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Chapter

Pain Testing in Endometriosis for the Clinician

John Jarrell

Abstract

Clinical pain testing has been used to ascertain the pathophysiology of many clinical conditions, but its use in the management of endometriosis has been limited. Although the testing can require the use of complex testing in the laboratory, this chapter is directed to look at a test for allodynia that can be applied in the clinic. The test for cutaneous allodynia is validated, does not require sophisticated tools, and is readily accepted by woman. The presence of allodynia in certain gynecological presentations can indicate the woman's pain system has become sensitized. Uses of the test in clinical encounters with women suffering from endometriosis and possible uses in future are presented.

Keywords: pelvic pain, pain testing, pain sensitization, visceral pain, endometriosis

1. Introduction

The object of this chapter is to introduce and describe pain testing for gynecologists to use at the bedside. Although the subject's description of pain is still the best method of assessing pain, the use of objective pain measures permit independent quantification that is useful in explaining a more complete picture of a disease process, and it is also of help in documenting change in response to medical or surgical intervention. Formal pain testing has now provided new information on the pain mechanisms in chronic pancreatitis, dysmenorrhea, painful bladder syndrome, osteoporosis, and low back pain to name a few conditions [1–5]. Central sensitization has been identified as a component of persistent pelvic pain, with and without endometriosis [3–5]. This summary is intended to provide several examples where testing gives both the woman and the gynecologist a fuller appreciation of the clinical problem of pain.

Clinical pain testing has been used to ascertain the pathophysiology of many clinical conditions, but its use in the management of endometriosis has been limited. Although the testing can require the use of complex testing in the laboratory, this chapter is directed to look at a test for allodynia that can be applied in the clinic. The test for cutaneous allodynia is validated, does not require sophisticated tools, and is readily accepted by woman. The presence of allodynia in certain gynecological presentations can indicate the woman's pain system has become sensitized. Uses of the test in clinical encounters with women suffering from endometriosis and possible uses in future are presented.

2. Visceral pain physiology

The physiological basis for pain testing is viscero-somatic pain referral. One of the first such observations was made by Sir James Mackenzie (1853–1925). Although known primarily for his work on cardiac physiology, arrhythmias, and heart disease, he wrote a book in 1913 that provides insight into how we might understand the clinical signs of pelvic disease [6]. Mackenzie provided a diagram of a man with biliary colic who had pain radiating to his right upper quadrant (**Figure 1**). This painful area was also found to have an area of allodynia in the same area. Allodynia is defined as pain from a non-painful source. The allodynia can be static or dynamic depending on the mode of testing. Static allodynia is direct pressure on the skin, while dynamic allodynia uses movement across the affected area. Notably, Mackenzie found a small area within the region of allodynia that was particularly tender and corresponded to the anterior cutaneous nerve that passed through the abdominal wall fascia. Mackenzie correctly noted that not only the colicky pain was referred to the right upper quadrant but also there was also a tiny muscular component of this referral, centered on the tender ninth thoracic nerve as it perforates the abdominal wall fascia.

This simple diagram is the basis for the clinical testing of women's pelvic pain at the bedside. Most of the causes of pain in the pelvis associated with endometriosis are due to inflammatory processes. These are considered nociceptive influences on the afferent nervous system that pass to the spinal cord primarily in the T12 and L1 segments. The viscero-somatic referral then initiates efferent activity through the corresponding anterior cutaneous nerves to the lower abdomen. The result of the efferent activity is the pattern of allodynia and tender areas in a similar fashion to Mackenzie (**Figure 1**). There are many variations of the presentation, unilateral, bilateral, with both equal and unequal sizes of the allodynia [6].

Another contributor was Sir Henry Head (1861–1940) who, mapped out the referral patterns of the body of many illnesses that initially became the Head zones but later evolved to be the dermatomes. The accompanying figure demonstrates the ovarian zones (**Figure 2**) [7].

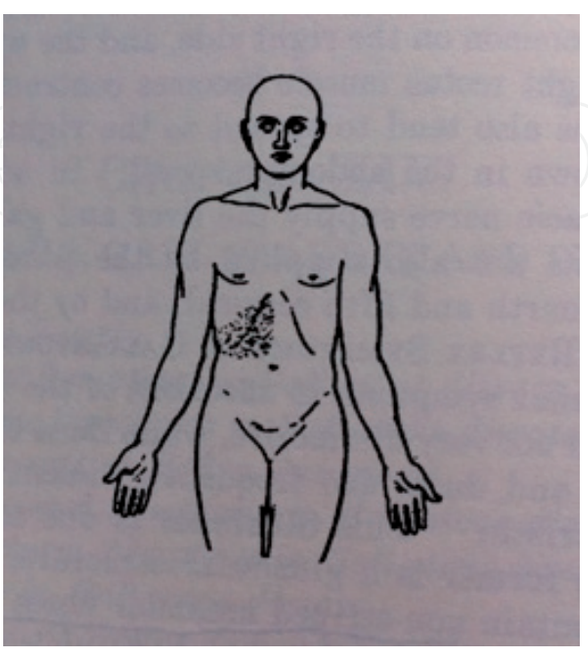

Figure 1.
Location of right upper quadrant allodynia associated with tenderness in the region of ninth anterior cutaneous nerve due to biliary colic.

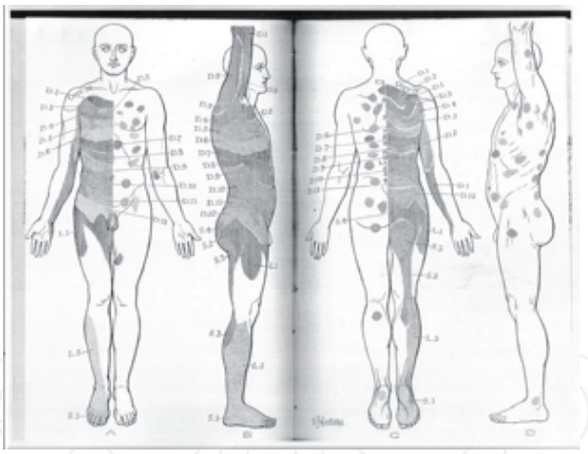

Figure 2.
Demonstration of the Head zones.

More recent studies of the visceral-somatic referral and guidelines for the management of associated persistent pain have been reported [8–12].

3. Detection of allodynia and expansion

To detect allodynia, a cotton-tipped applicator is slowly drawn down from the midclavicular line toward the pubic region along the imagined border of the rectus abdominus muscle. It is necessary to start the test outside the area of allodynia. Starting within will not detect the necessary changes. As the applicator is positioned, the woman is asked to note if there is any sudden change in sensation or the onset of a sharp pain. When this is announced, the level is marked off with a body marker. An example of two small areas of allodynia containing trigger points associated with the T12 anterior cutaneous nerves is shown in **Figure 3**.

An extreme example of severe chronic pelvic pain demonstrates how large the area of allodynia can become—this degree is unusual (**Figure 4**). The delineation of allodynia that is marked off with a pen can stimulate spinal activity such that there is an almost immediate shift in the borders of allodynia (**Figure 4**). These shifts in the levels of sensation correspond to "jumps" taking place in the spinal cord, segment by segment.

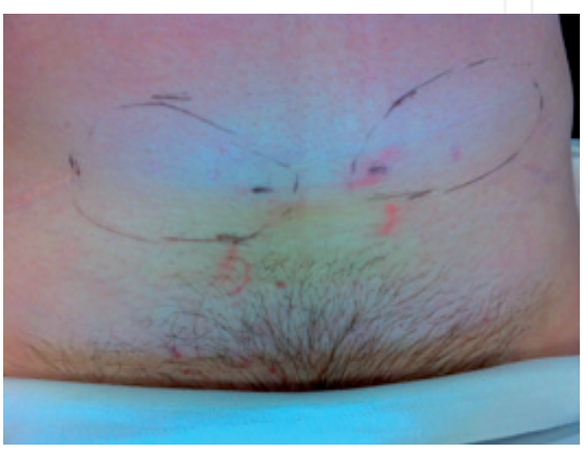

Figure 3.
Small areas of allodynia containing painful trigger points of T12 anterior cutaneous nerves.

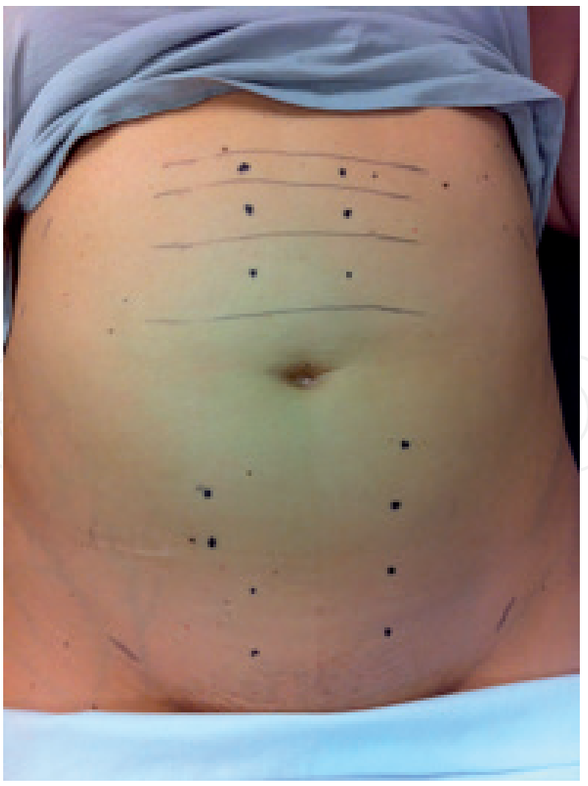

Figure 4.
An example of allodynia expansion upward by dermatome with each test for allodynia in a woman with severe pelvic pain.

4. Hyperalgesia and location of trigger points on the abdomen

Associated with the allodynia, one can determine the presence of hyperalgesia, which is an increased pain sensation from a painful source. The examining finger can detect this when gently applied to the area (**Figure 5**). The examination has to be gentle as a pressure of only 15–20 g can evoke severe pain from the small nodular trigger point (**Figure 5**). The location of the trigger point has been marked in **Figure 6**.

A more sophisticated way of determining the degree of hyperalgesia is with an algometer. This instrument will determine the pressure pain threshold. Measures of pressure pain thresholds are reduced in the areas affected by pain sensitization. In many cases of severe chronic pelvic pain, it is possible to put only the mildest

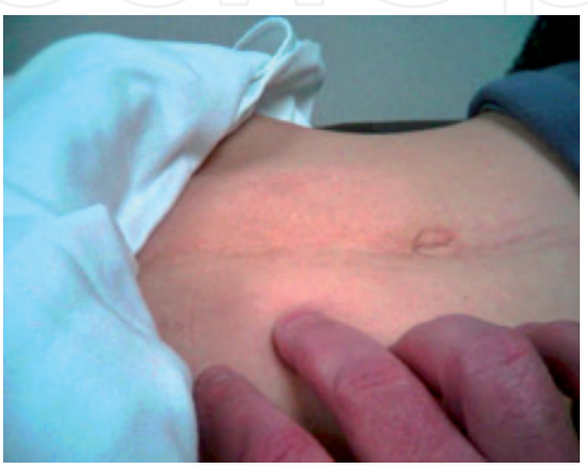

Figure 5.
Localizing a viscerally related trigger point with gentle pressure from the pulp of the examining finger.

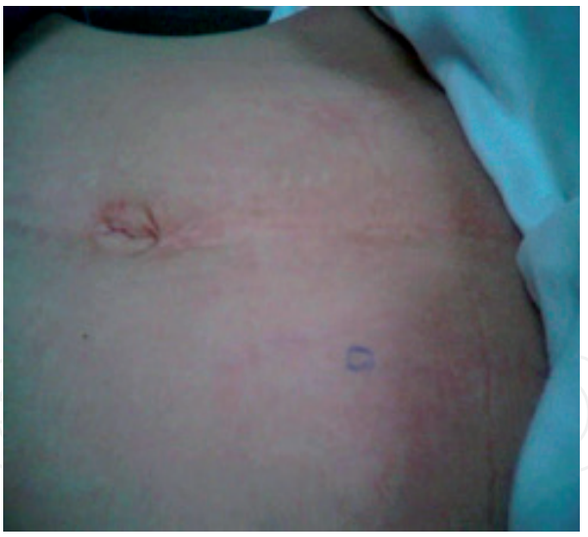

Figure 6.
The location of the trigger point corresponds to the right anterior cutaneous nerve from T12 spinal nerve.

pressure in the region of the anterior cutaneous nerve to have the induced pain threshold recorded.

5. Validity of allodynia testing in pelvic pain

In order to have faith in allodynia, it is important to ensure the test has reliability. In a cohort of 81 women with chronic pelvic pain, the presence of allodynia was significantly associated with those who were suffering from visceral disease [13].

The positive predictive values for pelvic visceral disease were as follows:

Abdominal cutaneous allodynia	93%
Perineal cutaneous allodynia	91%
Abdominal myofascial trigger points	93%
Perineal myofascial trigger points	81%
Reduced pain thresholds	79%

The likelihood ratio (+) and 95% C.I. for the detection of visceral sources of pain were as follows:

Abdominal cutaneous allodynia	4.19 (1.46, 12.0)
Perineal cutaneous allodynia	2.91 (1.19, 7.11)
Abdominal myofascial trigger points	4.19 (1.46, 12.0)
Pelvic myofascial trigger points	1.35 (0.86, 2.13)
Reduced pain thresholds	1.14 (0.85, 1.52), [13]

In another study of validity, a total of 22 females with chronic pelvic pain were compared to 23 pain-free controls and 12 cyclic pain patients. Participants were evaluated by two clinicians. Investigators mapped the abdomen with the cotton-tipped applicator, outlined the areas of allodynia with a body pen, photographed the abdomen, and wiped off the marking before the second investigator repeated the test. The interrater reliability resulted in 98% agreement for the three study

groups. The cotton-tipped applicator test showed 73% sensitivity and 100% specificity for differentiating patients with chronic pelvic pain from pain-free patients [14]. At present, there do not appear to be pain-testing techniques that specifically identify endometriosis independent from other visceral diseases. It is arguable, however, that the experience of pain may have greater relevance depending on the clinical situation as described in relation to the negative laparoscopy.

6. The negative laparoscopy

A comparison of the results of pain testing was done in women investigated for pelvic pain between 69 with confirmed endometriosis compared to 35 who had a negative laparoscopy [15]. When women with a negative laparoscopy were compared to those with confirmed endometriosis, there were no differences in age, gravidity, parity, menarche, and frequency of dyspareunia or duration of severe dysmenorrhea. There were no differences in the frequency of abdominal wall allodynia or of pressure pain thresholds. These tests give validation to the women who otherwise have no explanation and it also raises the possibility that dysmenorrhea may be the source of the pelvic pain. These results are consistent with testing of women with persistent pelvic pain with and without endometriosis [3].

7. Prediction of postoperative pain

There has been a great deal of interest in the prediction of postoperative pain, but most of the studies have not included laparoscopic pelvic surgery. The situation is very complex with a wide number of variables having a role such as preoperative pain, depression, previous surgery, gender, and opiate use and abuse. A study of the assessment of predicting postoperative pain considered these elements but also included testing for the presence of allodynia and hyperalgesia before and after 6 months following laparoscopic surgery for non-acute pain. Hyperalgesia was identified with the use of a Somedic Algometer (Somedic SenseLab AB, Norra Mellby 1129 SE-280 10 Sösdala, Sweden). In women who underwent tubal ligation, pain levels were low before and after the procedure. In 61 women who underwent surgery for non-acute pain, pain levels at 6 months and all psychologic test scores were reduced significantly compared with baseline ($P < .001$ and $P = .001$, respectively). Among those women with positive results on the quantitative pain tests of sensitization at baseline, average postoperative pain was also significantly reduced ($P < .001$). Univariate analysis demonstrated only tests of sensitization were correlated with the reduction in average pain level ($P = .01$). Regression analysis suggested that baseline pain, catastrophizing, and the presence of cutaneous allodynia significantly predicted pain levels after 6 months. We had anticipated sensitization would have predicted more pain, but we have interpreted the results to indicate the reduction in pain may be due to the successful removal of a nociceptive source in the pelvis. At present, pain testing does not indicate whether surgery should or should not be done; that remains a clinical decision.

8. Detection of sensitization in relation to psychological status

Also, a secondary analysis reviewed the changes in pain and psychological measures of stress (Pain Disability Index, Pain Catastrophizing Scale, CES-D (Center

for Epidemiologic Studies Depression Scale)), depression scale, and the McGill Pain Scale (short form) as the presence of pain sensitization. Preoperatively, the psychological test scores correlated significantly with the pain scores. Post-laparoscopic surgery pain and psychosocial test scores were reduced and remained significantly correlated. The presence of preoperative pain sensitization was associated with trends to greater baseline and 6-month postoperative changes in average pain and measures of psychological distress [16].

9. Relationship to pelvic floor

In a study of 112 women with chronic pelvic pain assessed for pain in the abdominal wall, perineum, levator ani, and obturator internus, the number of myofascial trigger points was predicted by the number of previous laparoscopies adjusted for age. Both the presence of visceral disease and endometriosis were significantly associated with higher numbers of myofascial dysfunction than the absence of these conditions [17]. These findings suggested that prior surgery may aggravate pain sensitization. The available studies using pain testing do not indicate they can discriminate endometriosis from other visceral diseases [3, 13, 18]. It should also be noted here the test for allodynia on the perineum was validated as noted above [13].

10. Possible future benefits of pain testing

It has long been known that the extent of disease does not have a correlation with the severity of pain. Many women with minimal disease are severely incapacitated with their pain. Alternatively, but less common, are women with severe stage 4 disease without pelvic pain. Many gynecologists have seen women who have had repeated procedures for minimal disease despite having no change in their pain [18]. The techniques of pain testing can provide an assessment indicating peripheral and central sensitization have altered pain physiology and possibly eliminate the need for repetitive laparoscopic surgery of limited, if any, benefit.

There have been several blinded controlled trials of the excision versus sham excision of endometriosis for the management of pain [19–22]. The results have differed; in several, there was a reduction in pain; in another that was extended out 14 years post-randomization, there was no difference between the sham excision and excision. Perhaps it may not be the surgeons' expertise, the degree of disease, or prior pelvic surgery, but the differences may possibly be explained by the womens' pain sensitization. Pain testing might have a unifying feature to allow comparisons of cohorts of subjects in clinical trials.

Many surgeons have had the unsettling experience of having one of their women undergo what is considered a straightforward operation of hysterectomy, tubal ligation, or laparoscopic excision of endometriosis in which the woman returns with severe incapacitating pelvic pain. The reason is not in the operative procedure that was uncomplicated, but it is difficult at times to persuade that to the woman involved. Possibly, there was a preexisting state that made this possible. In reviewing women presenting with postoperative onset of chronic pelvic pain, there is commonly a history of pain preceding the operation. This can take the form of severe dysmenorrhea, repetitive bouts of cystitis, or prior kidney stones. Pain causes chronic pain and while it is possible to generate chronic pelvic pain from an isolated procedure, it is much more common to see there was a previous pattern of repetitive pain. The shift to a chronic pain state might be identified as a risk with pain testing for sensitization.

Also, there is a troubling experience of undertaking an operative laparoscopy anticipating there is going to be endometriosis present and instead finding no disease whatsoever. Again, this leads to difficult explanations and often the patient will seek yet another laparoscopy.

These examples are fundamentally issues of pain and pain management. In order to have a strategy to inform these situations, pain testing might be of assistance.

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