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Chronic pelvic pain: 11 critical questions about causes and care

An expert explores anatomic and mechanistic bases of chronic pelvic pain in women to clarify optimal diagnosis, management, and treatment

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CASE

Multisystem involvement makes diagnosis and treatment thorny

Sara B. is a 26-year-old gravida 4, para 3, abortus 1 who visits your office to be evaluated for chronic pelvic pain. She says her pain is most intense before and during her period and with intercourse. It is located primarily in her abdominopelvic area, but radiates to her lower extremities and lumbosacral back. It appears to be related to bowel function and meets Rome II criteria for irritable bowel syndrome (criteria developed by a panel of experts convened by the Rome Foundation).

Sara B. reports that she voids at least 20 times a day and once during the night. She has a history of depression, for which she takes sertraline (Zoloft), but no history of physical or sexual abuse. When she underwent laparoscopy more than 1 year ago, endometriosis was diagnosed visually.

Upon physical examination, you identify 13 positive fibromyalgia points, moderate tenderness of the posterior levator ani muscles, severe tenderness of the bladder, and moderate tenderness of the uterine fundus. You also find moderate tenderness in the adnexa and uterosacral ligaments bilaterally. Your tentative diagnosis: endometriosis, interstitial cystitis, fibromyalgia, and irritable bowel syndrome.

How do you confirm the diagnosis? And what treatment should you offer to her?

Chronic pelvic pain (CPP) is anything but simple. Sara B.'s case illustrates some of the complexity involved in the diagnostic evaluation and treatment of this disorder. Very rarely is the pain localized to one organ or system. More commonly, it involves multiple

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organs or anatomic areas within the pelvic region.

To confirm the diagnosis in Sara's case, the next step would be a potassium chloride sensitivity test for interstitial cystitis. I would also start her on desipramine for fibromyalgia, and perform laparoscopy and cystoscopy with hydrodistention to explore the diagnosis further.

In Sara's case, let's assume that the repeat laparoscopy reveals glomerulations of the bladder but no recurrent endometriosis. I would administer oral pentosan polysulfate sodium and instill heparin and lidocaine in her bladder to improve her voiding pattern significantly (to the range of four to six times a day without nocturia). I would also prescribe continuous oral contraceptives to suppress her menses and alleviate some of her pain. In addition, I would be interested to see what a transjugular pelvic venogram would reveal. If it were to suggest severe pelvic congestion syndrome, I might perform embolization of both ovarian veins to provide additional relief.

Clearly, when confronted with a case as intricate as Sara's, there are many ways to organize your thinking about the potential diagnoses that may cause or contribute to CPP. This article focuses on anatomic and mechanistic bases for evaluation of this disorder as a means of tailoring treatment appropriately. It explores these topics by addressing 11 critical questions, ranging from how pain is described to what to do about it.

FAST TRACK

Fifteen percent of women 18 to 50 years old reported chronic pelvic pain in a survey conducted by the Gallup organization

1. How is pain defined?

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.[1]

Pain is defined in this way to make it clear that it is not just a sensory experience, but both a sensory and emotional experience. This means that the pain is always subjective and is not the same in all individuals—nor does it remain the same in the same person.

Individuals base their descriptions of pain on their unique prior experience of it. Many people report pain in the absence of tissue damage or any likely pathophysiologic cause, often for psychological reasons. If they regard their experience as pain and report it as they would pain caused by tissue damage, it should be accepted as pain. In defining pain, it is best to deliberately avoid tying pain to the stimulus.

What about CPP? There is no generally accepted definition. The American College of Obstetricians and Gynecologists (ACOG) defines it as noncyclic pain of at least 6 months' duration that localizes to the anatomic pelvis, lumbosacral back, buttocks, or anterior abdominal wall at or below the umbilicus and that is severe enough to cause functional disability or lead to medical care.[2]

2. How many women suffer chronic pelvic pain?

Chronic pelvic pain is more common than is generally recognized. Here are some estimates:

- A US study conducted by the Gallup organization found that 15% of women 18 to 50 years old had CPP[3]
- A survey of women in family medicine and ObGyn offices found that 39% had CPP, although only 8% reported having it more often than "sometimes"[4]
- The Oxfordshire Women's Health Study, a postal questionnaire survey of a random sample of women 18 to 49 years old in the general UK population, found a prevalence of 24%[5]
- A primary-care database in a UK study of women 15 to 73 years old found a prevalence of 38 cases for every 1,000 women. (The database contained annualized data that excluded women who had only dysmenorrhea or dyspareunia.) Although the study likely underestimated the prevalence of CPP, the finding does make it possible to compare prevalences in the same population: asthma (37/1,000), back pain (41/1,000), and migraine (21/1,000).[6]

3. What are the main types of pain involved?

They are nociceptive, inflammatory, and neuropathic pain.

Nociceptive pain occurs in response to a noxious stimulus that alerts the organism to impending tissue injury. One way to think of nociceptive pain is as "normal" or physiologic pain (**FIGURE**).

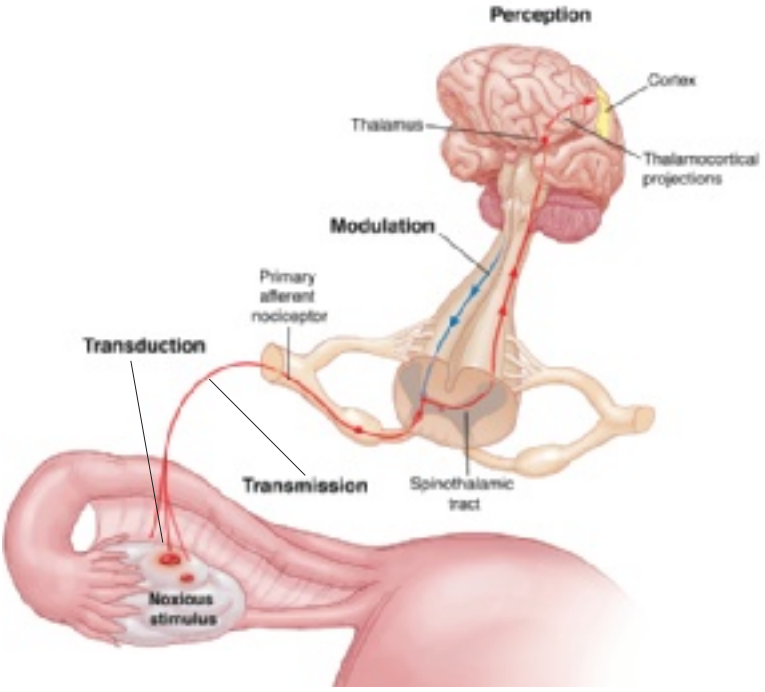
Acute pelvic pain is usually nociceptive in origin. CPP is usually not solely nociceptive in origin. It often involves inflammatory or neuropathic pain, or both (**TABLE 1**, page 30).

Inflammatory pain arises in response to tissue injury and the resulting inflammatory process. In some cases, the inflammatory response is actually a source of tissue injury (e.g., rheumatoid arthritis). Inflammatory pain may be an important mechanism in both acute and chronic pelvic pain.

Neuropathic pain is produced by damage to or dysfunction of neurons in the peripheral or central nervous system. It is not physiologic and is often a significant mechanism in the generation of CPP.

An understanding of inflammatory and neuropathic mechanisms is not esoteric, but has clinical significance.

FIGURE Noxious stimulus is often the trigger in acute and chronic pain



Nociceptive pain is a response to a noxious stimulus, alerting the organism to impending tissue injury. Four fundamental processes are involved in nociceptive pain: **transduction,** in which the stimulus is converted to a biochemical signal; **transmission,** in which the signal is transported from the peripheral nervous system to the dorsal ganglion and central nervous system; **modulation,** in which the intensity of the signal is increased or decreased; and **perception,** in which the organism experiences the pain.

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4. Is chronic pelvic pain a disease—or a symptom?

My experience caring for patients who have CPP suggests that chronic pain is a disease, whereas acute pain is a symptom. This concept is controversial in gynecology, and CPP is often labeled as only a symptom, not a diagnosis.[7] The search for one underlying disease means that the woman who has CPP frequently undergoes multiple surgical and other invasive procedures, often with incomplete or insignificant diagnoses and responses.

The assumption that CPP is always due to a specific pathologic process in somatic structures or viscera (nociceptive pain) excludes the possibility that CPP can be caused by prolonged or permanent dysfunction of the peripheral or central nervous system, or both (neuropathic pain), or by psychological mechanisms (central pain). Clinical knowledge lags behind basic science in this area and is not at all concrete.

Our ability to accurately diagnose neuropathic or inflammatory pain leaves room for improvement.

5. Is chronic pelvic pain a gynecologic disorder?

Gynecologists have traditionally thought of CPP as either gynecologic or nongynecologic in origin, but this framework has very limited clinical utility. An anatomic and mechanistic classification (**TABLE 1**, page 30) represents a far richer strategic approach to the diagnostic evaluation of CPP, allowing more comprehensive and effective treatment.

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TABLE 1 Anatomic and mechanistic classification of pain

Central
- Neurogenic
- Psychogenic

Peripheral
- Somatic
  - —Neuropathic
  - —Inflammatory
  - —Nociceptive
    - Myofascial
    - Skeletal
    - Cutaneous
- Visceral
  - —Neuropathic
  - —Inflammatory
  - —Nociceptive
    - Gynecologic
    - Urologic
    - Gastrointestinal

FAST TRACK

Not all viscera generate pain, possibly owing to a lack of sensory receptors or appropriate nociceptive stimulus

6. What distinguishes visceral from somatic pain?

In addition to recognizing the importance of nociceptive, inflammatory, and neuropathic mechanisms in the generation of CPP, it is useful to classify potential causes anatomically (TABLE 1). In the broadest anatomic categories, pain may be central or peripheral, or both. Central pain can be psychogenic or neurogenic, and peripheral pain can be visceral or somatic.

Visceral sources of CPP include the reproductive, genitourinary, and gastrointestinal (GI) tracts. Mechanistically, as has been discussed, visceral pain can be neuropathic, inflammatory, or nociceptive.

Potential **somatic** sources of CPP are myofascial, skeletal, and cutaneous. Mechanisms leading to somatic CPP can be neuropathic, inflammatory, or nociceptive.

Somatic pain is better understood than visceral pain, but knowledge about the latter has been expanding rapidly. Several characteristics distinguish visceral pain:

- Not all viscera generate pain, possibly owing to a lack of sensory receptors or appropriate nociceptive stimulus
- Visceral pain is not always linked to injury and, therefore, may be functional
- Visceral pain frequently results in somatic referral of pain, possibly due to central convergence of visceral and somatic afferents
- Visceral pain tends to be diffuse or poorly localized, probably because of the low concentration of nociceptive afferents within viscera (only 2% to 10% of total afferents to the spinal cord originate from visceral nociceptors).[8]

It is not clear whether there are visceral neurons dedicated solely to nociception; it appears that viscera utilize sympathetic and parasympathetic neurons as nociceptors. It also is important to note that the stimuli that activate somatic nociceptors—cutting, crushing, and burning, for example—do not generally cause visceral pain. Visceral nociceptive pain is generated in response to:

- distention of a viscous or organ capsule
- spasm of visceral muscular fibers
- ischemia from vascular disturbances
- hemorrhage
- neoplasm
- inflammation
- traction on mesentery.

Another characteristic that distinguishes visceral from somatic nociception: Visceral nociception utilizes a dorsal midline pathway within the central nervous system, in addition to the lateral spinothalamic tract pathway utilized by somatic nociception.

Although this anatomic and mechanistic classification is clinically useful in the diagnostic evaluation of CPP, it is an oversimplification. Most patients—like Sara B., described in the opening case—have multiple anatomic and mechanistic causes of their pain.

7. What are the primary visceral causes of chronic pelvic pain?

A limited number of visceral and somatic diagnoses are backed by level-A evidence as having a causal relationship with CPP (TABLE 2, page 33). A few are discussed here.

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Disorders of the reproductive tract

Endometriosis is the most common gynecologic diagnosis in women who have CPP. There is significant epidemiologic evidence that endometriosis causes CPP. There is also strong evidence that endometriosis is a risk factor for CPP.

For example, human and animal experimental data suggest that women who have endometriosis have more episodes of urinary calculosis—and more severe pain—than women who do not have endometriosis.[9,10] They also are more likely to report vaginal pain than are women who do not have endometriosis, and that vaginal pain is more likely to be severe.

Such viscerovisceral interactions may play a significant role in CPP in women and may explain why some women who have a history of endometriosis have persistent pelvic pain after their endometriosis is gone, or even appear to develop other pain syndromes, such as interstitial cystitis.[11]

Our introductory case illustrates these concepts. Sara B.'s history is classic for endometriosis-associated pelvic pain; that was her original diagnosis. Although her pelvic pain recurred and persisted, a repeat laparoscopy found no endometriosis—but it did reveal evidence of interstitial cystitis and painful bladder syndrome (IC/PBS). Could Sara's current pain be neuropathic or inflammatory?

Treatment of IC/PBS targets neuropathic and inflammatory pain mechanisms, but this approach has not been fully explored for endometriosis. Might the visceral pain mechanisms be as important as the end-organ diagnoses? Clearly, this area merits further attention in gynecology.

Pelvic inflammatory disease (PID) often causes CPP. Approximately 18% to 35% of all women who have acute PID develop CPP.[12,13] The actual mechanisms by which CPP results from PID are not known, but it seems likely that both inflammatory and neuropathic mechanisms are important. Adhesive disease secondary to PID may also contribute to CPP by generating nociceptive pain. The route of treatment of PID—parenteral or oral antibiotics—does not appear to affect the odds of developing CPP.

Pelvic congestion syndrome is a controversial diagnosis that is uncommon in the United States. However, a well-designed study from Turkey suggests that about 40% of women who

TABLE 2 Disorders that may cause CPP or make it worse*

Reproductive tract
- Endometriosis
- Pelvic inflammatory disease
- Pelvic congestion syndrome
- Ovarian remnant syndrome
- Ovarian retention syndrome (residual ovary syndrome)
- Gynecologic malignancy (especially late-stage)
- Tuberculosis salpingitis

Urinary tract
- Interstitial cystitis
- Urethral syndrome
- Bladder malignancy
- Radiation cystitis

Gastrointestinal tract
- Irritable bowel syndrome
- Carcinoma of the colon
- Constipation
- Inflammatory bowel disease

Musculoskeletal system
- Abdominal wall myofascial pain (trigger points)
- Pelvic floor myalgia (levator ani or piriformis syndrome)
- Chronic coccygeal pain
- Faulty or poor posture
- Neuralgia of iliohypogastric, ilioinguinal, and/or genitofemoral nerves
- Peripartum pelvic pain syndrome
- Abdominal cutaneous nerve entrapment in surgical scar

Depression

Somatization disorder

* Disorders with Level-A evidence, i.e., good and consistent scientific evidence of a causal relationship to CPP

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About 18% to 35% of all women who have acute pelvic inflammatory disease develop chronic pelvic pain

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consult a gynecologist about CPP may have this syndrome.[14] In Sara's case, pelvic congestion syndrome was diagnosed after venous dilation and delayed emptying were confirmed by selective ovarian venography (transcervical venography is another option).[15] This approach is recommended.

According to the data, the most effective treatment of pelvic congestion syndrome is a high-dose progestin or gonadotropin-releasing hormone (GnRH) agonist.[14,16] Only observational data back treatment with ovarian venous embolization, which was performed in Sara's case.[8]

Urinary tract disorders

Interstitial cystitis/painful bladder syndrome is the most common urologic diagnosis among women who have CPP. Recent evidence suggests that 38% to 81% of women who are given a diagnosis of a reproductive-tract disorder may in fact have IC/PBS.[17,18] Much of the recent evidence regarding interstitial cystitis suggests that inflammatory and neuropathic mechanisms are crucial in the generation of CPP; therefore, much of the treatment focuses on inflammatory and neuropathic pain.[19,20]

For example, among the treatments that alleviate IC/PBS to some degree are:

- amitriptyline, widely used for neuropathic pain[21]
- gapabentin, an anticonvulsant used to treat neuropathic pain[22]
- antihistamines directed at inflammation[23]
- intravesical instillation of a local anesthetic agent, which may target both inflammatory and neuropathic pain mechanisms.[24]

Although these therapies have not been widely studied for their efficacy in gynecologic disorders, they are likely to produce similar results.

Disorders of the GI tract

Irritable bowel syndrome is the most common GI diagnosis in women who have CPP. It is a clinical diagnosis, usually based on the Rome III criteria (**TABLE 3**). (Sara B. was evaluated when Rome II criteria were in use.)

TABLE 3 Rome III criteria for irritable bowel syndrome

Two or more criteria must be present to make the diagnosis.

Over the past 3 months, have you had at least 3 days when you have had abdominal pain or discomfort that:

- was relieved with a bowel movement?
- began with a change in how often you were having a bowel movement?
- began with a change in the form or appearance of the stool or bowel movement?

Data from a primary-care database in the United Kingdom suggest that irritable bowel syndrome may be the most common diagnosis in women who have CPP (about 38% of patients).[25] In some cases, irritable bowel syndrome presents primarily with lower abdominal or pelvic pain, so it must be considered in the differential diagnosis of CPP. It seems likely that the pain in irritable bowel syndrome is not simply nociceptive, but that inflammatory and nociceptive mechanisms play an important role, as well.[26,27]

8. What are the main somatic causes of chronic pelvic pain?

Abdominal wall myofascial pain syndrome

When there are trigger points and myofascial pain of the lower abdominal wall muscles or pelvic floor muscles, they often present as CPP.

The underlying mechanisms responsible for myofascial pain syndrome are not clear. Nociceptive pain seems to be an important mechanism, but it is not clear whether inflammatory and neuropathic changes occur in some patients with this syndrome.

Many women who have myofascial pain syndrome and CPP respond poorly to traditional treatment with physical therapy and trigger-point injections; this may be due to inflammatory or neuropathic changes, or both.

Pelvic floor tension myalgia

Pain due to abnormal tension of the pelvic floor muscles is well-described. In many cases,

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Interstitial cystitis/painful bladder syndrome is the most common urologic diagnosis among women who have chronic pelvic pain

pelvic floor tension myalgia is a secondary phenomenon, as pelvic floor muscles react to the persistent presence of pelvic pain, which often has a visceral basis. In other cases, pelvic floor tension myalgia is a primary phenomenon and most likely represents myofascial pain syndrome of one or more of the pelvic floor muscles.

9. Are multiple anatomic sites and mechanisms the "norm"?

They may not be the norm, but it is not unusual to discover multiple diagnoses when evaluating a patient for CPP. Most published studies of women from primary-care practices suggest that 25% to 50% of patients have more than one diagnosis,[5,25,28] and anecdotal experience from referral practices suggests that most women in such practices have more than one diagnosis. The most common diagnoses in most published series are endometriosis, adhesions, irritable bowel syndrome, and interstitial cystitis.[18,29–31] The absence of somatic diagnoses in these series probably reflects the gynecologist's tendency to concentrate on visceral elements in CPP.

10. When multiple systems are involved, is the pain greater?

Yes. Women who have more than one organ system involved in CPP have greater pain than women who have only one system involved. For example, 43% of patients who have CPP without GI or urologic symptoms had moderate or severe pain (mean visual analog score of 3.8), whereas 71% of women who had CPP and both GI and urologic symptoms had moderate to severe pain (mean visual analog scale score of 5.4).[28]

Pain is also more consistent in women who have multisystem symptoms. Women who have CPP are more likely than the general population to have dysmenorrhea (81% versus 58%) and dyspareunia (41% versus 14%). The severity of pain with intercourse and with menses is greater in women who have CPP and GI and urologic symptoms than in those who have no GI and urologic symptoms.

11. How is treatment affected by multiple diagnoses?

The presence of multiple diagnoses often reflects neuropathic changes and neuropathic pain. An accurate diagnosis of all pain generators, including neuropathic pain, seems vital to improving our management and treatment of women who have CPP.

For example, in Sara B.'s case, I prescribed norethindrone acetate to suppress menses, based on her history of endometriosis-associated pelvic pain and menstrual exacerbation of her symptoms. I prescribed oral pentosan polysulfate sodium and intravesical lidocaine and heparin for interstitial cystitis/painful bladder syndrome. And I gave Sara amitriptyline for both fibromyalgia and interstitial cystitis/painful bladder syndrome (as well as suspected neuropathic pain).

I also recommended a low-fat, high-fiber diet to help alleviate her irritable bowel syndrome.

FAST TRACK

It is not unusual to discover multiple diagnoses when evaluating a patient for chronic pelvic pain

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