Chapter

1 Chronic pelvic pain: spectrum of the disorder

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Historical perspective

The following quote from M. Renaer summarizes succinctly the status at the end of the twentieth century with regard to chronic pelvic pain in women [1].

> This shows that women tend to ascribe lower abdominal and low back pain to gynecological causes although it may just as well have an orthopedic, a gastrointestinal, or a parietal origin. It also draws attention to the fact, already pointed out by Martius in 1939, that chronic pain complaints frequently have a combined origin.

Also of interest in this excellent treatise on pelvic pain is the emphasis on finding a "diagnosis" for the pelvic pain, yet paradoxically admitting that in the majority of women there is no obvious cause. Hence Marcel Renaer coined the term "chronic pelvic pain without obvious pathology." The previous two centuries had been marked by multiple discoveries in anatomy and physiology, the advent of synthetic drugs, and the embryonic understanding of genetics and epigenetics. However, it should be said that "Western" medicine grew to become a rigid Cartesian discipline: every condition had to be precisely described and named. Pathognomonic signs are adored and every medical student is drilled to recognize them without fail. In other words, medical books have been turned into bibles. Every effect has to have a cause, preferably a single one, fitting neatly into a box, which, in turn, fits into the "algorithm" of that particular condition. It so happens however that *the book is often wrong and the patient always right* (I do not know who said this first, but I am happy to claim it!).

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This takes us to the key change in management of chronic pelvic pain in women: *Chronic pelvic pain is a diagnosis in its own right*. The twenty-first century sees emphasis move away from diagnosis toward management. In parallel, accepting chronic pelvic pain as a stand-alone diagnosis, also allows us to avoid the trap of searching for a singular cure with its inherent and often inexorable disappointment. We can now focus on providing the pain sufferer with the best options for management of her condition. This approach could be termed "*mechanism-specific therapy*," meaning that the various and often multiple aspects involved in the generation of pain are identified and addressed if at all possible in a concerted effort. This approach requires the availability of a team of dedicated professionals. Typically such a team comprises a physician with knowledge of the semiology of pain and the pharmacology of the appropriate medications, a physiotherapist experienced in the "hands-on" identification of musculoskeletal abnormalities often seen in pain syndromes and a psychologist trained in techniques such as self-hypnosis.

Still, a lot of ground is to be covered before progress will be noticeable on a large scale. Hopefully this manual will contribute substantially to this effort.

Pathophysiology

First and foremost, *"pain" per se is a normal function of our body*. I agree with Professor Cousins, cofounder of the Australian Faculty of Pain Medicine, that pain is a vital function on a par with breathing, pulse, blood pressure, and so on. Life without pain, on a physiological level, is not possible. Pain started its biological history as a defense mechanism and this is still a fairly important aspect of its function. However, pain has evolved into a complex neurophysiological process between the initiating impulse and the conscious interpretation that ensues. There is the purely electrochemical chain of events but also a rational as well as an emotional component. These latter components have their roots in the social, religious, educational, and cultural history of the individual.

Professor Roger Robert (Chapter 2) describes in great detail, and with passion, the detail of neuroanatomy. What makes pelvic pain unique is that the pelvis brings together elements of locomotion with the visceral as well as the sexual organs. Each organ system – musculoskeletal, gastrointestinal, neurovascular, urogenital – can contribute to pelvic pain, and several systems can do so simultaneously.

The crux of the matter in pain management is defining when pain is "normal" and when it is "abnormal." Everyone has experienced an episode when one of the visceral functions was perceived as painful. Yet where do we draw the line? Every definition written in various textbooks is purely arbitrary (and usually contains a number "three" somewhere). From a practical point of view, *pain loses its normalcy when the perception of pain no longer adds to a particular function and, as a result, the individual no longer can complete that particular function or perform a related task*. The latter definition provides some added flexibility in pain management as the individual has to a certain extent at least, a choice in setting her "tasks."

This definition of pain also highlights the fact that there is not a lot of difference between, for example, a migraine and dysmenorrhea ("a headache in the pelvis"). Hence there is a need for any practitioner involved in pain management to understand pain beyond what might be called "the presenting organ system." It should also come as no surprise that the management of apparently separate conditions, such as chronic pelvic pain, irritable bowel syndrome, and migraine, often involves the same management strategies, at least in part.

The electrochemical aspect of pain (Figure 1.1) is most obvious when there is one major event as the stimulus, such as an injury or a surgical intervention. Episiotomy or cesarean section scars are ready examples of "major" stimulations causing pelvic pain.

The "rational" component of pain is somewhat difficult to explain. One example is the pain perceived with a needlestick. The individual "knows" that a needlestick hurts and thus anticipates experiencing pain. It has been shown that watching the needle piercing the skin reduces the intensity of pain, as opposed to turning one's head away. The rational component in pain physiology tends to reduce the intensity of the perceived pain. It can be said that a number of events in the female pelvis are anticipated to cause discomfort, such

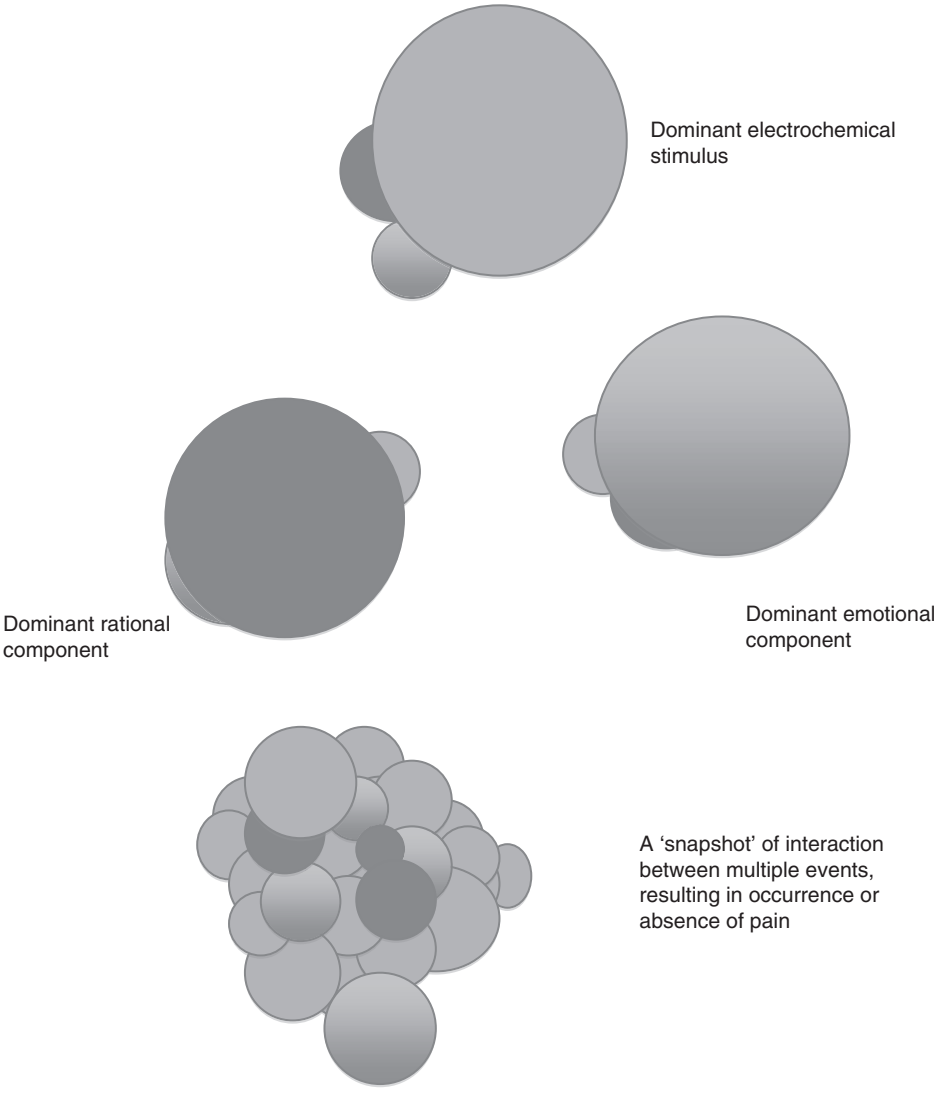

Figure 1.1 The components of the pain experience.

as menstruation. Knowing when menstruation will occur, such as with the help of oral contraceptive medication, can reduce the perceived intensity of pelvic pain.

The emotional component of pain physiology is omnipresent of course and in itself excessively complex, as it is influenced by a host of elements varying from the cultural to the religious background of the individual. Additionally, in women, the influence of the mother–daughter relationship cannot be stressed enough. The experience of pelvic pain by the mother will influence through learned behavior how the daughter will come to face physical events such as ovulation and menstruation, but also events such as intercourse, insertion of tampons, and so on. An obvious example of how emotion can influence pain is dysmenorrhea during the menstrual cycles following a miscarriage. It can be safely assumed that the electrochemical aspects of pain associated with menses are reasonably constant in an individual, yet it is no surprise that a woman will experience more pain with menses in the months following an event such as a miscarriage.

At any given moment, there is a host of electrochemical events occurring in the body. Each of these events is subject to various rational and emotional influences. Few of these events will be perceived as uncomfortable and even fewer will be perceived as painful.

The electrochemical chain of reactions that is involved in the genesis of pain perception is far more complex than a simple straightforward line of communication between the periphery and the cerebral cortex. Not only are there various sensors (mechanical, temperature, etc.), there are also various types of "wire" connected to these sensors, with varying dominance, speed, and connections. Every single synaptic space is subject to the humeral environment as well as the down- and upregulatory stimuli from neighboring cells.

The stimulus

Every stimulus reaching our body, or generated within our body, is potentially a trigger for a painful sensation: light, sound, muscle contraction, pressure on skin, and so on. For a stimulus to become a trigger, a sensor needs to be stimulated either directly, for example by the photon or by pressure, or through the mediation of a chemical substance. Lactic acid produced during intense muscle exercise can stimulate neural receptors, for example.

Because pain is an important regulatory function of the body, there are specific receptors that will generate a signal which is unmistakably seen as "painful" by the body. These receptors are called nociceptors. Some of these nociceptors are highly developed, such as in joints, others are barely more than the end of a nerve fiber, exposed to the humeral environment and triggered by chemicals released during inflammatory processes, for example cytokines and prostaglandins.

The signal

The human body is fitted with a dual sensory system: somatic sensory and sympathetic sensory. Nociceptors within both systems are primarily linked to the central nervous system through C-fibers, which are unmyelinated and, therefore, slow. In parallel, additional information from the same site, is gained through other fibers and carried along. That information involves factors such as temperature, mechanical pressure, and tension. These stimuli involve the thicker, thus faster, fibers of the A class.

The posterior horn of the spine is the first relay post in the system, except for the fibers of the sympathetic system, which involve the prevertebral ganglia and will anastomose

with the spine at the level of the thoracolumbar junction. This anatomical particularity may in part explain the great variability in response to treatment modalities such as sacral neuromodulation.

Additionally, there is widespread variability between individuals in the distribution of the visceral sympathetic and parasympathetic innervation, making it completely unpredictable which "course" a particular signal emerging from the pelvic viscera will take.

At the level of the posterior horn, the signal is subject to external influences, which will either alter or augment it, or even completely obliterate it.

The signal from the nociceptors at the level of the posterior horn will immediately spread to neighboring dermatomes, before moving up to the lower centers of the brain (Chapter 2).

In parallel with the signal from the nociceptors, information on temperature, pressure, position and so on is carried simultaneously to the corresponding lower brain centers. The brain, to interpret the train of signals arriving, will use this additional information. This, in turn, will influence the reaction the brain will initiate.

Knowledge about a number of phenomena specific to neurotransmission has emerged in recent times, including central sensitization and neuroplasticity.

Central sensitization is defined as activity-driven augmentation of sensory signaling in the central nervous system, which persists after the stimulus has been withdrawn. Of note is that the augmentation occurs within the fibers affected by a particular stimulation, which clearly differentiates central sensitization from other phenomena such as neuroplasticity.

The augmentation is expressed by a reduction in threshold at the site of stimulation. In other words, repeat stimulation at the same site needs less intensity to generate a response. In addition, the area immediately adjacent to the initial site of stimulation becomes more responsive to stimulation and, with continued repeat stimulation, there is expansion of this receptive field. These changes, which in general render the initial stimulated area more "sensitive," persist for some time after the stimulus is withdrawn. There is no general rule as to how long the hypersensitivity persists in a "normal" individual. It is well known that a scar, for example, can remain sensitive for quite some time after it has apparently completely healed. When is this hypersensitivity considered to be abnormal? There is some indication that if the hypersensitivity persists beyond two years, resolution is less likely to occur.

Abnormal regulation of this physiological phenomenon, which we call central sensitization, plays an important role in chronic pain, particularly in persistent pain after surgical intervention or other type of major physical injury, such as a motor vehicle accident.

The concept of neuroplasticity is a significant departure from previous dogma that the nervous system, once developed in early childhood, would remain unchanged throughout life except for deterioration with advancing age. Neuroplasticity is defined as the ability of the nervous system to respond to intrinsic or extrinsic stimuli by reorganizing its structure, function, and connections. Neuroplasticity is said to be adaptive if the reorganization results in a beneficial outcome for the body. It is said to be maladaptive if the reorganization results in harming the body. Chronic pain is thought to be, in part, the result of a maladaptive neuroplastic change in our nervous system.

Neuroplasticity is, of course, invaluable for the recovery from conditions such as stroke and spinal trauma.

The interpretation

Once all signals originating from the zone of interest have reached the cerebral cortex, the process of interpretation begins. Only recently have researchers been able to get a glimpse at cerebral activity by interpretation of the information received through measurements using magnetic resonance imaging (MRI) and positron emission tomography.

It is only when the various signals have reached the cortex, that pain is experienced.

The reaction

Reaction to a "noxious" stimulus (i.e. a signal originating from a nociceptor) occurs even before the signal reaches the central nervous system. These initial reactions are what can be called "reflexes." They are primitive and innate, the equivalent of a scream in response to being startled, but on a tissular and organ level. Such reactions can be channeled through the same nerve fibers in retrograde fashion or through a short neural circle, involving few neurons. The result of this primitive reflex is vasodilatation, sweating, and contraction of nearby muscles. Retrograde activity in nerve fibers is called neurogenic inflammation, as that activity mostly results in vasodilatation and the release of cytokines and other stimulators of inflammation from mast cells.

From an individual's perspective, dealing with this multitude of events depends on a variety of factors, which as a whole could be labeled "self-treatment capability." In my opinion, the most important of these factors is knowledge: knowledge about the events that could cause discomfort, knowledge about the effectiveness of various remedies, and so on. Every day, in clinical practice, clinicians are confronted with the fact that increasing the patient's knowledge about her condition will invariably increase her ability to cope. It should also be said that in many cases rational statements are incorrect. This in itself often has a devastating effect on the patient's ability to manage. In some cases, it is exceedingly difficult to set the record straight, especially when the individual is surrounded by a tight cocoon of family and "friends" who subscribe to the same belief system.

Where self-management often goes wrong is in the emotional department. The tendency to catastrophize, for example, and exaggerate the potential negative outcomes is a real issue. Catastrophizing is a normal phase in self-management. Considering the worse-case scenario is a necessary step in the process of managing pain, as for many other situations in daily life. However, most individuals will quickly shake off these type of emotions.

Patients with chronic pelvic or perineal pain will, in most cases, present to a health-care provider when they have exhausted their self-treatment capabilities. Some patients will wait years, even decades, before presenting themselves for help. In other cases, patients cry for help but are channeled in the wrong direction and do not get appropriate support.

Prevalence

Measuring prevalence of pelvic pain in the general population is difficult to say the least. The greatest issue is in the definition of pelvic pain. In addition, there is a traditional impulse to "qualify" the pain symptom and to use terms such as dysmenorrhea, dyspareunia, dyschezia, and "non-menstrual" pelvic pain. Each of these symptoms/syndromes can be considered a subset of pelvic pain. This leads to the question of whether all

Table 1.1 Incidence of pelvic pain in a cohort of 1200 women

Variable	Endometriosis present (n = 201)	Adhesions present (n = 278)	No pathology identified (n = 721)
Dysmenorrhea	137 (68%)	140 (50%)	358 (50%)
Dyspareunia	75 (37%)	93 (33%)	168 (23%)
Pain after intercourse	29 (14%)	42 (15%)	72 (10%)
Pelvic pain (non-menstrual)	118 (59%)	165 (59%)	346 (48%)

Source: from Mahmood *et al.*, 1991 [3].

pain symptoms should be "pooled" in a large "pelvic pain" basket, or should the "organ-specific" terms be kept. Confusing the matter further is the tendency to identify endometriosis as the main, if not sole, "cause" of pelvic pain.

Then there is the issue of normalcy of pain. Every woman will at some point in her lifetime experience pelvic pain. Therefore, what is the point of measuring prevalence? There are a few studies from the late twentieth century showing that pelvic pain affected a large proportion of women. To interpret these numbers it is essential that the definition of pain be taken into account. Pooling several articles together will result in aberrant numbers as often the respective definitions are diverging.

A review article in 1998 noted that there were no community-based studies evaluating the incidence of pelvic pain in women in the UK [2]. A single meaningful paper was identified, published by Mahmood *et al.* [3], reporting on a survey involving 1200 patients admitted to an Aberdeen (Scotland) hospital. Half of this cohort of patients underwent sterilization, 312 were investigated for infertility, 156 for pain, and 134 underwent hysterectomy for excessive menstrual bleeding. The findings on incidence of pain are shown in Table 1.1.

The incidence of pelvic pain in the subset of patients undergoing sterilization was 39%. This figure would, therefore, come closest to the incidence of pelvic pain in the general population. Zondervan *et al.* considered that number too high [2]. The conclusion of these authors was that pain as such was not a valid criterion to diagnose endometriosis. This could probably be turned around to state that endometriosis does not necessarily involve pelvic pain.

The dissociation between endometriosis and pelvic pain has been recently confirmed by a study performed on 57 subjects suffering chronic pelvic pain [4], showing that the pain score was inversely related to quality of life but that the presence or absence of endometriosis has no impact on that relationship.

The only study from the twentieth century which could truly be considered to be community based was published by Mathias *et al.* in 1996 [5]. This study was based on a telephone survey of 17 927 individuals performed in 1994 in the USA. Of this group, 5263 women were identified as subjects and 773 admitted having suffered pelvic pain for the past three months, leading the authors to estimate the incidence of pelvic pain in the community to be 14.7% among women of childbearing age. This is approximately three

times less than the incidence of pelvic pain reported by Mahmood *et al.* in a hospital community [3]. Of particular interest is the finding by Mathias *et al.* that 61% of women with pelvic pain did not have a diagnosis [5]. The authors also paid attention to the impact of pelvic pain on the quality of life of the individual and the impact on productivity. Among 548 women who were employed at the time of the survey, 82 (15%) reported having taken time off work and 247 (45%) admitted to being less efficient at work when in pain.

Measuring the impact of pelvic pain on the individual and on society through the individual's contribution, or lack thereof, is obviously of paramount importance. A recent publication has reported on the overall effect endometriosis has on patients [6]. The term "burden" in the title of the article is aptly used instead of cost, as this study is among the first to show that hidden costs, such as the inability to work properly when in pain, are far greater than the cost of treatment through medication and surgery. This study has also highlighted that the degree of impact on quality of life correlates most with increasing burden of the condition.

There are two aspects to pelvic pain that deserve closer scrutiny when it comes to prevalence, namely the incidence of sexual dysfunction and the coexistence of musculoskeletal disorders. Neither one of these specific aspects has had much attention in the scientific community until recently. Tu *et al.* [7] performed a retrospective review of 987 patients from a chronic pelvic pain clinic and found that 217 (22%) had levator ani tenderness and 138 (14%) had piriformis tenderness. There is no readily available comparator with the general population. However, these findings confirm that pelvic pain involves the musculoskeletal system as well as the visceral organs. This musculoskeletal involvement can be secondary through muscular reaction to visceral pain or can be linked to a greater incidence of central sensitization. Clinical experience shows that addressing the musculoskeletal component of pain seems to contribute to overall improvement.

The impact of pelvic pain on sexual function should not surprise anyone. The incidence of sexual difficulties in the general population is estimated to be between 30 and 40%. Ambler *et al.* found that up to 73% of individuals suffering any type of chronic pain (n = 237) experience sexual difficulties [8]. A study on a smaller population of 19 women with specific pelvic pain, not surprisingly, identified a similar proportion of sexual dysfunction [9].

Symptomatology

The patient's account of her problem remains the foremost important source of information for the physician. I often remind trainees that we need to "read" the patient who presents with complaints of pelvic pain: demeanor, gait, level of detail, posture, attitude, desire to progress, the presence and attitude of family members or friends, and so on. Many patients will give an "interpreted" account of their symptoms, such as labeling their pain ("ovarian" or "menstrual") or recount what another doctor told them. Efforts should be made to redirect toward a primitive account of events.

By definition, when dealing with chronic pain, symptoms have been present for some time and possible initiating events – if at all present – are often a faded memory. It is important to understand that symptoms are variable over time and that this variability is non-linear.

It must be emphasized that symptoms are important with regard to identifying the various organ systems involved in the process and to arrive at a meaningful mechanism-oriented approach in treatment. It has been known for some time that the coexistence of dysmenorrhea, dyspareunia, and dyschezia indicates the presence of endometriosis in nearly all women. Similar symptom clusters can point in the direction of clinical entities such as levator ani syndrome, painful bladder syndrome, and so on.

Investigation

A patient with pelvic pain visiting a urologist is likely to undergo a cystoscopy; one visiting a colorectal surgeon is likely to undergo a colonoscopy, and one visiting a gynecologist is likely to undergo a laparoscopy. Yet are any of these interventions necessary in every patient presenting with chronic pelvic pain? The short answer is "no." Routine investigations are a curse and a blessing at the same time. Every specialist looks at the patient with tinted glasses and that is unavoidable. However what should be avoidable is the use of an investigation as the one and only means of evaluation of pelvic pain. A negative laparoscopy does not mean that the patient has no pelvic pain or that the pain is "idiopathic." The "gunshot approach" to pelvic pain is still prevalent unfortunately: chasing the "cause" of pelvic pain and eliminating it, much like the hunter shooting down prey.

Routine investigation of the patient involves an encompassing physical examination and a minimum of laboratory investigations. The objective of routine laboratory investigations is to identify the occasional chronic autoimmune or other inflammatory condition. In practice, the "laboratory set" in our clinic consists of erythrocyte sedimentation rate, C-reactive protein, anti-nuclear antibodies, and creatine kinase.

The value of imaging, such as sonography, of the pelvic viscera has increased significantly in recent years. This is discussed in detail further in Chapter 3.

Management

The typical Western cause–effect model does poorly in management of pain. In particular it implies unrealistic expectations: remove the cause will equal removing the pain. It also dulls the clinician's acumen: looking for endometriosis because that is what I think causes pelvic pain (hence the specialist–specific intervention link) and, therefore, not seeing anything else.

Use of the ubiquitous and often unidirectional treatment algorithm is also not helpful in the management of pain. As clinicians, we have to allow ourselves to move "up and down" the tree and be willing to start over at any time.

A social healthcare system is a true blessing overall. However, a social healthcare system can also engender a "state–provider" or "mother-state"–patient dependency. In particular, systems such as the "workers' compensation" schemes often prevent the patient from continuing progress as long as the administrative process is ongoing or a dispute unresolved.

A core principle of treatment of pelvic pain is that the patient is responsible for her care, not the healthcare provider. The patient needs to be willing to improve and to understand how she will achieve that objective. The healthcare provider's role is to make the various treatment options available. And here lies the challenge: the challenge for the physician to identify the various organ systems involved in the electrochemical pathways,

to increase whatever rational thought processes are present, and to provide emotional support. Suffice to say that these challenges are more than a single person job: hence, a multidisciplinary approach to achieve a "multimodal" treatment regimen. This sentence summarizes well the current approach to pain management and for most chronic conditions. As a healthcare provider advances into her/his specialty, her/his knowledge increases and in parallel – most of the time – there is a reduction in the width of her/his area of interest. For optimal evaluation of a patient's status, it will, therefore, be necessary to involve several practitioners who will provide different, hopefully converging, opinions and treatment options. The treatment regimen is equally multifaceted. It is safe to say that the days of handing out prescriptions as the chief mode of treatment are over. Various treatment modalities, traditional or alternative, and some defended vigorously by their proponents, are being promoted as greatly effective in the treatment of chronic pelvic pain. However, I believe the patient will be better off if she can decide for herself which path to follow.

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