Contents

Chapter 1

Introduction to Chronic Pelvic Pain

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Editor's Introduction

Pelvic pain is a condition which is much more common than perceived by the medical and general community. Because it affects the most private aspects of human life such as sexuality and reproduction, patients are not willing to discuss it with their families, friends, and loved ones. Medical providers are also very likely to dismiss the symptoms and blame it on a psychological or psychiatric conditions. Chronic pelvic pain is real, it is common, and it is almost always due to some identifiable disease or injury. Patients with pelvic pain need to be heard and treated with dignity and respect, and the majority of them can be helped.

In at the conquer'd doors they crowd! I am possess'd!
Embody all presences outlaw'd or suffering,
See myself in prison shaped like another man,
And feel the dull unintermitted pain.
Walt Whitman, *Song of Myself*

Pain is one of the most feared and dreaded human sensations. It is derived from the Latin *poena* – punishment. Pain, thirst, and hunger responses are considered to be the most primordial of human emotions [1]. Unlike higher emotions such as love, hate, and anger, these primordial sensations involve lower brain regions such as the medulla, midbrain, and hypothalamus. Pain may occur as an acute event or as a persistent, long-term symptom. While acute pain or nociception serves as an alert of trauma and impending damage, chronic pain is a disease and can easily become one of the most debilitating conditions that one can endure.

In 1979 the International Association for the Study of Pain (IASP) defined pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" [2]. This definition is incomplete because it excludes the clinically significant social and cognitive components of pain. Also, describing pain merely as an unpleasant sensation minimizes patient suffering and may influence bias in the approach of practitioners.

Over the years our understanding of pain has changed dramatically. The pain experience is characterized by tremendous interindividual variability. By definition, pain is a subjective and personal experience, inherently making clinical practice and research challenging. A multitude of biological and psychological factors contribute to these differences: genetic, psychosocial, and demographic processes inherently influence each other, contributing to the overall pain experience. Historically, pain researchers have focused intellectual pursuits on legitimizing these differences.

Nociceptive pain originates in damaged tissues, usually secondary to a noxious stimulus, and neuropathic pain is caused by a disease of the nervous system. Superficial nociceptive pain originates in the pain receptors (nociceptors) located in the skin. Deep nociceptive pain may be either somatic or visceral. Deep somatic nociceptors located in the muscles, tendons, ligaments, bones, and blood vessels usually produce dull and poorly localized pain. Deep visceral nociceptive pain originates in the visceral receptors and may be well localized; however, this localization rarely corresponds with the area of injury because of pain referral patterns. This phenomenon is commonly seen in conditions such as painful bladder syndrome, in which presenting symptoms may include back or vulvar pain. Neuropathic pain may originate in the peripheral or central nervous system, as a result of disease or intrinsic malfunction. Peripheral neuropathic pain is more common, producing sensations of burning, tingling, electrical shocks, or pins and needles. Table 1.1 outlines common terms used in clinical descriptions of abnormal pain function.

Acute pain is an essential evolutionary sensation that prompts a change in position or behavior, usually in response to some noxious stimulus, with the

Table 1.1 Common terms used in pain conditions

Allodynia	Pain in response to the stimulus that is normally non painful
Hyperalgesia	Exaggerated response to a stimulus that is normally painful
Central sensitization	Up-regulation of central nervous system, causing the sensation of higher intensity pain with less provocation. Allodynia and hyperalgesia are signs of central sensitization
Analgesia	Absence of pain in response to painful stimulus
Dysesthesia	An unpleasant abnormal sensation. May be spontaneous or evoked
Paresthesia	An abnormal sensation. Unlike dysesthesia it does not need to be unpleasant
Hyperesthesia	Increased sensitivity to stimulation
Allotriesthesia	Pain caused by the sensation of a foreign body in the absence of a foreign body
Neuralgia	Pain in the distribution of the nerve. By definition it does not require nerve injury
Neuritis	Pain caused by inflammation of the nerve
Neuropathy	A disturbance of function or pathological change in a nerve
Noxious stimulus	A stimulus that is strong enough to damage normal tissues, usually prompting a reactive pain response
Peripheral sensitization	Increased sensitivity to an afferent nerve stimulus. Occurs after injury to the area, which results in the flare-up response
Nociceptive pain	Pain originating in the pain receptors in the skin (superficial), muscles, tendons, blood vessels (deep), or visceral organs, usually secondary to a noxious stimulus
Neuropathic pain	Pain originating in the peripheral or central nervous system, resulting from disease or intrinsic malfunction
Wind-up phenomenon	Perceived increase in pain intensity due to repetitive painful stimulus. Caused by activation of normally dormant receptors
Viscerosomatic convergence	Noxious stimulus to the viscera triggers pain referred to somatic sites
Viscerovisceral convergence	Noxious stimulus to the viscera triggers pain referred to other visceral sites
Functional somatic syndrome	Physical symptoms that are poorly explained. Encompasses conditions like chronic fatigue, fibromyalgia, irritable bowel syndrome, tension headache, and others
Somatization	Manifestation of mental phenomena as physical symptoms
Conversion disorder	Neurological symptoms such as numbness, blindness, or paralysis in the absence of organic cause and traced back to a psychological trigger

goal of preventing any further damage to tissues. Pain has been studied in numerous animal species, including fish and invertebrates such as the fruit fly. Across species, it has been demonstrated that acute pain serves not only as a warning of external trauma, but also as a symptom of numerous internal disease processes. In humans, acute pain may serve as a lifesaving symptom of medical emergencies such as myocardial infarction. Chronic pain, on the other hand, does not always serve a clear essential purpose and can actually become a disease of its own. The general mechanism of chronic pain has clear differences from that of acute pain. The majority of patients who experience tissue trauma with acute pain will heal without any sequelae. After physical healing is complete, a small percentage of these patients will continue to experience pain. Chronic pain may result from a number of other mechanisms including degenerative disease resulting from aging or overuse, and abnormal or insufficient healing following acute physical trauma. Chronic pain may also present as a primary condition, lacking any identifiable cause. It is theorized that in some instances, the central nervous system may produce independent pain input without an external or internal pain stimulus. Regardless of origin, the mechanism of chronic pain generally has some relation to musculoskeletal or nervous system function.

Maladaptive plasticity changes in the nervous system that lead to a disruption in function, producing a disease state, have been described in a large number of clinical trials and animal studies. Additionally, these changes may also occur in sensory conduction pathways between the peripheral and central nervous system, resulting in the development and maintenance of chronic pain. Central sensitization represents the manner in which pain is uncoupled from the clear noxious stimulus that defines acute nociceptive pain. Instead, the features of pain are reflective of the functional state of the central nervous system, the memory of persistent pain, and the associated sensory conduction pathways. Central sensitization results in an alteration of the induction, spatial extent, intensity, and duration of pain [3].

A key difference between an acute episode of pain and chronic pain is that the persistence of this sensation can lead to a number of adverse sequelae including physical suffering, sleep disorders, fatigue, and substance abuse. Because chronic pain and mood control share the same neurotransmitters, these patients often suffer from mood disorders such as depression, bipolar disease, obsessive–compulsive disorder, and posttraumatic stress disorder. Persistent pain can also lead to significant social concerns including difficulty with intimacy, strain on personal relationships, and poor professional performance. Decline in physical activity in patients with chronic pain often causes weight gain, deconditioning, and other secondary morbidities.

Prevalence and Impact of Chronic Pain

The prevalence of chronic pain is difficult to estimate. In the industrialized world anywhere from 20% to 50% of people suffer from pain for more than 6 months during some point in their lifetime. In the United States the prevalence of chronic pain is approximately 30.7%, translating to an estimate of 90 million people living in pain. Chronic pelvic pain affects 5.7%–26.6% of reproductive-age women, with variation in these numbers influenced by population characteristics [4]. It is estimated that one in seven women meet clinical criteria of chronic pelvic pain at some point in their lives. In women the prevalence of chronic pelvic pain is higher than that of asthma, diabetes, and coronary artery disease and almost as high as that of back pain [5].

This vast number of affected individuals has led to significant social and economic sequelae. The total annual cost associated with pain in the United States has been estimated to be between 560 and 635 billion dollars, which is higher than the combined annual cost associated with heart disease and cancer. Other studies estimate the economic impact of chronic pain to be 3% of GDP.

Between 1999 and 2016, more than 630,000 people died from a drug overdose in the United States. In 2016, an estimated 48.5 million persons in the United States reported use of illicit drugs or misuse of prescription drugs in the past year, of which 4.3% were prescription pain relievers; this translates to 2 million individuals [6]. In 2017 healthcare providers wrote on average 58.5 prescriptions per 100 persons. Even though opioid prescribing continued to decrease through 2017, more efforts are needed to help healthcare providers adopt and maintain safe prescribing habits.

The Diagnostic Challenges of Chronic Pelvic Pain

Chronic pelvic pain is a common and often underdiagnosed condition occurring in both women and men. Although this book specifically focuses on chronic pelvic pain in women, chronic pain in men is equally frequent and devastating, with similar challenges in diagnosis and management.

The International Pelvic Pain Society defines chronic pelvic pain as pain located in the pelvis, persisting for 6 months or longer, with or without association with menstrual cycles and severe enough to cause functional disability [7]. Up to one in seven women meet this clinical criterion over the span of their lifetime. Despite this high prevalence, the condition remains relatively underdiagnosed and untreated. This is at least in part due to the suboptimal education of clinicians on the subject of female chronic pelvic pain. In the United States, most medical school curricula lack even a single lecture dedicated to chronic pelvic pain in women, and postgraduate obstetrics and gynecology training tends to limit this training to endometriosis and painful bladder syndrome. This approach produces clinicians who are ill prepared for the diagnosis and management of the wide range of gynecological and nongynecological conditions that can lead to chronic pelvic pain.

Most women with pelvic pain have more than one condition contributing to their pain, further complicating diagnostic workup. This is commonly true in

the case of endometriosis. Dr. Fred Howard, a pioneer in the area of chronic female pelvic pain in the United States, made an observation in his practice that more than three-quarters of patients with endometriosis and pelvic pain have another etiology contributing to their pain, in addition to their endometriosis. This means that if the only intervention offered to these women is treatment of endometriotic lesions, more than half will likely not experience adequate improvement in their chronic pain.

The diagnosis of pelvic pain is further challenged by the fact that many patients with chronic pelvic pain do not have easily identifiable pathology. The American College of Obstetricians and Gynecologists (ACOG) highlights bloodwork, ultrasonography, cystoscopy, sigmoidoscopy, colonoscopy, and laparoscopy as potential workup modalities that may be helpful in working toward a diagnosis in patients with chronic pelvic pain, based on presenting symptoms [8]. It has been reported that up to 30% of women with pelvic pain have completely normal findings on laparoscopy [9]. In the remaining 70% of patients the most common surgical findings were lesions consistent with endometriosis and adhesions. The severity of endometriosis and adhesions tends to be only marginally correlated with the severity of chronic pelvic pain [10]. Only deep infiltrating endometriosis has been shown to be associated with more pain [11]. In light of the inconsistent findings in the clinical workup of patients with chronic pelvic pain, ACOG has previously concluded that "few, if any of the diseases thought to cause chronic pelvic pain meet traditional epidemiological criteria of causality"[12].

A final key point is that more than 70% of the causes of chronic pelvic pain may be nongynecological, further contributing to diagnostic challenges. Musculoskeletal causes of pain are often overlooked in the evaluation and workup of chronic pelvic pain, and data regarding the true prevalence are limited. Based on a retrospective, cross-sectional study conducted using a population in a single chronic pelvic pain specialty clinic, Tu et al. estimated that the prevalence of pelvic floor musculoskeletal disorders in their patients was 14%–22% [13]. Based on our practice experience, which is approaching two decades of work, this is a gross underestimation. Up to 74% of patients with chronic pelvic pain will have an identifiable abdominal wall trigger point with proper clinical evaluation, and 71% have focal areas of pain along the pelvic floor muscles (ie. levator ani, obturator interni) and piriformis muscles on vaginal exam [14]. The most common musculoskeletal contributor to chronic pelvic pain is spasm of the pelvic floor muscles. This spasm may be primary or secondary. Causes of primary spasm are unknown but it may be due to genetic abnormalities or inherent diseases of the muscles that make them more prone to spasm. Secondary spastic pelvic floor may result from irritation of pelvic viscera, physical pelvic trauma, or psychological insult. Irritation of the pelvic viscera may be associated with endometriosis or pelvic inflammatory disease (PID). Accidents, athletic activity, or simply overworking pelvic and lower extremity muscles can lead to pelvic trauma. Pelvic surgery and childbirth with seemingly uncomplicated clinical course may provoke pelvic floor muscle spasms. Psychological insult may include psychological trauma and sexual violence. Musculoskeletal causes of pain will be discussed in detail in Chapter 20.

Another common cause of chronic pelvic pain is painful bladder syndrome. It will be discussed in detail in Chapter 9. Painful bladder syndrome is also often referred to as interstitial cystitis or bladder pain syndrome. This syndrome often coexists with other pelvic pain disorders. Painful bladder syndrome is not simply a disease of the bladder; it is a condition mediated by the intricate connection between the viscera, muscles, and central nervous system. Table 1.2 lists a number of other gynecological and nongynecological conditions that may manifest as chronic pelvic pain.

Table 1.2 Causes of chronic pelvic pain

Gynecological
Endometriosis
Adenomyosis
Primary dysmenorrhea
Pelvic congestion
Pelvic masses
Ovarian entrapment/remnant
Pelvic infections/pelvic inflammatory disease
Surgical
Adhesions
Urological
Interstitial cystitis/bladder pain syndrome
Urethritis
Urolithiasis
Gastroenterological
Irritable bowel syndrome

Table 1.2 (cont.)

Diverticulitis
Ileitis
Chronic appendicitis
Neurological
Nerve entrapment
Complex regional pain syndrome
Musculoskeletal
Spastic pelvic floor syndrome
Sacroiliac joint instability
Psychosomatic
Physical and/or sexual abuse
Depression
Anxiety
Personality disorder

We hope that this text will serve as a primary resource for addressing the challenges that clinicians face in caring for chronic pelvic pain patients. The following chapters will assist in defining the theories and components of chronic pelvic pain development. They will also provide diagnosis and management algorithms that can be used to optimize the care for these patients.

Five Things You Need to Know

- Chronic pelvic pain is defined as pain located in the pelvis, persisting for 6 months or longer, with or without association with menstrual cycles and severe enough to cause functional disability.
- In the industrialized world anywhere from 20% to 50% of people suffer from pain for more than 6 months during some point in their lifetime.
- Up to 70% of patients with chronic pelvic pain have a nongynecological cause of their pain.
- More than 60% of patients with chronic pelvic pain treated in general obstetrics/gynecology practice do not have a proper diagnosis.
- Most patients with chronic pelvic pain have multiple reasons for pain: endometriosis, interstitial cystitis, and irritable bowel syndrome coexist in many of these patients.

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Chapter 2

Neurobiological Basis of Pelvic Pain

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Editor's Introduction

Nerve pain is more often than not a cause of pelvic pain. This is particularly true in patients in whom pain started after pelvic trauma, surgery, or vaginal delivery. Unfortunately, most of gynecologists who are often physicians of primary contact for pelvic pain patients are not trained in recognizing and treating patients with nerve injury pain. Patients with nerve injury pain can almost always pinpoint the moment when the pain started. It is often unilateral and neuropathic in nature. Patients have a burning, tingling sensation often associated with increased sensitivity to stimuli analogous to skin pain after sunburn. Pain is often exacerbated by body movements and certain body positions. It is very important for the first provider who sees patients with pelvic pain that pain may be related to nerve injury because expeditious treatment increases the chances of recovery. It is also important to instruct patients to avoid activity that started the pain in the first place and minimize activity that exacerbates the pain. Trial of muscle relaxants, gabapentin, or pregabalin may be appropriate first treatment; however, prompt referral to physical therapy, neurology, or a specialized pelvic pain center is often necessary.

Introduction

Chronic pain is defined by the International Academy for the Study of Pain as "pain without apparent biological value that has persisted beyond the normal tissue healing time (usually taken to be 3 months)" [1]. It has been estimated that more than 30% of Americans suffer from chronic pain. According to the 2011 Institute of Medicine Report "Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research," pain is a significant problem costing US society at least $560 to $635 billion annually [2]. Although repeat estimates have not been published, the rates of chronic pain and accompanying opioid abuse have only been increasing. The understanding of the pathophysiology of pain is constantly evolving and this chapter attempts to summarize our current knowledge.

Pertinent Anatomy

Abdominal and pelvic pain can originate from the gynecological, urological, gastrointestinal, neurological, or musculoskeletal systems. Often pain may stem from multiple systems simultaneously. To understand the complex interplay between these systems and structures, one must understand the neuroanatomy involved. Abdominal and pelvic pain can stem from the somatic system (T12–S5) or the visceral system (T10–S5). Somatic pain arises from skin, muscles, joints, and the pleural and peritoneal lining. Visceral pain arises from the hollow organs of the abdominopelvic cavity including the bladder, bowel, uterus, and fallopian tubes. The complexity of pelvic pain is in part related to the interactions between these two systems. Of importance, the visceral nerves converge on the same somatic levels in the thoracic, lumbar, and sacral spinal cord. This is termed viscerosomatic convergence and can result in visceral pain being perceived in somatic regions. With time, muscles innervated by the stimulated somatic nerves can develop trigger points leading to worsening somatic pain. Viscerovisceral convergence can also occur, leading to referred symptoms in other organs. This neural convergence can also be useful therapeutically to treat pain.

Somatic Pain

Peripheral neuropathic pain typically has a very specific localization along nerve distributions. Nerve injury can occur through a variety of mechanisms

such as trauma, stretch, compression, fibrosis, or entrapment. Understanding neuroanatomical relationships, especially within the pelvis, is vital to both diagnosis and treatment.

The abdominal wall is innervated by the thoracoabdominal intercostal nerves (T6–T12) along with the iliohypogastric and ilioinguinal nerves. The intercostal nerves travel between the transversus abdominis and internal oblique muscles within the transversus abdominis plane (TAP). At the midaxillary line, perforating branches diverge to innervate the lateral abdominal wall. The segmental nerves of T6–T9 perforate the abdominal wall along the path of the anterior costal margin. The remaining intercostal nerves perforate the rectus abdominis sheath, providing sensation to the anterior abdominal wall. Near the anterior superior iliac spine (ASIS) the ilioinguinal and iliohypogastric nerves, which previously ran within the TAP, transition to travel between the internal and external oblique muscles.

The iliohypogastric nerve arises from the T12–L1 spinal segments. It travels through the psoas and transversus abdominis muscle, coursing medially below the internal oblique. It splits into two branches, with the anterior branch piercing the external oblique muscle at the level of the ASIS to provide cutaneous sensation to the mons pubis and the lateral branch to the posterolateral gluteal region. This nerve converges on the dorsal horn structures shared by the distal fallopian tube and ovary.

The ilioinguinal nerve arises from L1–L2 spinal segments. It follows a course similar to that of the iliohypogastric nerve but enters the inguinal canal 2 cm medial to the ASIS. It exits the superficial inguinal ring to provide sensation to the groin, labia majora, and the medial aspect of the thigh. It converges with the neurons of the proximal fallopian tube and uterine fundus.

The genitofemoral nerve also arises from the L1–L2 spinal segments and converges with neurons from the proximal fallopian tube and uterine fundus. It courses through the psoas muscle, exiting along its medial border at the L4 vertebral level, where it divides into a genital and femoral branch. The genital branch supplies the mons pubis and labia majora while the femoral branch supplies the skin of the femoral triangle. It can commonly be injured as a result of postappendectomy fibrosis or hernia repair.

The obturator nerve arises from L2–L4 spinal segments and travels along the pelvic sidewall, exiting the pelvis through a tunnel in the pubic ramus, and then divides into two branches. The anterior branch sends motor fibers to the adductor longus, adductor brevis, and gracilis and sensory fibers to the distal medial two thirds of the thigh. The posterior branch sends motor fibers to the adductor magnus and sensory fibers to the knee joint.

The lateral femoral cutaneous nerve arises from L2–L3. It courses over the iliacus muscle, passing under the inguinal ligament to provide sensory fibers to the upper outer thigh. Although it does not innervate any structures in the pelvis, it converges with neurons from the uterus in the dorsal horn.

The pudendal nerve arises from S2–S4. It carries motor, sensory, and autonomic fibers. The sensory component of the nerve innervates the clitoris, labia, distal one third of the vagina, perineum, and rectum. The motor component innervates the external urethral sphincter, perineal muscles, and external anal sphincter. After exiting the sacrum, it travels inferiorly and laterally on the anterior surface of the piriformis muscle. Once it enters the gluteal region it joins the pudendal artery and vein, which accompany the nerve through its course. It briefly exits the pelvis through the greater sciatic foramen and reenters through the lesser sciatic foramen, where it passes between the sacrospinous and sacrotuberous ligaments approximately 1 cm medial to the ischial spine. In this location the nerve is the most dorsal structure. It then travels through the aponeurosis of the obturator internus muscle, an area referred to as Alcock's canal. On exiting the canal, it divides into the inferior rectal nerve, the perineal nerve, and the dorsal clitoral (penile) nerve. The pudendal nerve converges in the dorsal horn on neurons from the cervix, uterosacral ligaments, and vulvovaginal region. Reference Chapter 15 for further detailed information about the pudendal nerve and its involvement in chronic pelvic pain.

The nerve to the levator ani is separate from the pudendal nerve. This nerve arises from S3–S5 and travels along the superior surface of the coccygeal muscle and innervates the coccygeus, iliococcygeus, pubococcygeus, and puborectalis [3]. The nerves to the levator ani and the pudendal nerve run approximately 5–6 mm from one another at the level of the ischial spine; therefore, a pudendal nerve block often results in a block of both.