppression of ovarian follicular development and ovulation, leading to a hypoestrogenic state.

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Pelvic PT can be considered for patients with pain reproducible with palpation of the pelvic floor, abdominal wall, paraspinal lumbar muscles, or sacroiliac joints.

Combined estrogen-progestin formulations and progestin-only options are often considered first-line therapy for dysmenorrhea and endometriosis. Continuous administration, with the goal of inducing amenorrhea, is effective in the treatment of dysmenorrhea. Several randomized controlled trials have shown that different types of hormone suppression agents are, essentially, equally effective. Treatment recommendations therefore should focus on adverse effects, cost, and patient preference. GnRH agonists and norethindrone are not FDA approved for the treatment of endometriosis.

It may be appropriate to consider use of hormone suppression therapy in patients with menstrual exacerbation of pain symptoms, including those with a history of endometriosis. We generally advise patients that the goal is amenorrhea and that achieving it often involves a process of trying different formulations to find the best fit. Remember that GnRH agonists are dependent on a functional hypothalamic-pituitary-ovarian axis, and they are unlikely to be effective in women with suspected residual endometriosis who have had a bilateral oophorectomy.

Physical therapy
For CPP, PT typically targets musculoskeletal dysfunction in the pelvic floor, abdominal wall, hips, and back. Interventions include muscle control, mobilization, and biofeedback. Pelvic PT has been shown to improve pain and dyspareunia in patients with CPP, coccydynia, and vestibulodynia. One large study found a significant, patient-directed decrease in pain medication use after pelvic floor PT. Pelvic PT for patients with interstitial cystitis and pelvic floor tenderness resulted in improved pain and bladder symptoms.

Pelvic PT can be considered for patients with pain reproducible with palpation of the pelvic floor, abdominal wall, paraspinal lumbar muscles, or sacroiliac joints. Best practices include referral to a therapist who has specialized training in CPP, including pelvic floor therapy. It is important to clearly list the indication for referral, as many of these therapists also treat stress urinary incontinence. The wrong exercises can result in increased hypercontractility of pelvic floor muscles, which can worsen pelvic pain.

It is also critical to clarify expectations with your patient at the time of PT referral. Specifically, advise patients that when beginning therapy, it is common to experience a temporary increase in discomfort of the pelvic muscles. Inform patients also to expect that their therapist will perform internal manipulation of the pelvic floor muscles through the vagina, as this can be surprising for some patients. Finally, counsel patients that their adherence to daily home exercises improves their chance of a durable, long-term successful response.

**CASE 1** Treatment recommendations
For treatment of this patient’s CPP, consider scheduled naproxen therapy during menses, continuous OCPs, and referral for pelvic floor PT.

**CASE 2** Patient with long-standing CPP, multiple diagnoses, and sleep problems
A 30-year-old woman (G2P2) reports having had CPP for 17 years. She is amenorrheic with continuous OCP treatment. She had experienced some improvement with pelvic PT. The patient reports that she has daily pain with intermittent pain flares and that she is exhausted and has poor sleep quality, which she attributes to pain. She has been diagnosed with interstitial cystitis, irritable bowel syndrome, and temporomandibular joint disorder. She has a history of depression, which she feels is well controlled with bupropion. Physical examination reveals that the patient has diffuse but mild pain in the pelvic floor and abdominal wall muscles.

What further pain management options can you offer for this patient?

**Managing pain, sleep disturbance, and depression**
This patient has been living with CPP for many years, and she has sleep difficulties that might be exacerbating pain or result from pain (or both). She is already on continuous OCPs and has had some relief with pelvic PT. Other options that may help with her multiple issues...
include antidepressants, cyclobenzaprine, and calcium channel blockers.

**Antidepressants**

Several classes of antidepressants have been used in the treatment of chronic pain conditions, specifically, tricyclic antidepressants (TCAs) and serotonin-norepinephrine reuptake inhibitors (SNRIs). Commonly used TCAs include amitriptyline, nortriptyline, desipramine, and doxepin. Commonly used SNRIs are duloxetine and milnacipran. Both TCAs and SNRIs increase the availability of norepinephrine and serotonin, which are thought to act on the descending pain inhibitory systems to decrease pain sensitivity. Of note, most selective serotonin reuptake inhibitors (SSRIs) at typical doses do not exert a significant enough impact on norepinephrine to be useful for chronic pain.22

Evidence is limited on the use of antidepressants for treating CPP. Amitriptyline is the most extensively studied antidepressant. Amitriptyline treatment resulted in modest pain improvement in patients with CPP and fibromyalgia.23,24 Bothserous anticholinergic effects, including fatigue, dry mouth, and constipation, often are reported with TCAs. Adverse effects tend to be less with nortriptyline or desipramine compared with amitriptyline, but possibly at the expense of efficacy.

While SNRIs have not yet been studied in CPP, several investigations have shown that they improve pain and quality of life in fibromyalgia patients.22,25

Antidepressant therapy may be appropriate for patients with suspected central pain amplification, widespread pain, and sleep disturbances. Best practices include patient education and careful discussion of this option with your patient. We suggest that clinicians explain that antidepressant medications alter the function of neurotransmitters, which modulate pain signals. While neurotransmitters also are involved in mood modulation, this is not the therapeutic goal in this circumstance. In addition, the doses used for the effective treatment of chronic pain are significantly lower than those needed to treat depression effectively.

Patients often need to hear that you believe that their pain is real and is not a manifestation of depression or another mood disorder. If you suspect that the patient also has untreated depression, address this as its own issue and use medications that have greater efficacy for mood symptoms.

Because many antidepressants can cause sedation, they are best taken before bedtime. Also, slow dose titration over several weeks will reduce the chance of bothersome adverse effects. Counsel patients that efficacy is not generally seen until at goal dose for several weeks. Be aware of interactions with other medications that can cause serotonin syndrome.

**Cyclobenzaprine**

Cyclobenzaprine is a muscle relaxant that also has activity in the central nervous system. The drug’s precise mechanism of action is not known, but it appears to potentiate norepinephrine and bind to serotonin receptors. Thus, it also likely has some TCA-like activity. Cyclobenzaprine has not been studied in patients with CPP. In fibromyalgia patients, however, it produced significant improvements in pain, sleep, fatigue, and tenderness.26,27 In our anecdotal experience with CPP patients, cyclobenzaprine has been one of the most impactful therapies. It hits the “chronic pain triad,” meaning that it helps with myofascial pain, neuropathic pain, and sleep disturbances.

Cyclobenzaprine treatment may be considered for patients with myofacial pain, sleep disturbances, and clinical symptoms of central pain amplification.
associated with improvements in pain, coping, mood, and functional status. Helping a patient to improve her sleep generally requires a multifaceted approach. It always involves “sleep hygiene” or a behavioral component, and pharmacologic assistance may be considered when improved sleep hygiene does not provide adequately improved sleep quality.

**Calcium channel blockers**

Gabapentin and pregabalin are calcium channel blockers that inhibit the reuptake of glutamate, norepinephrine, and substance P, which helps to decrease pain sensitivity. They also act as membrane stabilizers, reducing hyperexcitability of peripheral and central nerves. Studies have shown that in patients with CPP, gabapentin resulted in improved pain and mood symptoms with few adverse effects. Patients with fibromyalgia had improvements in pain, sleep, quality of life, fatigue, and anxiety with both gabapentin and pregabalin.

It is appropriate to consider use of gabapentin or pregabalin in patients with central pain amplification and sleep disturbances. Best practices include starting with a low dose at bedtime. Traditionally, gabapentin is given in 3 equal doses throughout the day. In our experience, patients report less daytime drowsiness and better sleep quality if two-thirds of the daily dose is given at night, with the remaining daily dose broken up into 2 smaller daytime doses. Slow titration over several weeks will reduce risk of bothersome adverse effects. Patients should be counseled that efficacy is not generally seen until treatment is at goal dose for several weeks.

**CASE 2  Treatment recommendations**

For this patient with daily pelvic pain, multiple diagnoses that have a pain component, and poor sleep quality, consider a treatment plan that includes scheduled cyclobenzaprine, improved sleep hygiene, and, if needed, gabapentin.

**CASE 3  Cesarean delivery, hysterectomy, and continued pelvic pain**

A 38-year-old woman (G2P2) has had CPP for the past 10 years. She developed persistent left lower-quadrant pain after cesarean delivery of her son. She had a hysterectomy 2 years ago for CPP, after which her pain worsened. She describes daily pain with intermittent flares. On examination, the patient has focal left lower-quadrant pain lateral to the left apex of her Pfannenstiel incision.

What treatment approach would be appropriate for this patient?

**Focal pain requires a precisely targeted treatment**

This patient with focal left lower-quadrant pain is a candidate for anesthetic trigger point injections in the affected area near her Pfannenstiel incision.

**Anesthetic injections**

Consider the presence of trigger points and peripheral neuropathy in patients with focal abdominal wall pain. Trigger points are focal, palpable nodules within muscles. They are markedly painful to palpation and are associated with referred pain, motor dysfunction, and occasionally autonomic symptoms. They frequently are seen in abdominal wall or pelvic floor muscles in patients with CPP and are caused by abnormal neuromuscular depolarization.

The ilioinguinal, iliohypogastric, and genitofemoral nerves are in close proximity to Pfannenstiel and laparoscopic port site incisions. These nerves may be injured directly during surgery, but they also may be compressed by postoperative scarring.

Anesthetics, such as lidocaine and bupivacaine, which act as sodium channel blockers, can be injected into this area, and improvement often substantially outlasts the anesthetic’s duration of action. While these drugs’ mechanism of action is not clear, theories include altered function of sodium channels on sensory nerves with repeated anesthetic exposure, dry needling that occurs during injection, hydrodissection of tight connective tissue bands surrounding neuromuscular bundles, or depletion of substance P and neuropeptides as a result of injection.
In several studies, patients with CPP reported decreased pain with lidocaine injections in pelvic floor or abdominal wall trigger points.36-38 Patients with fibromyalgia reported improvement in pain and a decreased need for NSAIDs with bupivacaine trigger point injections.39 While abdominal wall nerve blocks have not been extensively studied in patients with chronic neuropathic pain following gynecologic surgery, they have been shown to substantially improve chronic neuropathic pain following inguinal hernia repair.40

Anesthetic injections appropriately may be considered in patients with focal pain in a muscle or in the distribution of abdominal wall nerves, palpation of which reproduces pain symptoms. Patients with diffuse pain are less likely to benefit from anesthetic injections. Best practices include careful examination with attention to areas of prior abdominal incisions.

Our practice is to inject each affected area with a mix of 9 mL of 1% lidocaine and 1 mL of sodium bicarbonate. If a patient reports at least 24 hours of improvement, we repeat the injection in 2 to 4 weeks. The goal is for the patient to experience a progressively longer duration of benefit with subsequent injections. We perform repeat injections shortly after pain begins to recur at that site. The patient should eventually graduate from receiving regular injections and may return for a remedial injection if pain recurs.

**CASE 3  Treatment recommendations**

For this patient with persistent focal left-lower quadrant pain and a defined trigger point near her Pfannenstiel incision, consider anesthetic injection in the left lower quadrant.

**Work toward realistic symptom improvement**

Remember that living with chronic pain is exhausting, and empathy with a patient-centered approach is the most important ingredient for patient improvement and satisfaction. Discuss realistic expectations with patients. Remind them that there is no magic bullet for the complex problem of CPP, and that chronic conditions generally do not improve overnight. Focus on improving the patient’s function and quality of life, and applaud symptom improvement rather than focusing on complete pain resolution.

As these visits often require a good deal of patient education, budget more appointment time if feasible. We find that scheduling frequent return visits (approximately every 3 to 4 months) allows timely treatment follow-up so that changes may be made if needed. If you have maximized your available treatment options, referring the patient to a specialist with additional training in CPP is a sensible next step.

**References**

2. Mathias SD, Kuppermann M, Liberman RE, Lipschutz RC, Steege JE. Chronic pelvic pain: prevalence, health-related

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