Chronic Pelvic Pain: A Case Study and Management

Series Editors: Matthew F. Davies, MD, FACOG
Associate Professor of Obstetrics and Gynecology, Residency Program Director, Chief, Division of Women’s Health and Division of Medical Education in Obstetrics and Gynecology, Pennsylvania State University College of Medicine, Department of Obstetrics and Gynecology, Hershey, PA

Jordan G. Pritzker, MD, MBA, FACOG
Assistant Professor, Albert Einstein College of Medicine, Montefiore Medical Center, Bronx, NY, Obstetrics and Gynecology Faculty Practice, Women’s Comprehensive Health Center, Long Island Jewish Medical Center, New Hyde Park, NY

Contributor: Joseph E. Patruno, MD
Assistant Professor of Obstetrics and Gynecology, Medical Student Clerkship Director, Associate Residency Program Director, Pennsylvania State University College of Medicine, Hershey, PA

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Joseph E. Patruno, MD, and Matthew F. Davies, MD, FACOG

I. INTRODUCTION

Chronic pelvic pain (CPP) in women is a common problem that has substantial effects on both the patient and society. This debilitating and often enigmatic condition afflicts 15% of reproductive age women in the United States and accounts for more than 10% of gynecologic referrals. The ramifications of pelvic pain (eg, loss of productivity, effects on family, and cost to society) are considerable.

CPP, defined as nonmenstrual pain of at least 3 months’ duration or menstrual-related pain that persists for more than 6 months, may afflict women in any age group. The most common population affected by chronic pain, however, is women between 18 and 50 years of age. In evaluating the symptom of chronic pelvic pain, various gynecologic and non-gynecologic causes should be considered. The most common non-gynecologic causes of CPP include conditions of the gastrointestinal (GI), urologic, and/or musculoskeletal system. Also, psychiatric illnesses may manifest as or contribute to symptoms of CPP. Common gynecologic explanations for CPP include endometriosis, pelvic adhesive disease, and structural lesions of the uterus and ovaries (eg, cysts and leiomyomas).

The medical community has become more familiar with the physiology and causes of CPP; however, ideal diagnostic algorithms and management protocols have not been established. Because gynecologists often see these patients, they should be familiar with all the conditions in the broad differential diagnosis and be able to provide both diagnostic and therapeutic recommendations.

II. CASE PATIENT I PRESENTATION

Patient 1 is a 28-year-old nulligravida married woman who presents with a 12-month history of worsening pelvic pain. The pain is constant and described as “achy” in nature with intermittent sharp “stabbing” episodes. Her symptoms are worse immediately before, and during, her menses. She also notes worsening dyspareunia with deep penetration during the past several months. A review of systems is pertinent for intermittent constipation and diarrhea but is negative for bladder symptoms such as dysuria, increased frequency, or hematuria. Her cycles occur every 30 days, last approximately 1 week, and are described as “very heavy.” She denies a history of abnormal Papanicolaou (Pap) smears, sexually transmitted diseases, or pelvic inflammatory disease. Additionally, there is no history of abdominal surgeries or medical co-morbidity (eg, GI, musculoskeletal, or psychiatric disorder). She denies any prior or current sexual, physical, or emotional abuse. Notably, patient 1 mentions that she and her spouse have been unable to conceive during the past 2 years.

Which of the following presenting complaints is most consistent with a diagnosis other than endometriosis?

A) Deep dyspareunia  
B) Intermittent bowel dysfunction  
C) Primary infertility  
D) Progressive dysmenorrhea

DISCUSSION

The correct answer is B. Patients with CPP often present a diagnostic dilemma because several conditions may explain their pain symptoms. It is essential to obtain a complete and accurate history and to ask certain questions as described in Table 1. In this case, patient 1 meets the criteria for CPP because she has had symptoms for more than 6 months. The fact that her pain is exacerbated by menses should alert the practitioner to a likely gynecologic origin, and endometriosis is the most likely cause. Approximately 71% to 87% of women with pelvic pain have endometriosis. Common associated symptoms of endometriosis include dysmenorrhea, menorrhagia, and deep dyspareunia. In patients with infertility (with or without associated CPP), 25% are found by laparoscopy to have evidence of endometriosis. Patients with endometriosis only rarely present with bowel or
bladder symptoms. Such symptoms more often suggest an intrinsic bowel or bladder disorder, respectively. For a GI etiology, irritable bowel syndrome (IBS) is the most common explanation. Unfortunately, 61% of patients with this functional bowel abnormality have associated dysmenorrhea, and the distinction between endometriosis and IBS may be difficult to make based on symptoms alone. For urologic pain, a key question is how the pain relates to voiding. The classic history for interstitial cystitis is that the pain is worse with a full bladder and relieved (briefly) by voiding. Pain during voiding suggests urinary tract infection (UTI), external irritation (such as vaginitis), pelvic floor dysfunction, urethritis, or urethral diverticulum. If the pain does not start until after voiding, this suggests bladder spasms or pain with coaptation of a sensitive bladder mucosa.

Incidence and Economic Effect of CPP

In reproductive-age women seeking the care of a gynecologist, it is estimated that 2% to 10% of visits are for CPP. Based on a recent Gallup poll, more than 9 million North American women have CPP. The condition remains debilitating, with 50% of women having to restrict or avoid usual activities, and 26% of those afflicted missing at least one-half day of work monthly secondary to symptoms. In addition to costs relating to lost productivity, the diagnosis and treatment of CPP leads to substantial health care expenditures. Of the nearly 4 million laparoscopies performed annually, 10% to 35% are scheduled secondary to complaints of pelvic pain. Similarly, CPP is the primary indication for 70,000 hysterectomies performed every year in the United States. Overall, the financial cost of CPP to society is estimated at nearly 3 billion dollars annually.

Physiology and the Evolution of Pelvic Pain

CPP (like other pain syndromes) is caused by a complex interaction between various neural pathways, local immune responses within the pelvic cavity, and psychologic perception. Chronic pain is not the same as longer-lasting acute pain. The National Institutes of Health (NIH) consensus conference organized a description of pain families. CPP belongs to the category of “chronic pain not associated with malignant disease.” In short, pain is a product of physical and cognitive factors.

The stimuli that cause such pain can be divided into 3 major categories: 1) structural abnormalities that are present (eg, endometriosis); 2) psychophysiological (eg, persistent muscle spasms); and 3) somatic (eg, internalizers of stress that manifest as pain). The cause of pain may be isolated to any of these categories, or it may be secondary to a combination of these categories. The normal response to pain typically evokes 4 unique phases:

1. Nociception, or the origination and detection of a neurologic signal as produced by a noxious stimulus
2. Pain, or the recognition of the signal or stimulus
3. Suffering, or the affective response to the stimulus
4. Pain behavior, or the adaptive changes that occur secondary to the stimulus

Two main neural pain fiber types have been identified that, when stimulated, lead to pain. Slow pain fibers, which are affected in cases of visceral peritoneal irritation, produce characteristic pain described as burning or aching. This pain is often diffuse and difficult to localize. An example of pain mediated through these fibers is that from either inflammation or ischemia. Fast fibers, conversely, result in the perception of sharp and often well-localized pain symptoms. Such fibers are affected in cases of acute pain where

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Table 1. Essential Questions for the Patient Presenting with Chronic Pelvic Pain

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
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</thead>
<tbody>
<tr>
<td>Where is your pain?</td>
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<tr>
<td>When did it start?</td>
<td></td>
</tr>
<tr>
<td>What makes it better or worse?</td>
<td></td>
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<tr>
<td>Do you have pain with menstrual periods?</td>
<td></td>
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<tr>
<td>Do you have pain with intercourse?</td>
<td></td>
</tr>
<tr>
<td>Do you have pain in other parts of your body?</td>
<td></td>
</tr>
<tr>
<td>What diagnostic studies have been done? What did they show?</td>
<td></td>
</tr>
<tr>
<td>What treatments have been tried? How did they work?</td>
<td></td>
</tr>
<tr>
<td>Are you depressed?</td>
<td></td>
</tr>
<tr>
<td>How do you sleep?</td>
<td></td>
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<tr>
<td>Do you have bowel symptoms, such as diarrhea and/or constipation?</td>
<td></td>
</tr>
<tr>
<td>Do you have urinary symptoms, such as pain with urination, frequent urination, and/or incomplete urination?</td>
<td></td>
</tr>
<tr>
<td>Have you seen other doctors?</td>
<td></td>
</tr>
</tbody>
</table>

Adapted with permission from Scialli AR. Evaluating the patient with chronic pelvic pain. OBG Manage 2000;(Suppl):7–11.
stimulation of the parietal peritoneum results in symptoms. In these cases, the pain persists as long as the insult is present. In most cases of chronic pain, both slow and fast fibers are involved.

**Acute pain**, by definition, persists for less than 3 months and is frequently associated with an identifiable structural or physiologic process. Typically, patients can clearly remember when their symptoms began. **Chronic pain** is defined as symptoms that persist beyond a 6-month period; it often begins with a non-specific and poorly identifiable nociceptive event or process that is difficult to recall. Because the etiology of such pain is often much less obvious, it can prove frustrating to the patient and physician.

Mood is also considered an important modifier of pain symptoms. Syndromes such as clinical depression and other affective disorders have been shown to exacerbate pain symptoms. Whether mood disturbance leads to heightened pain sensation or alters an individual’s ability to cope with the pain may be difficult to discern. Certain antidepressant medications are effective for treating women with CPP (who do not necessarily meet the diagnostic criteria for depression) further lending merit to the association between the physical and cognitive state.

### III. EVALUATION STRATEGIES

**GENERAL OVERVIEW**

It is critical to approach CPP as a symptom and not a diagnosis. Because pelvic pain is a common primary complaint in female patients, gynecologists and other women’s health specialists need to methodically assess and manage this symptom. In addition to a detailed history, a comprehensive physical examination is critical at the time of the initial evaluation. Various laboratory and radiographic studies may also prove beneficial in assessing the patient with CPP. Standardized pain scoring tools and depression scales may provide a means to more objectively measure pain and its effect on the patient’s life. Finally, the gynecologist should seek the expertise of other medical specialists when indicated. Consultation is particularly important for patients with significant non-gynecologic symptoms or for those who fail to respond to gynecologic therapies.

**HISTORY**

When examining the patient with chronic pelvic pain, the pain symptom must be assessed in detail. If possible, the time when the pain was first noticed should be clarified. Additionally, the quality, distribution, intensity, and radiation pattern of the pain should be assessed. The temporal pattern of the pain is critical. Specifically, it is important to establish whether exacerbations occur with menstrual cycle, intercourse, and/or with bowel or bladder function. The review of systems should examine other pertinent symptoms such as affective distress, fatigue, menstrual irregularities, and systemic complaints. In addition, attention should be taken in evaluating coinciding pain symptoms affecting the musculoskeletal, urologic, or GI systems.

Important historical information includes past surgery, previous pelvic infections, infertility, and unusual obstetrical events. Finally, a detailed psychosocial history should be obtained, taking into account issues of abuse and past or coexisting affective disorders. How pain affects the patient’s life, and how situations and events alter the intensity of the pain should be reviewed. At this time, assessment of coping mechanisms, support structure, and any evidence of maladaptive coping mechanisms (eg, substance and/or alcohol abuse) should be sought.

Objective pain measurement tools are valuable in assessing patients with CPP. Several pain assessment intake forms are available to assist in this process. These intake forms allow for an organized and comprehensive evaluation of the pain and associated symptoms. The International Pelvic Pain Society has published a form that can be used when dealing with CPP patients. The physician may also improve the evaluation through the use of validated pain inventory tools, such as The McGill Pain Questionnaire and the Multidimensional Pain Inventory. These inventories allow for a better understanding of the patient’s perception of her pain and the effect of the symptom on both the patient’s life and on the lives of significant others. Formal psychological evaluation may be warranted in those women with a known history of psychiatric disease, past sexual or emotional abuse, or a positive review of systems on psychiatric screening tool. The Minnesota Multiphasic Personality Inventory and the Beck Depression Inventory are psychological testing instruments that may enhance the assessment of patients with CPP.

**PHYSICAL EXAMINATION**

A complete physical examination should be performed at the time of initial assessment in every patient with CPP. The patient’s affect should be evaluated because it might suggest depression or other mood disorder. A complete assessment of vital signs, head and neck, cardiopulmonary, and neurologic systems as well as the extremities should be performed.
Abdominal examination is critical in the assessment of a woman with CPP. At the time of examination, the patient should be asked to localize and point out pain sites as well as regions of radiation should they exist. Abdominal inspection should initially focus on deformity, distention, or visible masses. Any surgical scars should be noted. Auscultation of the abdomen should focus on the presence and quality of bowel sounds, especially in the patient with substantial GI symptoms. Palpation of the patient’s abdomen should be performed, checking for hepatosplenomegaly, fluid shift, rebound, rigidity, or guarding. With the patient in a sitting position, a back examination should include inspection and palpation of the thoracic and lumbar spines, looking for deformity or point tenderness. The costovertebral regions should also be palpated in assessing for focal discomfort.

The pelvic examination is another critical aspect of the physical examination. Evaluation of the external genitalia should focus on escutcheon, inguinal masses, or lymphadenopathy of the labia. Vestibular pain or paresthesia of the external genitalia should be noted. Speculum examination should allow for close visualization of the vaginal vault and the cervix. Specifically, the cervix should be assessed for position, lesions, friability, or purulent discharge. Pelvic support should be evaluated specifically assessing for a cystocele, enterocele, rectocele, or uterine prolapse. Bimanual examination will offer a more complete survey of the upper genital tract. Size, contour, and focal tenderness of the uterus and adnexa should be noted. Reproducible pain during the examination should be documented and isolated to specific regions of the pelvis if possible. The presence of cervical motion tenderness, parametrial thickening, or uterosacral ligament nodularity should also be noted and should prompt the physician to suspect gynecologic pathology. If pain is reproduced by palpating the bladder, this suggests interstitial cystitis or other intravesical pathology.

Finally, rectovaginal examination should focus on sphincter tone, the presence or absence of masses, tenderness, or fullness in the rectovaginal septum that might represent pathology. Hemoccult testing of the stool is recommended in those with focal GI symptoms.

LABORATORY STUDIES

Occasionally, laboratory testing may be of benefit in evaluating the patient with CPP. The patient’s history, as well as clinical findings, will dictate which laboratory tests may be of value. In those with risk factors for infection or whose examination suggests sexually transmitted disease, endocervical swabbing for Neisseria gonorrhoea and Chlamydia trachomatis should be performed. If pelvic infection is a consideration, a complete blood count with differential should also be obtained. Serum erythrocyte sedimentation rate (ESR) may also support the diagnosis of an infectious or inflammatory condition as the source of pain. A urinalysis and culture are vital to assess for cystitis in any patient with suprapubic pain, flank tenderness, or with frank urinary symptoms. A Pap smear, although not usually diagnostic of conditions that cause pain, should be performed on any patient who is a candidate for, and not up to date on, their cervical screening.

DIAGNOSTIC STUDIES

Imaging studies such as plain films, computed tomography (CT) scans, and magnetic resonance imaging (MRI) studies have a limited value in the assessment of CPP. Ultrasound of the pelvis, however, may provide important information in the evaluation of patients with pain, especially in those with inadequate, inconclusive, or abnormal pelvic examinations. Sonogram may also provide information regarding pathology of the hepatobiliary tract and urologic systems, which may present with abdominal or pelvic pain.

Although a surgical procedure, diagnostic laparoscopy in many cases serves as a critical diagnostic adjunct in assessing the woman with CPP. The access provided by the technique also allows for the surgical treatment of various pathologies. Laparoscopic pain mapping is a newer, as yet unproven procedure where patients are kept conscious during laparoscopy so they can note reproduction of pain when areas are stimulated. The technique has shown a reasonable correlation between sites of pain and the presence of pathology, such as adhesions and endometriosis. In cases with abnormal ultrasound findings, laparoscopy is an excellent method of confirming and potentially treating pathology. Notably, in those women with CPP and normal sonographic studies, laparoscopy still reveals significant pathology in 50% of cases.

Negative findings on diagnostic laparoscopy can be frustrating for the practitioner and the patient but still provide valuable information for deciding on further therapy.

Urodynamic study is helpful if pain is thought to be coming from the bladder. For some patients, involuntary bladder contractions will be found as the source of pain. With interstitial cystitis, the usual urodynamic findings are pain on bladder filling and reduced functional capacity, but no involuntary contractions. Office cystoscopy under local anesthesia is normal in most patients with interstitial cystitis except that bladder capacity is reduced, and cystoscopy is more painful for those with interstitial cystitis than for other patients. The only benefit of office cystoscopy is to rule out other intravesical causes for pain (such as stones or tumors). If interstitial cystitis is suspected and a
Table 2. Gynecologic Causes of Chronic Pelvic Pain

<table>
<thead>
<tr>
<th>Common causes</th>
<th>Less common causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endometriosis</td>
<td>Chronic pelvic infection</td>
</tr>
<tr>
<td>Adenomyosis</td>
<td>Uterine leiomyomata</td>
</tr>
<tr>
<td>Pelvic adhesive disease</td>
<td>Hydrosalpinx</td>
</tr>
<tr>
<td></td>
<td>Ovarian or tubal neoplasms</td>
</tr>
<tr>
<td></td>
<td>Pelvic congestion syndrome</td>
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bladder distention under anesthesia is planned, then office cystoscopy ahead of time is clearly redundant. Cystoscopy under anesthesia is the current diagnostic test for interstitial cystitis, and laparoscopy can be performed under the same anesthetic.17

REFERRAL
An important consideration in managing CPP is whether to refer patients to other physicians and health care specialists. It has been shown that a multidisciplinary approach in managing CPP improves symptoms in 75% of patients.21 In cases where an evaluation demonstrates no evidence of gynecologic pathology, or if the patient is experiencing significant non-gynecologic symptoms, referral to an appropriate specialist is critical. Depending on presenting symptoms, medical specialists who may benefit the patient include gastroenterologists, urologists, psychiatrists, neurologists, and/or orthopedists. More specialized diagnostic studies should be ordered, or in conjunction with, the appropriate specialist. Consultation with a psychiatrist or counselor may also benefit women with pertinent psychiatric or social histories. Finally, chronic pain clinics may offer patients alternatives for pain management when clear pathology is not evident and when the primary goal is to control symptoms and improve functional capacity.

IV. CAUSES, DIAGNOSIS, AND TREATMENT OF CHRONIC PELVIC PAIN

ETIOLOGIES AND DIAGNOSTIC ELEMENTS
Various gynecologic and non-gynecologic causes of CPP have been identified and should be familiar to the obstetrician-gynecologist. It is estimated that only 20% of women with CPP ever seek medical attention. Of these women, twice as many will seek consultation with an obstetrician-gynecologist as opposed to other primary care specialists.22 Appropriate diagnosis of CPP relies on a comprehensive history and physical examination, appropriate ancillary tests, and at times referral to other specialists. Despite extensive evaluation, approximately 61% of women with CPP are not assigned a specific pathologic diagnosis.1

The gynecologic causes for CPP can be categorized into common and less common conditions (Table 2), which are discussed in Section V. Common sources for pain include endometriosis, adenomyosis, and pelvic adhesions. Less frequent explanations for CPP are leiomyomas, ovarian or tubal neoplasms, chronic pelvic infections, and pelvic congestion syndrome. Non-gynecologic causes for CPP include GI problems, urinary tract problems, musculoskeletal problems, and psychiatric disorders (Table 3), which are discussed in Sections VI, VII, VIII, and IX.

CASE PATIENT 1 EXAMINATION
On physical examination, patient 1 is without acute distress. She is afebrile and has stable vital signs. Abdominal survey reveals normal bowel sounds without masses, rigidity, or guarding. On pelvic examination, the external genitalia and vagina are normal. Visually, the cervix is without lesions or mucopurulent discharge and is deviated towards the patient’s right vaginal wall. The cervix is small and nulliparous with a stenotic os that barely allows the passage of a sterile cotton swab. On palpation, the cervix is smooth and without frank cervical motion tenderness. The uterus is sharply retroverted, poorly mobile, and diffusely tender. Similarly, the ovaries are bilaterally tender but with a mobile mass noted in the left adnexal region. Nodularity is appreciated in the area of the right uterosacral ligament and in the rectovaginal septum. Transvaginal ultrasound reveals a normal uterus with a complex adnexal mass measuring 4.7 × 5.0 cm.

- Of the following therapies, what is the next most appropriate step in the management of patient 1?
  A) Intravenous antibiotics with clindamycin and gentamicin
  B) Cervical dilation
  C) Diagnostic and therapeutic laparoscopy
  D) Long-acting gonadotropin-releasing hormone (GnRH) agonist

Discussion
The correct answer is C. Intravenous antibiotic administration would be reasonable if the patient’s pain was...
caused by an active upper genital tract infection. The lack of fever, mucopurulent discharge, and cervical motion tenderness make acute pelvic infection unlikely. Cervical dilation may prove beneficial in cases of complete stenosis causing a hematometra (distention of the uterus with blood). Because this patient describes regular menstrual cycles, this diagnosis is also unlikely and therapeutic dilation would offer little benefit. However, the finding of a narrow cervical opening has been associated with endometriosis. In a recent study, 96% of patients with stenosis and pelvic pain were found to have laparoscopic evidence of endometriosis. It has been proposed that this finding may predispose a patient to retrograde menstrual flow, an accepted pathophysiologic principle behind the development of endometriosis. Endometriotic implants and/or scarring in the pelvic cavity may present as uterosacral nodularity or obliteration of the posterior cul-de-sac respectively, which is seen in 15% and 9% of patients with endometriosis, respectively. Lateral displacement of the cervix is seen in 14% to 28% of patients with the condition also presumed to be secondary to uterosacral fibrosis and scarring.

The use of GnRH agonists has been shown to offer pain relief in patients with endometriosis in more than 80% of cases. Many have advocated an empiric trial of such medications before offering surgery in women who are strongly suspected of having endometriosis. When compared to surgical management with laparoscopy, GnRH agonists have proven to be equally efficacious and less costly. GnRH agonists are marketed under several names (eg, goserelin acetate, leuprolide acetate, nafarelin acetate). The use of such medications has also been associated with the regression of small endometrial implants on second-look laparoscopy.

Diagnostic and operative laparoscopy is the most appropriate next step in patient 1’s care. The decision when to perform laparoscopy in cases of CPP is dictated by the practitioner’s level of suspicion that organic disease can be identified through surgery. The abnormal findings on examination, confirmed by the ultrasound, warrant surgical evaluation and treatment in this patient. Findings of focal upper genital tract tenderness, uterosacral ligament nodularity, and the identification of a complex adnexal mass are strongly suggestive of gynecologic pathology and, specifically, endometriosis. In patient 1, the pelvic mass likely represents an endometrioma, which is estimated to occur in 5% of patients with endometriosis. Medical therapy with GnRH agonists has been shown to decrease the size of endometriomas. However, complete resolution of such cysts typically requires operative therapy. In this case, the patient’s desire for fertility further supports the decision to proceed with laparoscopy. Surgical treatment will allow for assessment of tubal patency as well as the removal of the pathology that may be contributing to infertility and pain. Additionally, the technique may allow the identification of other less common explanations for pelvic pain such as appendiceal pathology. Also, with the development of microlaparoscopic surgery, the procedure can be performed under conscious sedation, allowing patients to assist in identifying their anatomic regions of pain which may or may not correlate with visible or microscopic pathology.

Many practitioners support an empiric trial of a GnRH agonist in those with presumed endometriosis but no evidence of endometrioma. There has been

### Table 3. Non-Gynecologic Causes of Chronic Pelvic Pain

<table>
<thead>
<tr>
<th>Gastrointestinal disorders</th>
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<tbody>
<tr>
<td>Functional bowel disease (eg, irritable bowel syndrome [IBS])</td>
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</tr>
<tr>
<td>Inflammatory bowel disease (IBD)</td>
<td></td>
</tr>
<tr>
<td>Diverticulitis</td>
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<tr>
<td>Chronic appendicitis</td>
<td></td>
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<tr>
<td>Colon carcinoma</td>
<td></td>
</tr>
<tr>
<td>Meckel’s diverticulum</td>
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</table>

<table>
<thead>
<tr>
<th>Urinary tract disorders</th>
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</tr>
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<tbody>
<tr>
<td>Urinary tract infection</td>
<td></td>
</tr>
<tr>
<td>Urethral syndrome</td>
<td></td>
</tr>
<tr>
<td>Interstitial cystitis</td>
<td></td>
</tr>
<tr>
<td>Chronic diverticula</td>
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</table>

<table>
<thead>
<tr>
<th>Musculoskeletal disorders</th>
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</tr>
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<tbody>
<tr>
<td>Hernia</td>
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<tr>
<td>Disc disease</td>
<td></td>
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<tr>
<td>Arthritis</td>
<td></td>
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<tr>
<td>Scoliosis or posture-related problems</td>
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<table>
<thead>
<tr>
<th>Pain processing disorders</th>
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<tbody>
<tr>
<td>Fibromyalgia</td>
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<table>
<thead>
<tr>
<th>Psychiatric disorders</th>
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<tbody>
<tr>
<td>Depression</td>
<td></td>
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<tr>
<td>Physical or sexual abuse</td>
<td></td>
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<tr>
<td>Somatization</td>
<td></td>
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<tr>
<td>Hypochondriasis</td>
<td></td>
</tr>
<tr>
<td>Opioid-seeking behavior</td>
<td></td>
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<tr>
<td>Factitious</td>
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increasing enthusiasm for establishing the diagnosis of endometriosis non-surgically, based on an appropriate work-up and response to aggressive anti-endometriosis therapy.\textsuperscript{35,36} A 3- to 6-month trial of such medication may offer diagnostic information and, in many cases, may provide therapeutic relief of symptoms. However, other medical options are available as discussed in the next section.

**V. GYNECOLOGIC CAUSES OF CHRONIC PELVIC PAIN**

**ENDOMETRIOSIS**

Endometriosis is common among women with CPP. It is estimated that up to 87\% of women with pelvic pain will be diagnosed with endometriosis.\textsuperscript{3,4} Endometriosis is defined as the presence of endometrial implants (glands and stroma) outside of the uterine cavity. The common locations of implants include the ovaries and fallopian tubes as well as the surface of the uterus, bowel, and/or peritoneum. Cyclic bleeding, stimulated by ovarian hormones, results in peritoneal irritation and scarring and, eventually, chronic pain. Disease volume does not necessarily correlate with symptom severity. Endometriosis is characterized by pelvic pain that is pronounced immediately before and during menses. Patients also describe menorrhagia and dyspareunia, the latter commonly occurring with deep penetration. Endometriosis may be suggested by various findings on pelvic examination as mentioned in the case study; however, the examination may be completely non-focal.

Gynecologists have traditionally used laparoscopy to confirm or exclude the diagnosis of endometriosis. A sensitive, noninvasive, radiographic method of diagnosing endometriosis has not been developed. Laparoscopy, as mentioned, may also provide therapeutic benefit allowing the surgeon to operatively manage the disease process. Both medical and surgical therapies are available to the gynecologist for the treatment of endometriosis (Figure 1). Additionally, expectant management may be a reasonable treatment option in women presumed to have mild endometriosis who want to preserve their fertility. The decision as to what treatment might be optimal should be based on several factors, including the severity of the patient’s symptoms, the extent of the disease, her age, and her reproductive desires.

**Medical Treatment**

Medical treatments for endometriosis fall into 3 main categories: analgesics, hormones, and hormonal suppressants. These medications differ in terms of efficacy and side effects. Analgesics are a standard of care in the management of many pain syndromes. Ideally, these medications should be used to improve symptoms while initiating therapy directed toward the underlying etiology of the pain.

Endometriosis and other gynecologic sources of pain may partly result from alterations in prostaglandins and other inflammatory mediators. Various prostaglandin synthetase inhibitors (nonsteroidal anti-inflammatory drugs [NSAIDs]) have proven beneficial in treating such symptoms. These medications are available by prescription and in over-the-counter preparations. A newer generation of NSAIDs, coined cyclooxygenase-2 (COX-2) inhibitors, seem to offer comparable analgesic efficacy, better dosing schedules, and fewer side effects than many traditional NSAID regimens. In 1999, rofecoxib (Vioxx) acquired an indication for the management of primary dysmenorrhea.\textsuperscript{37} Its use in the treatment of secondary dysmenorrhea caused by endometriosis is not as well studied.

Narcotic analgesics should only rarely be used with CPP related to endometriosis. Although narcotics may provide substantial pain relief, the potential addictive properties of such agents may be a problem in some patients (see Section X. “Opioid Therapy”). It has been demonstrated, however, that undertreating pain may be more likely to lead to chronic pain states and drug-seeking behavior than early, aggressive, short-course, effective therapies.\textsuperscript{11} Thus, the judicious use of opioid-containing analgesics may be useful in the treatment of CPP.

Oral contraceptive pills (OCPs) have traditionally been used in the management of CPP, especially if associated with the menstrual cycle or proven endometriosis. By combining both estrogen and progestin, this hormonal regimen stabilizes and then suppresses endometrial tissue growth. When used for at least 6 months, nearly all types of OCPs promote decidualization of endometriotic implants and improvement in pain symptoms.\textsuperscript{38} The use of OCPs in treating patients with endometriosis has a success rate of 75\% to 89\%.\textsuperscript{39} The common side effects of OCPs include nausea, headache, and breakthrough bleeding. Physicians should be familiar with these side effects because they may adversely affect patient compliance and, thus, the efficacy of such treatment.

Like OCPs, progestins used alone promote decidualization and dissolution of endometriotic lesions. Several progestins are commercially available and may provide benefit in the treatment of gynecologic sources of pelvic pain. Depot-medroxyprogesterone acetate (Depo-Provera)—a long-acting, intramuscularly administered progestin—is effective in the treatment of endometriosis-related pain. Research has demonstrated similar benefit.
using high-dose progestins, GnRH agonists, or danazol in treating such pain. Side effects—including breakthrough bleeding, amenorrhea, weight gain, depression, and edema—may decrease patient compliance and acceptance of such agents.

Danazol (Danocrine) is a synthetic androgen that functions as a suppressor of gonadotropins and an inhibitor of the enzymes responsible for ovarian steroid production. The agent has both agonistic and antagonistic effects on progesterone and androgen receptors; it promotes atrophic changes of endometriotic implants. Danazol, when administered for a 6-month period, has been shown to improve pelvic pain symptoms in 90% of endometriosis patients; the volume of endometriosis has been shown to decrease by 90% after treatment with this agent.

Surgical Treatment

Surgical procedures have traditionally been an important means of diagnosing and treating endometriosis. Conservative surgical procedures include diagnostic and therapeutic laparoscopy, which allows for the identification and removal of lesions and scarring while conserving the patient’s reproductive capacity. When pathology is detected, removal may be accomplished using ablation, sharp excision, or fulguration with laser. In women with endometriosis who are treated laparoscopically, documented rates of success range from 37% to 100%. In addition, related symptoms associated with endometriosis, including dyspareunia and dysmenorrhea, often improve considerably after surgical therapy.

Several conservative adjunctive laparoscopic surgical techniques have been advocated as treatment for CPP. Laparoscopic uterosacral nerve ablation involves the surgical interruption of sympathetic nerve fibers in the superior hypogastric plexus at the sacral level of the spinal column and has been recommended as a treatment for patients describing recurrence of significant pain occurring approximately 5 to 6 months after stopping the agent. Like danazol, side effects of GnRH agonists may be significant and include vaginal dryness, hot flashes, decreased libido, irritability, headache, and arthralgias. Also, because of the long-term adverse effect of these medications on bone mineral density, use for longer than 6 months is not recommended.

Figure 1. Algorithm for managing presumed endometriosis. GnRH = gonadotropin-releasing hormone; NSAIDs = nonsteroidal anti-inflammatory drugs; OCPs = oral contraceptive pills; PostOp = postoperative. (Adapted with permission from Schattman GL. When endometriosis is the most likely diagnosis. OBG Management 2000(Suppl):16.)
Adenomyosis involves the displacement of endometrium outside of the uterine cavity, like endometriosis, patients may present with pelvic pain. In adenomyosis, endometriotic lesions invade the uterine muscle wall. The symptoms of adenomyosis often mimic those of endometriosis and include pain, dyspareunia, and menorrhagia. Adenomyosis, however, often presents 1 to 2 decades later in a woman’s life than does endometriosis.

Physical findings of adenomyosis may be subtle and include only a mildly enlarged and tender uterus on pelvic examination. Diagnosis in the past was based on clinical suspicion and confirmed pathologically only after hysterectomy. Both transvaginal ultrasound and MRI are excellent noninvasive methods of diagnosing adenomyosis. Conservative treatment for adenomyosis relies on cyclic hormones and NSAIDs, although optimal treatment of the condition often involves removal of the uterus.

PELVIC ADHESIONS

Pelvic adhesive disease has been proposed as an important cause of CPP. Adhesions, which are fibrinous bands of scar tissue, are thought to cause pain by producing tension and traction on sensitive peritoneum in the pelvis and surrounding abdominal organs. In women with CPP, the reported incidence of operatively diagnosed adhesions ranges from 6% to 51%. Processes that may cause the formation of adhesions include intra-abdominal or gynecologic infection, pelvic surgery, or radiation exposure. Adhesion formation is estimated to occur in 55% to 90% of patients after reproductive pelvic surgery.

The exact relationship between CPP and pelvic adhesions remains controversial. In a recent meta-analysis, 61% of women with CPP evaluated laparoscopically were found to have pathology, with 25% having only adhesive disease to explain their symptoms. Adhesiolysis decreases symptoms in 60% to 90% of patients who undergo the procedure, suggesting that adhesions are correlated with pain.

The diagnosis of adhesions should be suspected in patients with the aforementioned risk factors. Confirmation of pelvic adhesive disease, however, requires surgical confirmation via laparotomy or laparoscopy. Radiographic studies and ultrasound have limited value in establishing the diagnosis. The treatment of choice with pelvic adhesive disease is adhesiolysis using ablation, laser cautery, or sharp excision. Unfortunately, recurrent adhesions occur in up to 97% of patients after such therapeutic procedures. Adhesive disease secondary to surgery may be decreased by using a meticulous operative technique and by minimizing tissue damage. It is not clear whether anti-adhesive adjuvant therapies (such as Gore-Tex, Interceed, Seprafilm, and Preclude) can prevent the condition.

LEIOMYOMAS

Leiomyomas are a common finding in reproductive-age women but are rarely thought to be a cause of pelvic pain. Patients will often describe a sense of “pressure” or fullness with leiomyomas as opposed to frank pain. These benign muscle tumors of the uterus are thought to cause pain because of a mass effect or if they degenerate. Fibroids may be associated with dysmenorrhea and menorrhagia and may also contribute to pelvic pain symptoms. The severity of symptoms seems to be related to the number, location, and size of the myomas.
The diagnosis of uterine fibroids is often made at the time of abdominal or pelvic examination. The finding of an enlarged uterus may be further confirmed by ultrasound or CT scan. Women with symptomatic fibroids may be managed conservatively with hormones and analgesics. Surgical treatment of fibroids traditionally includes myomectomy or hysterectomy. Newer treatment options include cryomyolysis; arterial embolization; or the VersaPoint system, which was recently re-approved by the US Food and Drug Administration.56–59

OTHER CONDITIONS
Chronic Infection and Hydrosalpinx

Chronic pelvic infection has also been proposed as a cause of CPP. In a recent laparoscopic series of 170 women with pain, however, only 3 patients with confirmed CPP had evidence of infection.3 Despite these findings, the diagnosis of CPP should be considered in those patients with a history of upper genital tract infection. The evaluation of such patients may reveal focal adnexal tenderness that may symptomatically improve with antibiotic therapy. Laparoscopy may further confirm the diagnosis if hydrosalpinx or peri-tubular adhesions are seen.

Pelvic Congestion

Like chronic infection, the diagnosis of pelvic congestion syndrome is a controversial etiology of CPP because the presence of dilated veins in the pelvises of women has been observed for nearly half a century.60 The diagnosis of pelvic congestion syndrome is established with the finding of pelvic veins measuring greater than 1 cm. This dilatation is a proposed cause of chronic pain. Certain procedures including ovarian vein ligation or embolization have provided some benefit of pain symptoms in small study groups diagnosed with pelvic congestion syndrome.61 Hysterectomy is the standard treatment for this condition.

VI. PELVIC PAIN CAUSED BY GASTROINTESTINAL CONDITIONS

The gynecologist should not overlook the possibility of non-gynecologic etiologies of pain when evaluating the patient with CPP because 40% of diagnostic laparoscopies demonstrate no gynecologic pathology.18 As with the gynecologic assessment, the practitioner should approach the evaluation of non-gynecologic organ systems (eg, GI tract, urinary tract) in an organized and complete manner.

GASTROINTESTINAL PAIN

Several GI conditions exist that may contribute to, or cause, pelvic pain. Because the bowel and gynecologic organs are anatomic neighbors and share neural innervation, it is not surprising that symptoms affecting these systems may be difficult to differentiate. Specific conditions of the GI tract that the gynecologist should consider in the patient with pelvic pain include IBS, inflammatory bowel disease (IBD), diverticulitis, and chronic appendicitis.

IBS is considered the most common non-gynecologic cause of pelvic pain. Of patients diagnosed with IBS, 80% are women. Symptoms of IBS include alterations in bowel function (constipation and diarrhea), abdominal distention, and pain lasting at least 3 months.62 The pathophysiologic explanation for the pain associated with IBS involves abnormal GI motility and augmented sensation of visceral stimuli.63,64 It has been documented that the intensity of bowel symptoms can vary with a woman’s menstrual cycle often making it difficult to distinguish between gynecologic and bowel dysfunction. Furthermore, 61% of women with dysmenorrhea meet diagnostic criteria for IBS.65

The diagnosis of IBS is often based on a characteristic history. Findings on physical examination supporting the diagnosis might include mild abdominal distention, hyperactive bowel sounds, and focal tenderness on rectal examination. Patients with functional bowel disease often undergo lower endoscopy or barium studies, which rarely demonstrate remarkable findings.

In patients diagnosed with IBS, treatment is based on symptoms. The condition may be characterized as diarrhea-dominant, constipation-dominant, or pain-dominant. These categories are rarely mutually exclusive, and therapy may be focused on a combination of symptoms. Diarrhea may be managed effectively using several anticholinergic agents targeted at reducing bowel motility. Constipation-dominant disease may be managed through increased fiber consumption. Fiber, which acts as a cathartic and stool softener, may be obtained through the natural diet or supplemental regimens such as lactulose, Fibercon, Metamucil, or sorbitol. Patients with abdominal pain as their primary symptom may also benefit from anticholinergics or antispasmodics. Behavioral therapy including stress management has also been shown to be beneficial in the management of functional bowel disease.66

IBD may be classified into 2 main categories: Crohn’s disease and ulcerative colitis. The condition can present with a multitude of symptoms; in mild cases, it may be mistaken for simple IBS. Abdominal pain is the hallmark

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of IBD and is thought to be caused by inflammatory changes within, and around, the bowel. IBD should be suspected in patients with persistent diarrhea, rectal bleeding, fever, and weight loss. Confirmation of IBD requires lower endoscopy and tissue biopsies, which should be performed by a gastroenterologist or general surgeon. Various medical and surgical therapies are available for the management of IBD.

Diverticular disease is a condition that can present with lower abdominal and pelvic pain; thus, it should be considered in the differential diagnosis, especially in women older than 40 years of age. Diverticula, which are anatomic outpocketings of the colon and rectum, may become infected or inflamed resulting in symptoms. Conservative treatment of the condition involves adherence to an appropriate diet and avoidance of certain foods that may exacerbate the condition. Like IBD, patients with diverticular disease can present with rectal bleeding and fever (if they have infection). Rarely, the condition may result in either abscess formation or peritonitis, requiring aggressive antibiotic and surgical management. The diagnosis once again can be confirmed either via endoscopy or by barium enema. If confirmed, it should be managed in conjunction with an appropriate bowel specialist.

Other bowel conditions that rarely present as CPP include chronic appendicitis and colon cancer. A full description of these entities is beyond the scope of this article.

VII. PELVIC PAIN CAUSED BY URINARY TRACT DISEASES

SURGICAL TREATMENT OF CASE PATIENT 1

Patient 1 is treated surgically for endometriosis, and follow-up therapy includes a GnRH agonist for 6 months. She is treated for hypoestrogenic side effects and tolerates the therapy adequately. Initially, she has a good response for most of her pain. During the next 18 months, however, she re-develops some of her original symptoms and is bothered by a generalized pain that is suprapubic in location, along with pain before voiding. Urinalysis is normal, and culture is negative for amounts of bacteria that would be associated with infection.

- **The next best step in her evaluation is:**
  A) Treat empirically with antibiotics
  B) Re-initiate treatment for endometriosis but this time use danazol
  C) Treat symptomatically with narcotic analgesics
  D) Refer for evaluation of the urinary tract
  E) Perform office cystoscopy

**Discussion**

The correct answer is D. Several conditions affecting the urinary tract may manifest with pelvic pain. In particular, any patient with midline or suprapubic pain should undergo bladder assessment. The important urologic processes to consider in the patient with CPP include infectious cystitis, urethral syndrome, renal calculi, and interstitial cystitis.

**Infectious Cystitis**

Bacterial infections of the bladder or urethra may present with either acute or chronic pain symptoms. The pain is often localized to the suprapubic region, but the pain may be vague and difficult to isolate to a particular region of the pelvis. Patients with cystitis may also describe focal urinary symptoms including dysuria, urgency, frequency, incontinence, or hematuria. Physical examination may confirm tenderness in the suprapubic region, at the bladder base, or along the urethra. The diagnosis of infectious cystitis relies on positive findings on a urinalysis and culture. Several efficacious and cost-effective oral antibiotic regimens are available to treat uncomplicated UTI. For patients diagnosed with chronic or recurrent UTIs, suppressive therapy with antibiotics may be warranted. Consultation with a urologist to rule out structural abnormalities of the urogenital tract might be considered if symptoms persist.

**Urethral Syndrome**

Urethral syndrome is characterized by bladder irritation, urinary symptoms, and pain which is often more pronounced with intercourse. Although the symptoms and signs of the syndrome mimic cystitis, urinalysis and urine culture are negative. Several infectious organisms including *C. trachomatis*, *Ureaplasma*, and *herpes simplex virus* have been proposed as possible etiologies of urethral syndrome. Acceptable therapy for the condition involves prolonged antibiotic treatment.

**Interstitial Cystitis**

Interstitial cystitis remains an enigmatic cause of CPP. Interstitial cystitis is a syndrome with prevalence estimates ranging from 44,000 to more than 1,000,000 in the United States. Approximately 90% of patients with interstitial cystitis are women. The causes are unknown, and treatments are empiric. The symptoms vary greatly among patients, and usually include a combination of the following: pelvic pain (which may radiate),
perineal pain, pain increased by holding urine (which leads to urinary frequency), nocturia, urinary urgency, and constant urge to void. Patients have various symptoms, clinical features (such as cystoscopic and biopsy findings), and responses to the different empiric treatments. Because of these variations, most investigators agree that interstitial cystitis is a multifactorial syndrome rather than a single disease.

The typical interstitial cystitis symptom is pelvic pain with only small amounts of urine in the bladder. The pain is typically relieved by voiding but soon recurs as the bladder fills. The resulting urinary frequency can be as often as 40 times in 24 hours. Another common symptom is a constant urge to void, which is very uncomfortable because it never goes away, even after voiding. Incontinence is not typical for interstitial cystitis. If incontinence is present, other diagnoses should be diligently sought. Also, pain during voiding is not typical for interstitial cystitis. This symptom suggests UTI, urethral diverticulum, or external irritation such as atrophic vulvitis.

The typical interstitial cystitis symptoms get worse the week before menses (somewhat similar to endometriosis, but interstitial cystitis symptoms do not usually flare with the onset of menses). Some interstitial cystitis patients notice that specific foods worsen their symptoms; especially coffee, alcohol, carbonated drinks, citrus, tomatoes, and chocolate. Some interstitial cystitis patients have dyspareunia; for others, sex is not painful, but the symptoms will flare the next day. It is common for stress to worsen symptoms.

Not all interstitial cystitis patients have the typical symptoms previously described. Some patients have continual pain (rather than just with a full bladder), and some have pain that is worse after voiding. Especially for those patients with continual pain, other pelvic pathology should be considered and carefully sought.

REFERRAL OF CASE PATIENT 1

Patient 1 is referred to a urologist who does an office evaluation and is concerned that she may have interstitial cystitis. However, it is uncertain if patient 1’s endometriosis is simply recurring.

• The most appropriate next step in the management of this patient is:
  A) Perform cystoscopy and bladder dilatation under anesthesia
  B) Begin empiric treatment for interstitial cystitis
  C) Begin empiric treatment for recurrent endometriosis
  D) Perform laparoscopy to rule out endometriosis and treat if present
  E) Both A and D

Discussion

The correct answer is E. A major problem in patients with interstitial cystitis is that no objective abnormalities are found on the usual urogynecologic evaluation, including office cystoscopy. The diagnostic procedure is to do a cystoscopy under anesthesia with bladder distention. If multiple submucosal hemorrhages (glomerulations) and/or bladder ulcers are observed, then the patient is diagnosed with interstitial cystitis. Until recently, many clinicians did not know that bladder distention under anesthesia was needed to diagnose interstitial cystitis. Therefore, interstitial cystitis was thought to be rare. Patients were often told “there is nothing wrong,” “it’s just stress,” and other unhelpful statements. The average interstitial cystitis patient required 4.5 years and 5 doctors to obtain the correct diagnosis. Fortunately, since the 1980s, more clinicians are recognizing the symptoms and accurately diagnosing interstitial cystitis.

One popular theory for interstitial cystitis is that the epithelium is deficient and permeable to urinary irritants. The normal bladder epithelium functions as a barrier to prevent urine from irritating the bladder. This has not been definitively proven, but several lines of evidence suggest it. If permeability truly is increased in interstitial cystitis, the reason(s) are still unknown. Ordinarily, large negatively charged molecules (such as glycoproteins and glycosaminoglycans [GAGs]) line the epithelium and provide a permeability barrier. Protamine sulfate, which neutralizes the negative charges, caused interstitial cystitis–like symptoms when placed into bladders of healthy volunteers. This result suggested that the epithelial glycocalyx is deficient in interstitial cystitis. Thus, GAG “replacements” are used for treatment; these replacements include heparin and hyaluronic acid, usually given intravesically, and pentosan polysulfate (Elmiron), usually given orally. All 3 agents are clearly beneficial for subsets of patients. However, the mechanism(s) for symptom relief are unknown.

Although ongoing infection has not been shown to cause interstitial cystitis, it is possible that infection might initiate interstitial cystitis. For example, infection may damage the epithelium, which then does not fully recover, or infection may initiate an autoimmune process. Urodynamic studies in interstitial cystitis are usually normal except for increased bladder sensitivity and smaller capacity. To meet the NIH criteria for interstitial cystitis, the patient must have an intense urge to void at
FURTHER SURGICAL TREATMENT OF CASE PATIENT 1

Patient 1 undergoes a combined procedure (ie, cystoscopy and laparoscopy under the same anesthesia); minimal endometriosis is found and treated. In addition, she is found to have typical findings of ulcerative interstitial cystitis. She does well from a pain standpoint after the procedure and comes on a regular basis for continuing follow up.

After 7 months, she is again developing pain with bladder distension, although her frequency is not to the point it was before the bladder distension under anesthesia.

150 mL or less, and a capacity of 350 mL or less. Occasionally, interstitial cystitis patients will have poor bladder compliance.

Detrusor instability (uninhibited bladder contraction) is an exclusion criterion for interstitial cystitis, using NIH criteria. Most interstitial cystitis researchers believe that detrusor instability is a separate and distinct entity from interstitial cystitis. The most dramatic evidence for this distinction is in treatment response: detrusor instability responds to anticholinergic agents but not to standard interstitial cystitis treatments such as dimethyl sulfoxide (DMSO). In contrast, interstitial cystitis does not respond to anticholinergics. However, interstitial cystitis and detrusor instability may co-exist in the same patient. These patients require both anticholinergics and standard interstitial cystitis treatments.

The usual diagnostic test for interstitial cystitis is a cystoscopy under anesthesia, with bladder distention at 80 cm of water pressure for 2 minutes. This test is accomplished simply by hanging the fluid 80 cm higher than the patient’s bladder and leaving the connections open. After distention, one may see multiple submucosal hemorrhages (glomerulations) or bladder ulcers, which often crack and bleed. In addition, if other gynecologic pathology is suspected, laparoscopy can be performed under the same anesthetic (which is referred to as the combined procedure). The main purpose of bladder biopsies is to rule out other causes of interstitial cystitis symptoms, primarily carcinoma in situ. No biopsy findings are specific for interstitial cystitis. A major concern with chronic pain is that changes referred to as neural plasticity may occur in the central nervous system (CNS) that amplify or perpetuate the pain signals, even if the initial noxious stimulus is no longer present. This is one hypothesis for why some interstitial cystitis patients have no relief when local anesthetics are placed into the bladder. This theory also explains why some interstitial cystitis patients have persistent pain after cystectomy.

• The best option for treating her is education and which of the following?
  A) Narcotic analgesics
  B) Anti-inflammatory agents
  C) Pentosan polysulfate (Elmiron)
  D) Repeat bladder distension under anesthesia
  E) Intravesical lidocaine

Discussion

The correct answer is C. Two key points should be made in the initial educational discussion with the patient. First, interstitial cystitis usually does not progress. Those patients who have debilitating symptoms usually start out with debilitating symptoms. Patients are greatly relieved to know that their condition will probably not get worse. The second key point is that no single treatment works for all patients. Treatment is by trials of empiric therapies, continuing to try different alternatives until the symptoms are controlled satisfactorily. Because most patients eventually achieve good symptom control, they should not become discouraged if the initial treatment does not improve their symptoms.

Many treatments are used for interstitial cystitis, but only a few have been subjected to placebo-controlled trials or to studies in which a disease marker was followed. Some of the more commonly used treatments are described in the next section.

CONSERVATIVE TREATMENTS

Many foods have been implicated in promoting symptoms of interstitial cystitis. Some patients give a very clear history: within 1 hour of eating an offending food, symptoms flare. Some of the classic offenders are coffee, chocolate, carbonated drinks, alcohol, citrus, and tomatoes. However, different patients may be affected by different foods.

Most interstitial cystitis patients should try a restricted diet for a short time (1–2 weeks). If symptoms improve, this suggests that certain offending foods were eliminated. The patient can then try eating specific foods (eg, coffee, chocolate), one at a time, to see whether that specific food will bother her. If a symptom flare is going to occur, it usually happens within 1 day (often within 1 hour) after eating the offending foods. The mechanism whereby these foods promote symptoms is unknown but may be related to acid, potassium, or amine precursors (eg, tyramine, tryptophan).

Another conservative treatment that often helps is a bladder-holding protocol. This is best suited for patients with frequency and urgency but not severe pain. The specific techniques vary but include diary keeping, timed voiding, and a gradual increase in voiding intervals.
ORAL DRUG TREATMENTS

Pentosan polysulfate (Elmiron) is the only oral drug for interstitial cystitis that is approved by the FDA. The other drugs listed in this section (ie, amitriptyline, antihistamines, calcium channel blockers, drugs for neuropathic pain, arginine, narcotics) are FDA approved for other conditions but not for interstitial cystitis. Pentosan polysulfate was superior to placebo in one trial held in the United States but was not superior in another trial held in Europe. A possible explanation is that the European interstitial cystitis population has a higher proportion of patients with bladder ulcers, whereas pentosan polysulfate is more effective in patients without ulcers. It proposes that action is replacing a deficient bladder epithelial glycocalyx. Side effects (eg, GI upset, alopecia) are rare. The main drawback is expense (approximately $150.00/month). Therapy for 3 to 6 months may be needed to achieve good symptom relief. The standard dose of pentosan polysulfate is 100 g taken orally three times daily with water, either 1 hour before or 2 hours after a meal.

Amitriptyline has several actions that may benefit interstitial cystitis, including antihistamine, anticholinergic, sedation (improved sleep), and inhibition of nociception in the CNS. It was beneficial in several open-label studies. The usual dose of amitriptyline is 25 to 75 mg at bedtime. Side effects include sedation, anticholinergic effects, and weight gain.

Antihistamines are potentially useful because mast cell activation may contribute to interstitial cystitis symptoms. The H1 blocker hydroxyzine (25 to 75 mg at bedtime) and the H2 blocker cimetidine (300 mg twice a day) were both effective in open-label studies. Side effects are minimal. Hydroxyzine is sedating, but this effect is often a benefit for patients with nocturia and consequent sleep deprivation.

Nifedipine (a calcium channel blocker) gave good relief in a small open-label study. Its mechanisms may be through increasing bladder blood flow, inhibiting detrusor contractions, or depressing cell-mediated immune response. Side effects include hypotension, dizziness, and edema. It is unknown whether other calcium channel blockers besides nifedipine would benefit interstitial cystitis in the same manner.

Oral L-arginine (1500 to 3000 mg per day in divided doses) was given to 10 patients for 6 months. All patients had significant improvement of their interstitial cystitis after 1 month, which continued for 6 months. The proposed mechanism was increased nitric oxide synthase activity.

If other measures fail, chronic narcotic agents may be very helpful for returning to a more normal lifestyle. The pain of interstitial cystitis is real, and the risk of addiction is low. It may be beneficial to collaborate with pain management specialists, who are experienced in chronic narcotic use.

Drugs for neuropathic pain include clonazepam, gabapentin, and mexitelene. There are no formal studies of these drugs in interstitial cystitis, but they are useful in other types of chronic pain. Consultation with a pain management specialist may be helpful in determining whether these agents will be useful.

Anticholinergics, antispasmodics, and bladder analgesics are generally not effective in interstitial cystitis. In fact, relief by these drugs is an exclusion criterion for interstitial cystitis (using NIH criteria).

INTRAVESICAL TREATMENTS

These treatments include bladder distention, DMSO, heparin, hyaluronic acid, cromolyn sodium, silver nitrate, sodium oxychlorosene, bacillus Calmette-Guérin (BCG), and intravesical cocktails.

Bladder distention can also be therapeutic. It helps only a subset of patients, but this subset usually achieves dramatic symptom relief for nearly 6 months or longer. The mechanism of symptom relief is unknown. Patients with severe bladder inflammation (who also tend to be older) are the most likely to have complete symptom relief.

DMSO is the only other FDA-approved agent for interstitial cystitis (besides pentosan polysulfate). A controlled study showed that DMSO was superior to placebo, with 53% of patients having significant improvement. The proposed mechanisms include anti-inflammatory effect, free radical scavenging, mast cell inhibition, and analgesia. The usual dose is 50 mL of 50% DMSO intravesically once a week. Instillation can be painful; therefore, it is better to instill 20 or 30 mL of 1% lidocaine, wait a few minutes, drain the lidocaine, and then instill the DMSO. Draining the lidocaine is important because DMSO promotes the absorption of lidocaine across the bladder wall. DMSO is sometimes combined with other agents (eg, heparin, steroids), but the safety and efficacy of these combinations have not been evaluated.

In an open-label study, 56% of interstitial cystitis patients had good relief using heparin (10,000 units intravesically 3 times a week). In another study, monthly heparin instillations (10,000 units) prolonged the response to DMSO. Heparin is thought to replace the bladder epithelial glycocalyx but may act by stabilizing mast cells or other mechanisms.

In an open-label study, weekly instillations of 40 mg of hyaluronic acid gave complete symptom relief in 25% of patients and partial relief in 46%. The results of a
placebo-controlled trial are still pending. It is thought to replace the glycocalyx, similar to heparin, but may also work by modulating the immune response or other mechanisms.101

In a pilot study, 9 patients received 100 mL of 4% cromolyn sodium daily for 12 days. Two patients were cured and 4 were improved. The proposed mechanism is stabilizing bladder mast cells.102

In a controlled study using 6 weekly instillations, 30 patients were treated with BCG; the response rate was 60% versus 27% for placebo.103 The mechanism is unknown, but it likely involves modulation of the bladder immune response. A multicenter controlled trial is planned.

Sodium oxychlorosene (Clorpactin) is a solution of hypochlorous acid (“bleach”) and detergent. It was originally used because interstitial cystitis was thought to be a chronic bladder wall infection that could be ameliorated by the germicide and detergent actions of Clorpactin. It is very painful to instill, so it is usually given under anesthesia. Because most practitioners also do a bladder distention at the same time, it is hard to tell whether the patient’s symptom relief is from the distention or the Clorpactin. The usual procedure is to fill the bladder to 50% capacity with freshly prepared 0.4% Clorpactin, dwell for 5 to 7 minutes, drain the bladder, and repeat 3 or 4 times.97 Afterwards, the bladder, perineum, and vagina are copiously irrigated with normal saline. It is essential to rule out vesicoureteral reflux before Clorpactin instillation. Patients must be warned that the symptoms will be worse for days to weeks after the procedure.97

Silver nitrate was first described to treat interstitial cystitis in 1944. The overall success rate was approximately 50%. It has never been evaluated in a placebo-controlled study. Instillation can be painful (requiring anesthesia), and because so many other treatments are now available, silver nitrate is rarely used.97

Various intravesical cocktails are anecdotally described, with ingredients including heparin, gentamicin, local anesthetics, steroids, sodium bicarbonate, and DMSO in various combinations. None has been rigorously evaluated.

ADJUVANT TREATMENTS

Transcutaneous electrical nerve stimulation had a good effect or remission in 54% of classic (ulcer) interstitial cystitis patients and 26% of non-ulcer patients.104 Other types of physical therapy are also used, but formal studies of physical therapy in interstitial cystitis have not been published. Some patients have relief with other adjuvant treatments including acupuncture and hypnosis.
focused non-gynecologic history and examination are critical in establishing the diagnosis of fibromyalgia. Laboratory studies are not necessary in establishing the diagnosis but should be ordered to rule out other illnesses that may be curable and mimic fibromyalgia. Conditions that are more common in patients with fibromyalgia include irritable bowel syndrome, interstitial cystitis, chronic headaches, and vulvodynia. These diagnoses, at least in part, are thought to be conditions associated with defects in normal pain processing. The symptom of pelvic pain in women diagnosed with fibromyalgia results from stimuli originating from various organs and systems. For instance, IBS, dysmenorrhea, and vulvodynia may all manifest with generalized diffuse pelvic pain.

Fibromyalgia is considered a chronic condition, and therapy should be geared towards the alleviation of symptoms. Several medical therapies have proven effective in treating the condition. Tricyclic antidepressants remain a first-line treatment for fibromyalgia. Skeletal muscle relaxants and hypnotics have also proven efficacious in the treatment of the disorder. Behavioral modifications including exercise, stress reduction, improved sleep hygiene, physical therapy, and cognitive behavioral therapy have also provided benefit in the treatment of fibromyalgia.

IX. PSYCHIATRIC DISORDERS

Several psychiatric conditions should be considered in the patient with CPP. Chronic pain syndromes are often influenced by both physical and mental factors. Additionally, mood is considered an important modifier of both the symptom and the perception of pain. Psychiatric diagnoses—including depression, personality disorder, anxiety disorder, and past sexual or physical abuse—should be considered and screened for by the gynecologist. In women with psychiatric ailments, it may be difficult to discriminate whether a psychological issue is the cause of, or merely a product of, the patient’s symptoms.

DEPRESSION

Depression affects 10% to 25% of females during their lifetime and is more common in women than men. In women with depression, pain is not an uncommon manifestation of the disorder. Symptoms associated with depression include altered diet and sleep patterns, decreased concentration, low energy, and feelings of helplessness and guilt. Factors that may contribute to depressive symptoms, which should be explored by the practitioner, include recent loss of social or emotional support.

Psychological counseling, support, and antidepressant therapy may be helpful as an adjunctive treatment in patients with CPP who meet criteria for depression. This treatment is especially germane in women with no clear organic explanation for their symptoms. Various antidepressants have been proposed to be effective in treating pain in appropriate patients. The best-established of these agents are the tricyclics, including amitriptyline and nortriptyline, which also have proven efficacy in the management of chronic pain syndromes. Although commonly prescribed for depressive symptoms, selective serotonin uptake inhibitors, such as sertraline, have not decreased symptoms in patients with chronic pain; however, the studies were small.

SEXUAL ABUSE

A history of sexual abuse is uncovered in 40% of women with symptoms of CPP. The basis for this association is speculative but likely reflects the development of depression or a pain processing alteration after such trauma. When such a history is uncovered, it is imperative that the clinician be empathetic and sensitive to the patient’s emotional state. Additionally, psychological counseling and antidepressant therapy is best offered by a psychologist or psychiatrist with a focus on sexual abuse issues. Any patient experiencing suicidal ideation should promptly be referred for psychiatric consultation.

Other psychiatric-related conditions that should be considered in the patient with chronic pain symptoms include somatization disorders, hypochondriasis, malingering, and drug-seeking behavior. These conditions should also be explored in conjunction with an appropriate psychiatric specialist.

X. GENERAL PRINCIPLES OF PAIN MANAGEMENT

Regardless of etiology, general pain management principles endorsed by the American College of Obstetricians and Gynecologists (ACOG) include:

1. Use of positive reinforcement
2. Assessment of psychological factors early in the evaluation
3. Identification and treatment of underlying disorders whenever possible
4. Treating the pain promptly
5. Considering use of different but synergistic treatment modalities
6. Using narcotic drugs with caution
As long ago as 1976, Fordye recommended that behavioral methods be used instead of nociceptive elements in long-term management of CPP. Further, he cited the prolonged use of potent narcotic analgesics in pain syndromes as a potential factor to “perpetuate” the pain behavior. In addition, many clinicians do not treat chronic pain states adequately for various other reasons (eg, potential for losing license, negative attitude about narcotic use for analgesia). As such, undertreatment of pain is a common problem in CPP, and the sequelae have been well documented. One other reason that patients with CPP are under-medicated for their pain is that, frequently, the pain is out of proportion to the disease findings.

**OPIOID THERAPY**

Multiple treatment options are available for these patients. Opioid analgesics are commonly used. Mu receptors to which opioids bind are found mostly in the gastrointestinal and central nervous system (CNS) tissue. Pure agonists bind only these receptors. In contrast, partial agonists bind to this receptor partly; agonist/antagonist agents bind the kappa receptor and block the mu receptor. The controversy of using opioid analgesics to which opioids bind are found mostly in the gastrointestinal and central nervous system (CNS) tissue. Pure agonists bind only these receptors. In contrast, partial agonists bind to this receptor partly; agonist/antagonist agents bind the kappa receptor and block the mu receptor. The controversy of using opioid analgesics for CPP is that it improves quality of life in some patients, whereas it worsens the functionality of other patients. Relief of pain may indeed be a necessary, immediate outcome of opioid use; however, functional improvement measures commonly used by experts in rehabilitation medicine must be assessed to see if improvement in meaningful activities has been achieved. Failure to see improvement is an indication for adjustment or change of the drug dose. There is very little literature on use of opioids for CPP. In related research on chronic pain in general, approximately 50% of non-cancer patients received relief with opioids and 16% received no significant relief.

**Maintenance Opioid Therapy**

So who, then, should receive maintenance opioid therapy for CPP? Portenoy developed 11 criteria as a useful guide to answer this question:

1. **Opioid therapy should only be considered after all other reasonable attempts at analgesia have failed.** While this includes medicinal and non-medicinal alternatives (physical therapy, behavioral therapy, injection of trigger points), the use of opioids may still be necessary to provide interim pain relief so that these other therapies may then be attempted. Without such interval pain relief, no real effort will be made to relieve the pain through a non-narcotic avenue.

2. **A history of substance abuse should be considered a relative contraindication.** If the person has primary substance abuse (the history of narcotic abuse antedates the present pain syndrome), then management is probably better in a substance abuse program. In contrast, if they have secondary abuse (abuse initiated from the present, undertreated pain syndrome), then management is still best in office-based practice. In contrast to these settings, a remote history of abuse is not considered a contraindication but simply warrants close observation and accounting of all prescriptions to avoid recurrence of abuse.

3. **A single practitioner should take primary responsibility for treatment.** This is particularly important when referral to chronic pain services is done so there is a clear “contract” between patient and providers as to who will be dispensing medications; only one pharmacy should be used. Such a contract brings with it the option of dismissal from practice if violated.

4. **Patients must be allowed to increase dosing on an acute basis when needed.** These rescue doses will be needed to cover “breakthrough” pain experienced...
by some patients. Of course, too frequent use of these rescue doses suggests that either the maintenance dose is too low or reflects a possible abuse situation; regardless, re-evaluation is needed.

(9) **Patients should be seen at regularly scheduled appointments.** These visits are used to monitor progress, recognize early signs of potential abuse of medications, and assess any undesired side effects that the patient may be experiencing. By letting the patient know this office policy early, the late evening or last minute request for more analgesia can be more effectively handled.

(10) **Breakthrough pain not relieved by small, temporary dose increases should be considered a reason for hospitalization for observation of response to dose escalation.** This assumes that history, physical examination, and physical therapy have been used to successfully remove external influences that are inciting or exacerbating agents.

(11) **Unacceptable behavior (acquiring drugs from others, uncontrolled dose escalation, aberrant behavior) should be considered grounds for tapering and then discontinuing maintenance therapy.** Although clinicians must believe their patients’ complaints of pain, they must also be wary of those whom they feel are abusing such medications.

### Barriers to Chronic Opioid Use

Fortunately, chronic opioid use results in tolerance to some of the cognitive, respiratory, and other non-specific CNS effects of these agents within days of initiation. Unfortunately, the chronic constipating effect does not resolve, and stimulatory laxatives need to be prescribed as softeners; bulk forming or saline/osmotic laxatives do not help these patients. Despite successful use of laxatives, there are still barriers to the use of chronic opioids to manage chronic pelvic pain and pain in general. These barriers include issues of tolerance, dependence, and eventually addiction.

### PAIN CLINICS AND NONTRADITIONAL APPROACHES TO PAIN MANAGEMENT

Specialized clinics have been developed in recent years for treating chronic pain syndromes such as CPP. Research has confirmed the benefit of a multidisciplinary approach in the management of chronic pain. Specifically, psychological, social, and dietary interventions have proven valuable in the treatment of the condition when combined with traditional pharmacological and surgical treatments. Pain clinics, which are typically operated by anesthesia services, may offer unique and effective treatment modalities for patients with chronic pain.

Pain clinics often play an important role in providing analgesia while helping patients discontinue addictive narcotic medications. Such clinics may also identify focal “trigger pain-points,” which may be managed with the administration of periodic regional anesthetic blocks. Additionally, newer pharmacological therapies including gabapentin (Neurontin) are being used with some benefit in such settings. This agent has proven efficacy in treating neuropathic pain in diabetic patients and in some chronic gynecologic pain syndromes.

Various nontraditional therapeutic modalities have been proposed for the management of CPP including acupuncture, aromatherapy, reflexology, massage, relaxation, and stress-reduction techniques. In general, however, evidence confirming the effectiveness of these interventions is lacking; thus, they should be recommended only with caution.

### XI. SUMMARY

Treating patients with CPP is often a challenge and can be frustrating for both the patient and the physician. Over time, however, symptoms of CPP can often be managed successfully. Both the woman and practitioner should be patient through the evaluation and treatment process; continuity of care should be a priority. Because gynecologists typically evaluate and treat CPP, they need to be familiar with the complexity of the condition. Differential diagnostic considerations in a patient with CPP should encompass both gynecologic and non-gynecologic possibilities. Endometriosis is the most common gynecologic cause for CPP. Non-gynecologic sources of pelvic pain include conditions involving the GI, urologic, and the musculoskeletal systems. Finally, both psychiatric disorders and pain processing abnormalities may contribute significantly to pain symptoms and, therefore, should not be ignored in the patient with CPP.

Providing optimal treatment to women with CPP should involve a multidisciplinary approach. Other medical specialties, counselors, and specialized clinics may provide important diagnostic information and offer alternative therapies in the treatment of CPP. The gynecologist has an integral role in caring for the patient with CPP. This role includes alleviating pain and offering the patient a reasonable expectation of return to normal function.
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