INTRODUCTION:

In the United States, nearly one-third of the population experiences severe chronic pain at some time in their lives. It is currently the most common cause of long-term disability affecting up to 50 million people. 12% of hysterectomies performed are due to chronic pelvic pain, yet 23% of these patients will still have pelvic pain postoperatively [1]. In addition, 40% of all laparoscopies are done for chronic pelvic pain, but when minimal endometriosis is found, only one-third will have resolution of symptoms after that surgery [2].

Common pelvic pain syndromes include functional bowel disease, myofascial pain syndromes, vulvodynia and/or dyspareunia syndromes, and interstitial cystitis. It is very common that these puzzling problems coexist in many of our patients with chronic pelvic pain syndromes. For example, 30% of patients with interstitial cystitis also have severe vulvodynia, 40% will have functional bowel disease and 85-90% will have pelvic floor tension myalgia. 30% of patients with interstitial cystitis will go on to be diagnosed to have fibromyalgia later in life. The pathophysiology of complex pelvic pain syndromes and why these so frequently coexist in our patients is easily explained once we understand the neuropathophysiology involved. The Key to this neuropathic response is the up regulation of the sacral cord. Important components of that up regulation include the activation of silent C-fibers arising from the viscera of the pelvis, and a resultant increase in noxious input to the dorsal horn causing biochemical changes that become permanent [3]. These changes result in the findings of allodynia with obvious sensory processing abnormalities, expansion of receptive fields, and neuropathic output states including neurogenic inflammation, hypertonic pelvic floor muscle dysfunction and the development of trigger points not only within the pelvic floor but also within the abdominal wall. Once we understand the importance of this neuropathology, suddenly we gain insight into why our
patients so often have coexisting pain syndromes and thus we can more easily explain this findings to our patients and provide a more effective therapeutic approach.

FUNCTIONAL BOWEL DISEASE:

Functional bowel disease is a classic example of visceral hyperalgesia. It is characterized by a chronic relapsing pattern of bloating and cramping pain with alterations in stool frequency and/or consistency. Often, the pain is relieved by defecation. It is present in 50-80% of patients with any form of chronic pelvic pain. It is three times more likely to be found in women than in men, and these women are three to four times more likely to have already undergone a hysterectomy frequently for the treatment of pain [4]. We also know that if a hysterectomy in a patient who has coexisting functional bowel disease was done for causes of pelvic pain, this patient is much more likely to have a poor outcome with significant pain or persistence of pain postoperatively (P value less than .05). Also, 50% of patients who have negative laparoscopies at the time of evaluation of chronic pelvic pain are often found to have functional bowel disease once they are referred to a clinic specializing in the identification and treatment of functional bowel disease [5].

Patients with functional bowel disease often give a history of certain foods worsening or inducing their symptoms. These sensitivities might include a high fat diet, lactose, sorbitol, caffeine or alcohol excess or simply chewing gum frequently. These sensitivities do not represent true food allergies as much as an exaggerated gastric colonic reflex that is brought on by the particular food products. Patients with functional bowel disease often have other GI symptoms including esophageal reflux and peptic ulcer disease. Research has demonstrated that the visceral hypersensitivity can be easily demonstrated in all parts of the GI tract even though the patient might present with symptoms primarily arising from just one part of the GI
tract (colon) [6]. 50-80% of patients with significant functional bowel disease often have associated problems of pelvic floor muscle dysfunction resulting in problems of hemorrhoids, anismus, obstructed defecation and generalized pelvic pain.

Treatment of functional bowel disease must be directed towards the particular symptomatology of the patient. In patients with primarily severe cramping pain related to spasms in the colon, multiple medications including Dicyclomine, Donnatal, Librax and Hyoscyamine are beneficial. In patients who primarily complain of gaseous distention and cramping, products such as Simethicone, peppermint oil (Colpermin) and Beano™ can be quite beneficial. In patients who primarily have constipation dominated symptoms, fiber supplements are key. Psyllium is quite beneficial and new osmotic laxatives, such as Miralax™, can be quite successful. On the other hand, if patients have predominantly diarrhea type symptomatology, then again fiber supplements, Psyllium, Loperamide and tricyclics are very beneficial. 10-20% of patients who have undergone a cholecystectomy will have bile salt related colitis and their diarrhea responds very nicely to Cholestyramine.

MYOFASCIAL PAIN SYNDROMES:

Myofascial pain syndromes represent a large group of muscle disorders that are characterized by hypersensitive or tender spots that are referred to as “trigger points.” (Figure 1) Trigger points are often found within taught bands that are quite tender to palpation, and patients usually demonstrate very
nicely the localization of those trigger points if they happen to be within the abdominal wall. Myofascial pain syndrome is the most common cause of chronic low back pain, shoulder or neck pain. 30-50% of individuals will have latent trigger points. There are multiple risk factors that can turn a latent trigger point into an active or symptomatic trigger point. The key finding on examination is that an active trigger point will produce not only a localized site of tenderness but typically a referral pattern of pain radiating into the area that the patient describes her general pain to be in. Myofascial pain syndromes are the most frequent cause of chronic disabling pain, particularly so in patients who have failed more traditional therapies for their pelvic pain disorders. Primary fibromyalgia can be differentiated from a more localized myofascial pain syndrome in that fibromyalgia has a widespread distribution.

Sinaki in 1977 described pelvic floor tension myalgia. This represents a myofascial pain syndrome that involves the pelvic floor muscles. The literature is filled with multiple separate syndromes that have been associated with many different pelvic pain disorders. These specific syndromes include levator syndrome, coccygodynia and proctalgia fugax [7]. These are all myofascial pain syndromes. Pelvic floor tension myalgia is a term that tends to consolidate all of these previously used terms under a single umbrella. Pelvic floor myofascial pain syndromes can be brought on either as a visceral muscular reflex as was described earlier, or as a primary injury to pelvic floor muscles. Examples of a reflexic pelvic muscle disorder would include any chronic painful inflammatory process within the pelvis since they can all potentially induce pelvic floor tension. These include endometriosis, functional bowel disease, chronic vulvar vestibulitis [8] or interstitial cystitis. Examples of primary injuries to the pelvic floor include pelvic floor reconstructive surgeries (particularly sacrospinous vault suspensions), extensive dissection within the pelvic floor, postoperative complications such as a large pelvic hematoma, a straddle injury, a broken tailbone or a difficult delivery (particularly ones associated with forceps). DeLancey has demonstrated that 29% of multiparous women have levator ani abnormalities on
MRI while nulliparous women have none [9]. It is important to note that many patients associate the onset of chronic pain with problems that developed post delivery. Finally, pelvic myofascial pain disorders can develop as a pelvic floor dysbehavior, which is often associated with pelvic muscles simply not working in a coordinated manner. A classic example of this would be a patient who has had bed-wetting or recurrent UTIs since her childhood and while those urologic symptoms may resolve with time, the underlying pelvic floor dysbehavior often persists. It is important to note that patients with a history of bed-wetting are ten times more likely to develop interstitial cystitis. (Figure 2)

Typical symptoms of pelvic floor tension myalgia include an achy pelvic discomfort often described as pressure. Patients are frequently referred for evaluation and/or have undergone surgery for pelvic relaxation when in fact there are no true anatomic deficiencies found. The patient often reports problems with urinary hesitancy, voiding dysfunction and anismus, and gives a very typical history of the discomfort being made worse with prolonged sitting, particularly on hard surfaces. Finally, one of the key symptoms includes dyspareunia, which goes on for several hours after the completion of intercourse (muscular pain is often delayed pain). On examination, these patients are found to have very little pelvic floor muscle awareness and have difficulty demonstrating a simple squeeze or relaxation. The keys to the digital exam are not only this poor muscle awareness and poor relaxation but also the muscles are quite tender to palpation. In these cases it is sometimes easy to observe taught bands and trigger points within the iliococcygeus or more commonly the pubococcygeus muscles near their insertion along the “white line” or behind the pubic symphysis. (Figure 3)
measurement of this pelvic floor muscle dysfunction is easily seen with urodynamic evaluation of urethral pressures (the urethral pressures tend to be exaggerated and extremely unstable). Objective evidence using surface EMG’s has also been demonstrated, particularly by authors such as Howard Glazer [8].

Therapy for pelvic floor tension myalgia includes the traditional therapies for any muscle disorders with the keys here being localized heat, muscle relaxants and neurolytic therapy. Particularly beneficial in this regard is the use of Amitriptyline or other tricyclics. The studies that show the best response in this myofascial disorder of the pelvic floor revolve around a specially trained physical therapist who is knowledgeable in soft tissue work including myofascial release, muscle mobilization and the use of diathermy or ultrasound heat therapy to help relax these muscles. Biofeedback is commonly added with emphasis not on performing Kegels but instead learning to relax the muscles or performing “reverse Kegels.”

Trigger point therapy, whether it involves the abdominal wall or the pelvic floor, is very important in the management of myofascial pain syndromes. If conservative therapy is not able to eradicate these highly sensitive localized areas of pain, then blocking the pain cycle with an injection of $\frac{1}{2}\%$ Lidocaine, using a series of three to five injections, is extremely beneficial. Trigger point injections therefore not only become therapeutic but they are also diagnostic, which will demonstrate to both the patient and you the importance of eradicating these areas of extreme tenderness.
VULVODYNIA:

The international study of vulvar disease in 1983 defined vulvodynia as the chronic vulvar discomfort that patients suffer with that is characterized by complaints of burning, stinging, irritation and/or rawness and this generally needs to be differentiated from problems of itching or pruritus vulvae. There are six different subtypes or subsets of vulvodynia [10]. The three most common, which will be covered in this text, include vulvar vestibulitis, cyclic vulvovaginitis, and dysesthetic vulvodynia. History is extremely important in these patients with the first and most important question being whether or not the discomfort is a continuous discomfort or one that occurs only with intercourse. When discomfort is present only with intercourse, then the primary diagnoses to be included in the differential includes vulvar vestibulitis, cyclic vulvovaginitis and primary pelvic floor muscle dysfunction.

Cycle vulvovaginitis typically includes a history of intercourse related flare of burning and irritation. Typically, these patients will have redness. They will describe fissures and a minimal discharge. These patients will often describe menstrual cycling of their symptomatic dyspareunia. Important in these patients is that yeast cultures must be obtained despite the minimal findings on wet prep and gross examination. These are also found to have colonization with fungal organisms and thus long-term antifungal therapy is certainly indicated with the classic treatment being Diflucan 150 mg each week for four to six months.

Vulvar vestibulitis, on the other hand, is found in patients who typically have dyspareunia with localized areas of pinpoint tenderness at the site of vestibular gland openings with the pain and discomfort always being reproduced by palpation to the area of the vestibule. We have now come to realize that these patients may have only the pinpoint tenderness and no punctate
areas of redness, and therefore the lack of redness should not limit this diagnosis being made.

An important associated finding in patients with vulvar vestibulitis is significant problems of pelvic floor tension myalgia and pelvic floor muscle dysfunction. Howard Glazer has demonstrated that in patients with severe vulvar vestibulitis who have failed all other therapy, pelvic floor rehabilitation and relaxation therapy has actually been found to be quite beneficial. Traditional therapy for vulvar vestibulitis typically includes topical steroids, Amitriptyline 25-50 mg q HS. Surgical excision (Woodruff procedure) (Figure 4) is very beneficial in patients who have first undergone treatment of their pelvic floor tension myalgia and whose symptoms are truly related to intercourse and not those patients who have shifted into a continuous form of vulvodynia (Woodruff procedures demonstrate a very poor outcome in those patients who have continuous pain and vulvar burning).

Dysesthetic vulvodynia represents patients who report continuous vulvar burning and discomfort, yet often have no skin changes whatsoever. Their burning and discomfort are often associated with the light touch of clothing that significantly aggravates the burning that is already present. These patients quite frequently have severe pelvic floor muscle tension disorders that are often associated with other forms of chronic pain syndromes such as urgency/frequency syndrome, interstitial cystitis, functional bowel disease and fibromyalgia. It is thought that dysesthetic vulvodynia has a neuropathic etiology and probably represents a classic example of visceral somatic hyperalgesia. Therefore, neurolytic agents such as Amitriptyline represent the mainstay of therapy. It is extremely important in patients with
dysesthetic vulvodynia to look for other sources of visceral pain with the vulvodynia representing only the referral hyperalgesia. It has been my experience and the experience of many others that if one performs a potassium chloride test in these patients (Parson’s test) it is often positive and therefore the patients actually have a form of interstitial cystitis [15]. Once the interstitial cystitis is treated, the vulvodynia resolves. Glazer has shown impressive results with pelvic floor rehabilitation in patients with dysesthetic vulvodynia [11]. Bergeron and Glazer have recently published an excellent study comparing behavioral therapy, biofeedback and vestibulectomy in the treatment of vulvar vestibulitis. They showed that vestibulectomy resulted in the best outcome in patients with vulvar vestibulitis [12]. The key is vulvar pain only with sex and therefore not dyesthetastic vulvodynia. (Figure 5) Pudendal neuralgia is simply dyesthetastic vulvodynia in which the patient has a known history of neurologic trauma such as lumbosacral disease, post delivery avulsion of the pelvic floor with resultant localized pudendal defects, etc. Neurolytic agents are again used for this subtype of neuropathic vulvodynia.

**INTERSTITIAL CYSTITIS:**

Interstitial cystitis represents a clinical syndrome with symptoms that include urgency, frequency, suprapubic pain and irritable voiding symptoms that are often made worse with
intercourse. Throughout the literature, inconsistent use of other nomenclatures including urethritis, urethral syndrome, trigonitis and chronic cystitis have been used to the point that NIDDK developed very strict criteria to define interstitial cystitis. However, it is now agreed that if we all stick to the strict criteria of interstitial cystitis, two-thirds of patients that might benefit by therapy for interstitial cystitis will not be diagnosed to have that disorder. The most important concept concerning this diagnosis is to remember that patients with urinary tract infections will have a positive urine culture. If patients repeatedly give symptoms that have been diagnosed to be urinary tract infections, it is paramount that we establish that diagnosis through the use of urine cultures, and if the patient repeatedly has negative cultures, we cannot say this patient has recurrent urinary tract infections.

Somewhere between 500,000 and 800,000 patients in the United States have interstitial cystitis. 90% of these are women. 50% are unable to work full-time and 60% report severe dyspareunia. The quality of life associated with this disorder is less than those patients on renal dialysis, and interstitial cystitis is highly associated with a history of having undergone a previous hysterectomy, having functional bowel disease and vulvodynia [13]. The key finding is frequent voids and by definition of the International Continence Society, voiding more than eight times in 24 hours would be considered excessive unless fluid intake is excessive. (Figure 6) The normal functional volume of a bladder is 8 to 12 oz. per void, and if your patient is repeatedly demonstrating voided amounts of less than or equal to 4 oz., this would be considered an obviously abnormal urolog. Key findings on physical examination include a generalized hypersensitivity of the bladder base and trigone with an
otherwise relatively negative exam. Somewhere between 75% and 95% of patients with interstitial cystitis are also found to have pelvic floor hypertonic disorders and therefore a careful pelvic floor exam is necessary. Office testing that is beneficial in evaluating patients thought to have interstitial cystitis includes a uroflow to assess voiding function (some 25% to 70% of patients with interstitial cystitis have intermittent flow with significant hesitancy), a catheterized urine sample obtained for a post void residual, a urinalysis, a microscopic examination to rule out significant hematuria, and the performance of a urine culture to rule out an infection. Recent data has demonstrated that 48% of patients that present with urgency/frequency symptoms compatible with interstitial cystitis and who give a history of these symptoms starting at the same time as a new sexual contact, are found to have Mycoplasma or Ureaplasma in their vaginal vault [14] (this is a slight twist of the old data concerning Chlamydial urethritis in patients found to have urethral syndrome). It is also important to note that standard Chlamydial tests will test negative in a patient with Ureaplasma or Mycoplasma. This infectious process easily responds to Azithromycin. Cystoscopy under general anesthesia is becoming an extremely controversy tool to be used solely for the purpose of ruling in interstitial cystitis. A cystourethroscopy in the office setting is important, particularly in older patients, to rule out a bladder malignancy (found in 5 out of 202 patients with symptoms of urgency/frequency syndrome), but the findings of petechial hemorrhage under general anesthesia is not diagnostic of interstitial cystitis, and in fact patients with no evidence of interstitial cystitis at all will demonstrate that cystoscopic finding when their bladder is over-distended.

Lowell Parsons in 1994 developed a simple test to look for a chemical hypersensitivity to the infusion of potassium chloride into the bladder referred to as the KCl test or Parsons test. (See appendix) He found that 70% of patients with the clinical diagnosis of interstitial cystitis had an excessive amount of pain and/or urgency when potassium chloride was instilled into the bladder as compared to saline (these substances are instilled in the bladder under a blinded condition
and patients are asked to grade their symptoms on a scale of 1 to 5. If the patient tests positive, this represents a manifestation of a GAG layer deficiency with resultant tendency for acids, potassium and other solutes to traverse through the normally protective GAG layer into the submucosal layers thus causing many of the symptoms and neuropathic changes that are found in interstitial cystitis. A very important finding was recently reported in OB/GYN (OB/GYN 2001;98:127) by Parsons et al. In this study, 134 patients with gynecologic diagnoses involving pelvic pain syndromes (including the diagnosis of chronic pelvic pain, vulvodynia, endometriosis and dyspareunia) were studied to determine if they had a positive KCl test. 79% to 100% of patients tested were found to have a positive KCl test. When these patients were asked to fill out a urologic questionnaire, 75% were found to have urologic symptoms. This test points out that this GAG layer deficiency is commonly seen in most patients with any form of pelvic pain disorder [15]. Thus, treatment should be directed towards this obvious GAG layer defect.

Treatment of interstitial cystitis (Figure 7) includes simple behavioral modification (maintaining a fluid intake of approximately 64 oz. per day), low acid diet, estrogen vaginal cream if the patient is hypoestrogenic and the treatment of pelvic floor muscle dysfunction that is so commonly seen. Pharmacologic therapy includes tricyclic antidepressants, the use of antihistamines (especially with a significant history of allergies), and the use of bladder anesthetics such as Pyridium™ or Urimax™ to alleviate intermittent flares of bladder symptomatology. Intravesical heparin and/or
the use of oral Elmiron™ has been shown to have an extremely high success rate in alleviation of bladder pain. As a follow-up to the previously mentioned data concerning gynecologic pain, unpublished data demonstrates that gynecologic pain seems to markedly improve in patients treated with Elmiron™. If patients fail to respond to traditional therapies of interstitial cystitis, a new modality that has been available since 1999 is sacral neuromodulation using InterStim™. The success rate for this type of neuromodulation has been found to be quite good in properly selected patients. Antidotally, sacral neuromodulation has also been demonstrated to alleviate significant functional bowel disease (both constipation and diarrhea varieties), vulvodynia, and pelvic pain.

**SUMMARY:**

Once we understand the neuropathic activation that occurs in the sacral cords of our patients with any form of prolonged pelvic pain disorder, it should not be surprising that these patients often have coexisting symptoms. Pelvic neuropathic hypersensitivity is a new term that attempts to unify the concepts of neuropathic up regulation and multisite involvement in our patients with chronic pelvic pain. (Figure 8) A basic rule of management of any patient with chronic
pain is therefore to identify each source of pain and to design therapy to treat each component of the pain. Thus through the combination of behavioral modification for bowel and bladder disorders, physical therapy for the myofascial problems including trigger point injections, and pharmacologic intervention to try to down regulate the neural cascade that has been initiated by the neuropathic response occurring within the spinal cord, we can provide these patients with the best outcome possible [16,17]. The initiation of early intervention is the key to preventing the development of these complex chronic pelvic pain syndromes. It is important to try to identify the original end organ insult, whether it is endometriosis, interstitial cystitis or pelvic muscle dysfunction, and to treat that original insult if it is still present. As stated earlier, one of the keys to these complex syndromes is the treatment of all sources of pain and dysfunction. Yet, our biggest challenge is to identify the characteristics that suggest the source of the pain has left the end organ and has become centralized or neuropathic in origin. These characteristics include symptoms of multisite visceral hyperalgesia and an allodynic exam. When this has occurred, it is important that we design interventions that will not further up regulate the sacral cord [18] (such as doing repeated surgeries), but instead down regulate the neuropathic changes by decreasing the “volume of pain” that the spinal cord sees so that the patient’s own modulating pathways can hopefully handle what is left behind.

Appendix
Potassium Leak Sensitivity Test for Interstitial Cystitis\textsuperscript{1,2}
Procedure of C. Lowell Parsons, MD

- Potassium sensitivity testing appears to be a simple and inexpensive method to aid in the diagnosis of interstitial cystitis. Approximately 75% of patients with interstitial cystitis respond positively to the potassium sensitivity test.
- This useful test identifies patients with abnormal permeability of the bladder epithelium. It is based on the hypothesis that normal individuals cannot distinguish between two intravesically placed solutions, one of potassium and the other of sterile water. In patients with abnormal epithelial permeability, instillation of potassium solution will provoke pain, urgency, and/or detrusor instability.
- The test is considered positive if the potassium instillation induces an increase in urgency and/or pain of 2 points or greater on a subjective grading scale of 0–5 and if the patient says that the potassium solution was worse than the water.
- Patients who are very sensitive to water alone should be asked if the symptoms with potassium were worse. If so, the test is positive; if not, the test is indeterminate. If the patient has had recent hydrocilation or dimethyl sulfoxide (DMSO) therapy, sensitivity to potassium can be reduced. A negative test in these patients is indeterminate.

Materials

- Specimen container
- One 14 French, disposable catheter (Robinson or equivalent; smaller diameter for men)
- Prepared by pharmacy for convenience, where possible:
  - 40 cc sterile water in a syringe
  - 40 cc potassium chloride solution in a syringe
    (16 mEq KCl in 40 mL water—a concentration of \(~400 \text{ mEq/L}\))
  - 10,000–20,000 units of heparin in 20 cc of 1% lidocaine in a syringe
  - Symptom Grading Scale Form (on a clipboard, with pen or pencil)
POTASSIUM SENSITIVITY
Symptom Grading Scale

Patient’s Name ___________________________ Date ________________________

Mark the lines to show how much pain or urgency each solution is making you feel.

Solution 1

PAIN

<table>
<thead>
<tr>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

URGENCY

<table>
<thead>
<tr>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
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</table>

Solution 2

PAIN

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<thead>
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<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>1</td>
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URGENCY

<table>
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<tr>
<th>None</th>
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<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
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</table>

1. Which solution was worse?
   ____ First solution   ____ Second solution   ____ Neither

2. Was the difference between the two solutions...
   ____ None   ____ Mild   ____ Moderate   ____ Severe
Complex Pelvic Pain Syndromes

Charles W. Butrick, M.D.

Director,
The Urogynecology Center
Overland Park, Kansas
September 2001
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