



## **Interdisciplinary Management of Pelvic Pain: Bridging the Gap Between Primary Care and Specialty Referral**

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Jennifer Hah MD, MS

### **Disclosures**

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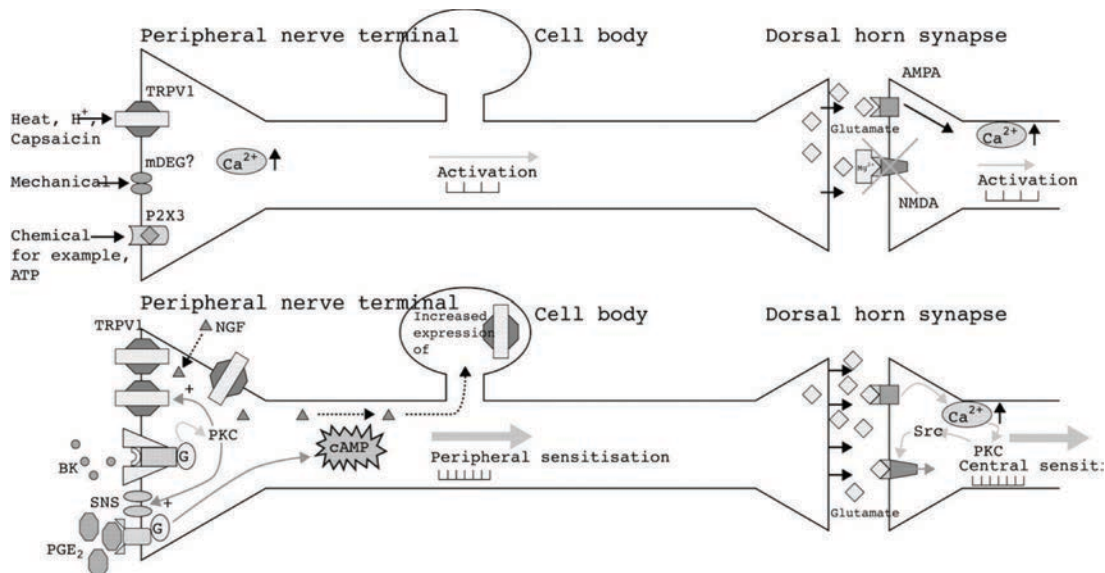
- Jennifer Hah has grant/research support from NIH NIDA R01 DA045027: Psychological Risk Factors for Persistent Opioid Use and Prevention of Chronic Opioid Use and Misuse After Surgery: Postoperative Motivational Interviewing and Guided Opioid Weaning



## Learning Objectives

- Describe the process of appropriate specialist referral and ongoing care by the primary care provider in the interdisciplinary management of chronic pelvic pain
- Differentiate bladder pain syndrome/interstitial cystitis from a myriad of other pelvic pain conditions including endometriosis, vulvodynia, and peripheral nerve entrapments
- Discuss evidence-based pain management strategies for the treatment of bladder pain syndrome/interstitial cystitis from the perspectives of a pain medicine specialist and a pain psychologist

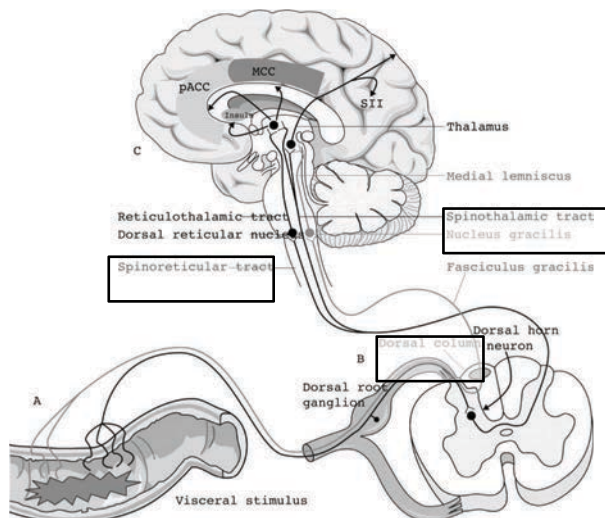
**PainWeek**



Matthews PJ, Aziz Q. Functional abdominal pain. Postgrad Med J. 2005;81(957):448-455.

**PainWeek**

Simplified diagram showing the major pain pathways from the viscera to the central nervous system.

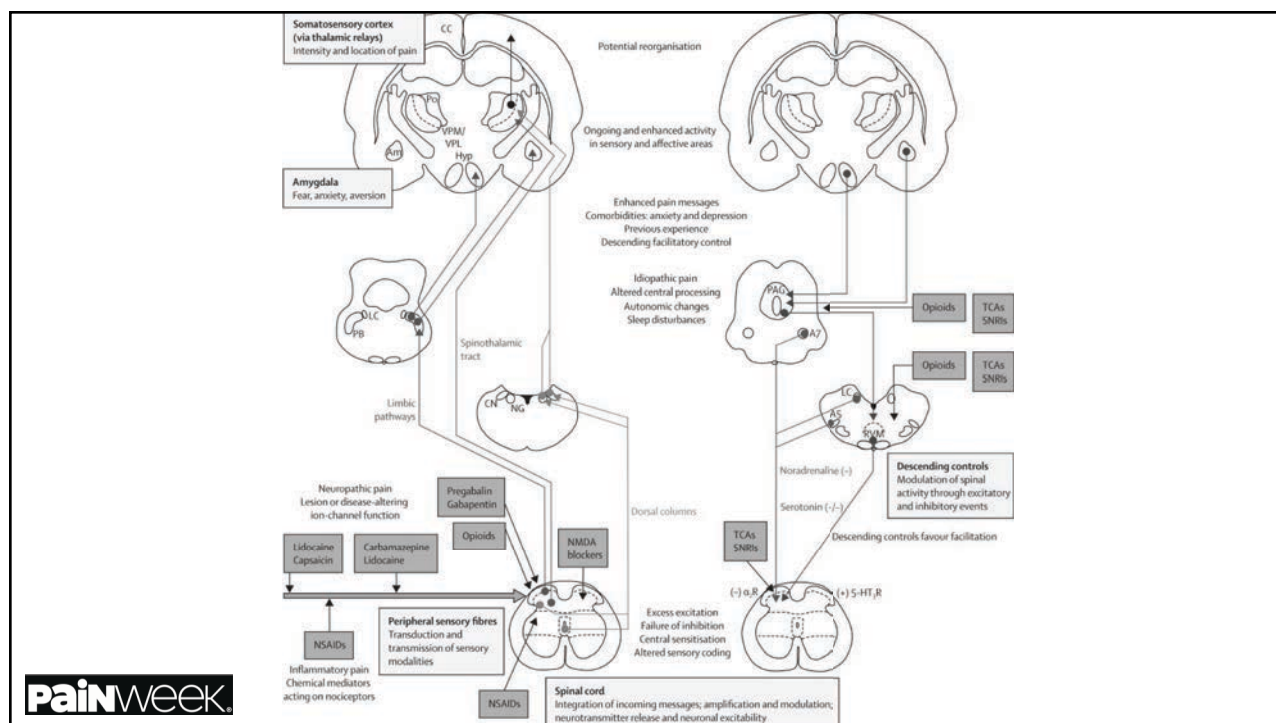


P J Matthews, and Q Aziz Postgrad Med J 2005;81:448-455

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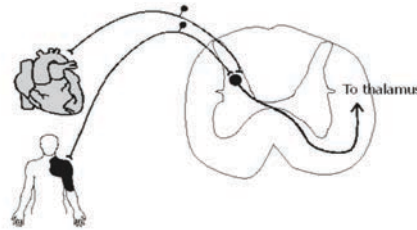
**PMJ**



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## Visceral Pain

- Diffuse and poorly localized
- Pain can refer to area innervated by same spinal segment as organ
- Vague discomfort
- Associated motor and autonomic reflexes
- Triggered by distention, contraction, ischemia, inflammation



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## Peripheral Visceral Innervation

- Visceral nociceptors
  - free nerve endings, large receptive fields
  - chemoreceptors sensitive to ischemia, inflammation, irritant, distention, contraction
  - stimulation  $\uparrow$  and afferent firing  $\uparrow$  (low-threshold mechanosensory afferents)
  - 50-90% of visceral afferents are silent until they are switched on (important role in central sensitization)

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## Visceral Nociceptors

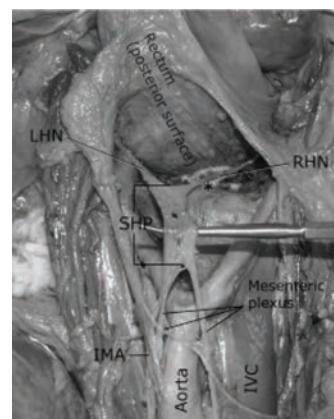
- Mucosal afferents
- Muscular afferents
- Serosal and Mesenteric afferents
- Muscular-mucosal afferents

• Keszthelyi, D., et al., *Revisiting concepts of visceral nociception in irritable bowel syndrome*. Eur J Pain, 2012. 16(10): p. 1444-54

**Pain**week.

## Peripheral Visceral Innervation

- Visceral afferent and efferent fibers are carried by spinal nerves
- Visceral afferents travel with autonomic nerves centrally
- Cell bodies reside in the dorsal root ganglia
- Large receptive field and low density of innervation by visceral afferents causes diffuse pain



Ripperda CM, Jackson LA, Phelan JN, Carrick KS, Corton MM. Anatomic relationships of the pelvic autonomic nervous system in female cadavers: clinical applications to pelvic surgery. Am J Obstet Gynecol 2016.

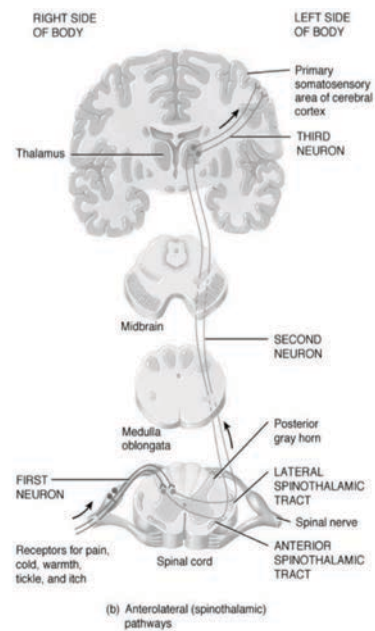
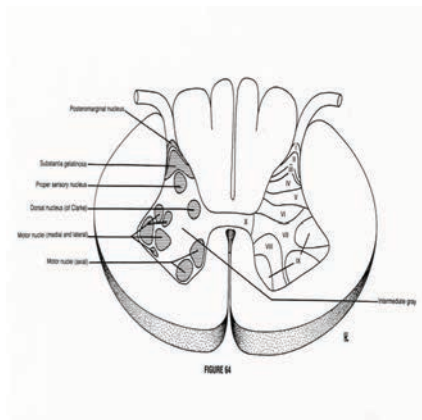
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## Visceral Pain

- Visceral afferents synapse above and below the entering segment
- Dorsal horn (lamina I and V)→dorsal column pathways, spinothalamic and spinoreticular tracts
- Autonomic spinal reflex:
  - sympathetic activation results in sweating and  $\uparrow$  BP
  - sympathetic inhibition or parasympathetic activation results in  $\downarrow$ BP, and bradycardia

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## Viscerosomatic Convergence



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## Viscerosomatic Convergence

- Pain originating from sacral sympathetic segments experienced in sacral somatic regions
- Visceral afferents reach upper lumbar/ lower thoracic spinal cord at same levels as visceral fibers from lower lumbar discs
- Sensory convergence from visceral afferents leads to somatic symptoms and vice versa
- Trigger points can develop in peripheral somatic tissue in response to increased nociceptive visceral input

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| Organ   | Level of CNS Entry of Visceral Afferents |
|---|--|
| Esophagus   | T2-T4, Nucleus tractus solitarius        |
| Stomach, duodenum, gallbladder, bile ducts, liver, pancreas | T5-T11                                   |
| Small intestines  | T8-T11                                   |
| Cecum and appendix  | T10-T12                                  |
| Colon to splenic flexure                                    | T10-L1                                   |
| Splenic flexure to rectum                                   | S2-S4                                    |
| Kidneys, ureters  | T10-T12 (L1,L2)                          |
| Bladder   | S2-S4                                    |
| Uterus  | T11-L2                                   |
| Testes  | T10                                      |
| Prostate  | S2-S4                                    |

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## Epigenetic and Environmental Influences

- Traumatic early life events produce long-term effects on the brain circuitry involved in visceral pain processing
- Chronic stress in adulthood predisposes to visceral pathology and pain states
- Chronic social stress in rats increases DNA methylation and histone acetylation of genes that regulate visceral pain sensation in the peripheral nervous system.
- In rats in which hypersensitivity to colonic distension had been experimentally induced, expression of the gene encoding the glucocorticoid receptor and cannabinoid CB1 receptors was reduced but expression of TRPV1 receptor increased in lumbosacral dorsal root ganglia

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## Enteric Nervous System

- Division of ANS
- GI motility, secretion, visceral sensation
- Myenteric and Submucous plexuses (sympathetic, parasympathetic, and enteric neurons)
- Can function autonomously
- Enteric neuronal plasticity contributes to visceral hypersensitivity

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## Superior Hypogastric Plexus

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- Anterior to L5 vertebral body and sacrum at bifurcation of common iliac vessels
- Union of aortic plexus, L3/L4 splanchnic nerves
- Divides into hypogastric nerves ( a.k.a. Middle Hypogastric Plexus)

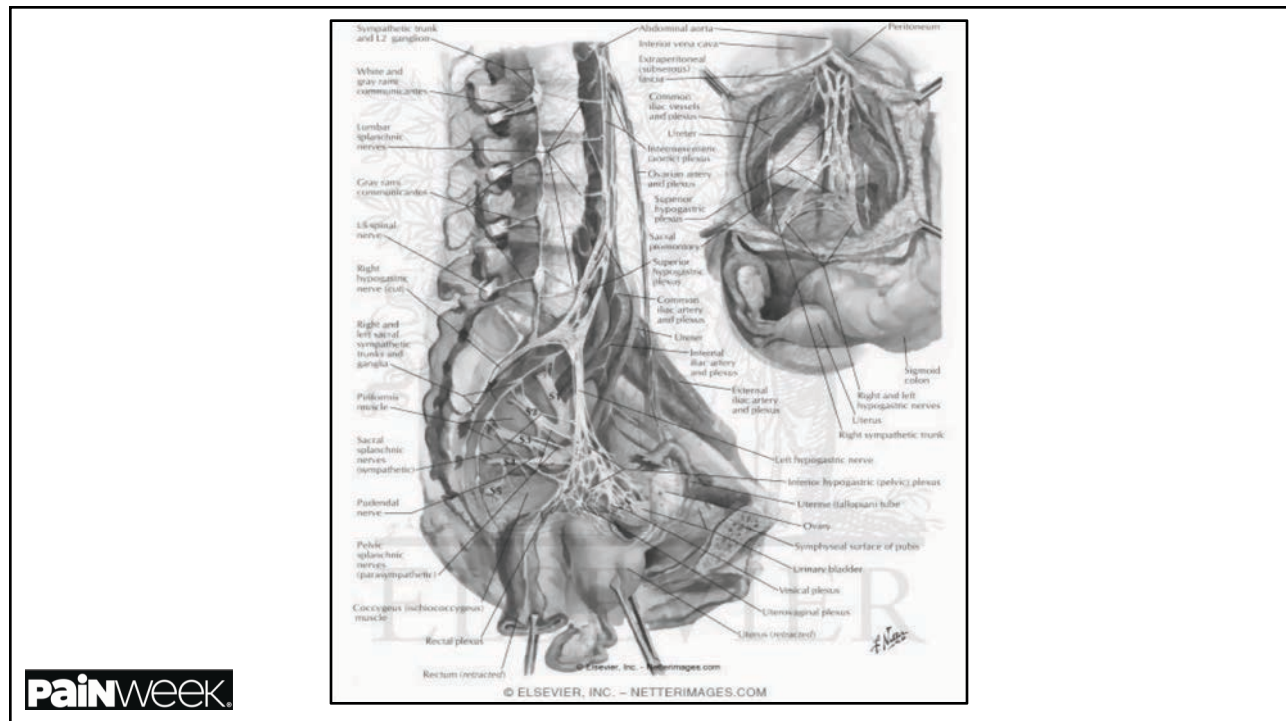
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## Superior Hypogastric Plexus

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- Sensory fibers transmit nociceptive impulses from uterus, cervix, fallopian tubes, bladder, rectum
- Visceral afferents with cell bodies in DRG of T10 to L2
- Parasympathetic nerves from S2-S4

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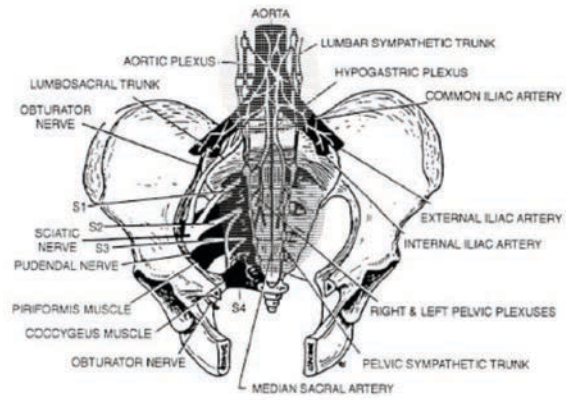


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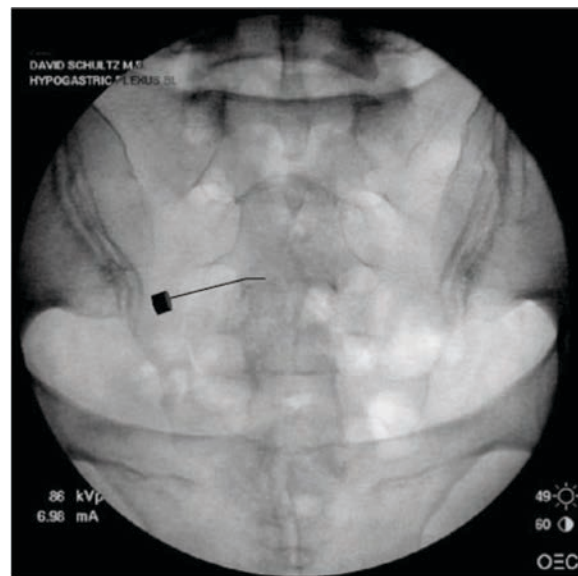
## Inferior Hypogastric Plexus

- Within bilateral presacral tissues on either side of rectum, ventral to S2, S3, S4 spinal segments
- The hypogastric nerves send branches to the internal iliac arteries and the IHP
- Also contribution from lowest lumbar splanchnic nerves, pelvic splanchnic nerves
- Branches to ovarian/testicular plexus, ureteric plexus, sigmoid colon
- Visceral afferents from bladder, penis, vagina, rectum, anus, perineum, and lower pelvis

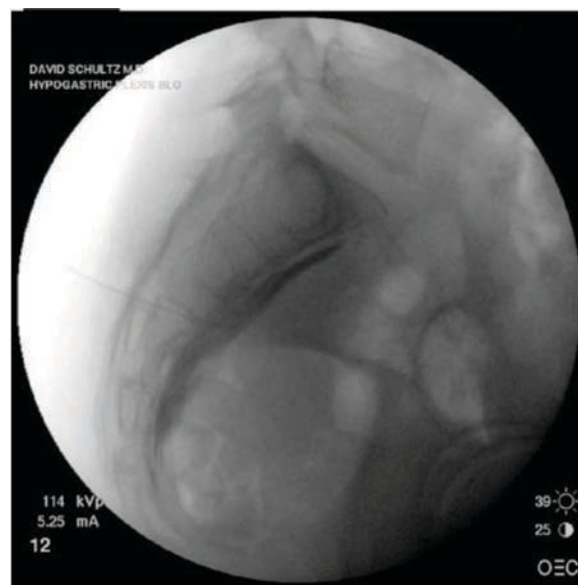
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**PainWeek**

## Inferior Hypogastric Plexus

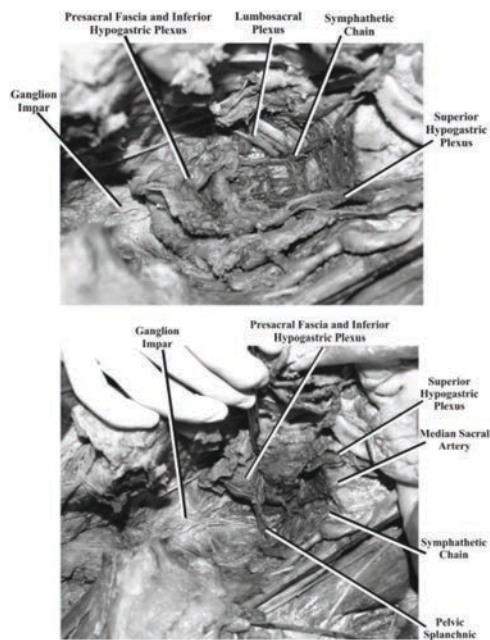
- Supplied by sacral splanchnics from S1 to S4 sympathetic ganglia (mostly postganglionic sympathetic fibers)
- Supplied by Nervi Erigentes (Pelvic Splanchnic Nerves): preganglionic parasympathetic fibers with cell bodies in S2, S3, and S4 (synapse with cell bodies of postganglionic parasympathetic neurons or viscera walls)
- Cell bodies of preganglionic sympathetic fibers originate from T9 to L2

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## Ganglion Impar

- Solitary retroperitoneal structure at the sacrococcygeal junction
- End of the 2 sympathetic chains
- Treats visceral pain in the perineal area
- Treats sympathetically mediated pain in the perineum, rectum, genitalia

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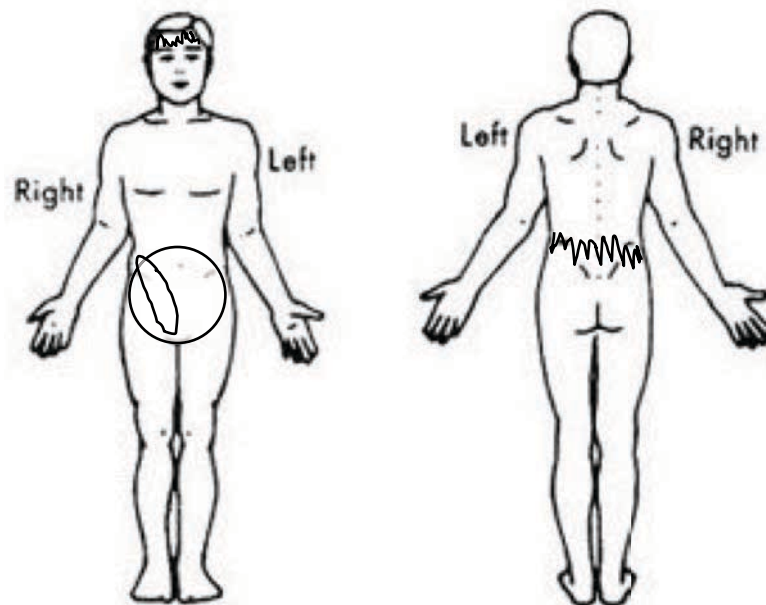


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## Case

- A 43 year-old female with a PMH of migraines, depression, and GERD presents to your office to establish care. She also has a long-standing history of pelvic pain, which has significantly worsened over the past year

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**Painweek.**

## Chronic Pelvic Pain

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- Nonmalignant pain perceived in the structures related to the pelvis that has been present for > 6 months or has a non-acute pain mechanism of shorter duration
- Disorders of urological, gynecological, gastrointestinal, musculoskeletal and nervous system
- Indication for 15-40% of laparoscopies and 12% of hysterectomies in the U.S

*Stacy, J., et al., Persistent pelvic pain: rising to the challenge. Aust N Z J Obstet Gynaecol, 2012. 52(6): p. 502-7*

*Yunker, A., et al., Systematic review of therapies for noncyclic chronic pelvic pain in women. Obstet Gynecol Surv, 2012. 67(7): p. 417-25*



## Terms

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- Pelvic Pain- pain arising from the visceral or somatic system encompassing structures supplied by the nervous tissue from T10 and below
- Pelvic Pain Syndrome- recurrent or persistent pain associated with symptoms suggesting involvement of the musculoskeletal, gynecological, urological, or gastrointestinal systems and the absence of inflammation or other specific pathology
- Pelvic floor- fascial and muscular layers that span the bony outlet of the pelvis



## Case

- She describes a sharp, shooting right groin pain radiating to her genitals and a dull, constant aching pain most notable in the suprapubic region
- Alleviating Factors: Rest, symptoms partially relieved by urination
- Exacerbating Factors: exercise, long car rides

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## Differential Diagnosis

| Gynecologic                         | Urologic                         | Gastrointestinal               | Musculoskeletal      |
|-------------------------------------|----------------------------------|--------------------------------|----------------------|
| Endometriosis                       | IC/PBS                           | Irritable Bowel Syndrome       | Pelvic Floor Myalgia |
| Adenomyosis                         | Chronic Urinary Tract Infections | Chronic Appendicitis           | Disc Disease         |
| Adhesions                           | Bladder Dysfunction              | Inflammatory Bowel Disease     | Nerve Entrapment     |
| Chronic Pelvic Inflammatory Disease | Bladder Stones                   | Constipation                   | Sacroiliac Disorders |
| Ovarian Cysts                       | Neoplasms                        | Chronic Intestinal Obstruction |                      |
| Ovarian Remnant Syndrome            |                                  | Diverticular Disease           |                      |
| Pelvic Congestion Syndrome          |                                  | Hernia                         |                      |
|                                     |                                  | Neoplasms                      |                      |

*Adapted from: Stacy, J., et al., Persistent pelvic pain: rising to the challenge. Aust N Z J Obstet Gynaecol, 2012. 52(6): p. 502-7*

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## Case

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- PSH: C-section 20 years ago, Exploratory laparoscopy with lysis of adhesions 5 years ago
- Medications: ibuprofen 200mg prn, sumatriptan 50mg prn, fluoxetine 20mg qd, famotidine 20mg BID, tramadol 50mg prn
- Social History: She is currently separated and going through a divorce. She has not been able to work over the last year due to pain, and had a previous history of suicidal ideations at age 18 due to a major life event

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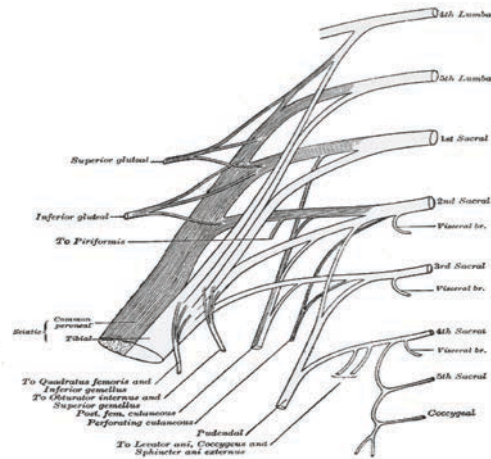
## Case

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- The patient is asking for a refill of her tramadol and referral to specialists as she has just moved to the area
- How would you proceed?

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## Sacral and Coccygeal Plexus



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## Iliohypogastric Nerve

- T12-L1
- Converge on dorsal horn structures shared with ipsilateral ovary and distal fallopian tube
- Cutaneous branch-anterior abdominal wall
- Motor branch-innervates TrA and internal oblique
- Sensory branch-groin and pubic symphysis

Apte, G., et al., Chronic female pelvic pain--part 1: clinical pathoanatomy and examination of the pelvic region. *Pain Pract*, 2012. 12(2): p. 88-110

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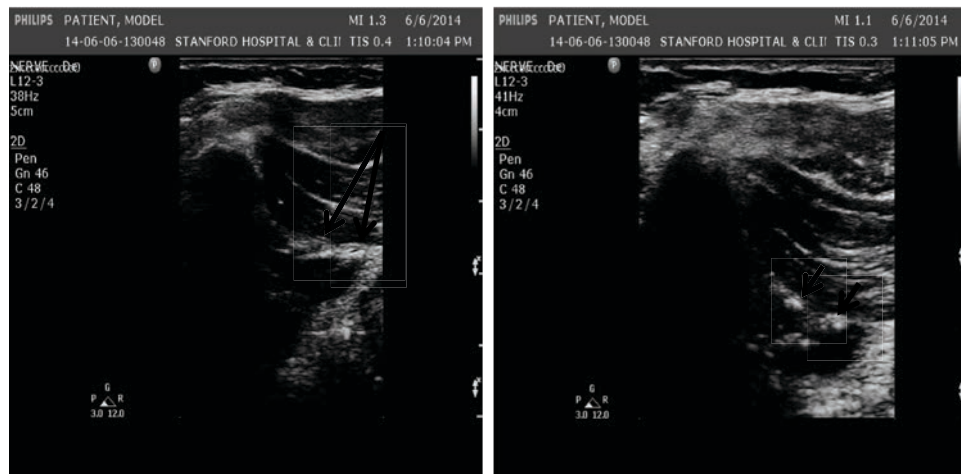
## Ilioinguinal Nerve

- T12-L1
- Converge on dorsal horn structures shared with proximal fallopian tubes and uterine fundus
- Enters inguinal canal 2cm medial to ASIS
- Sensory to groin, mons, labia, inner thigh
- Entrapment by suture at lateral edges of Pfannenstiel's incision
- Trauma during needle bladder suspension



Apte, G., et al., *Chronic female pelvic pain--part 1: clinical pathoanatomy and examination of the pelvic region*. *Pain Pract*, 2012. 12(2): p. 88-110

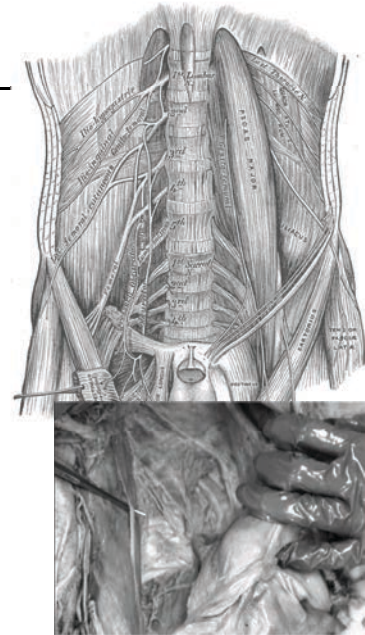
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## Genitofemoral Nerve

- L1-L2
- Converge on dorsal horn structures shared with proximal fallopian tube and uterine fundus
- Genital branch-skin of mons pubis and labia majora
- Femoral branch-skin of the femoral triangle
- Right genitofemoral neuralgia due to postappendectomy perineural fibrosis at exit through psoas

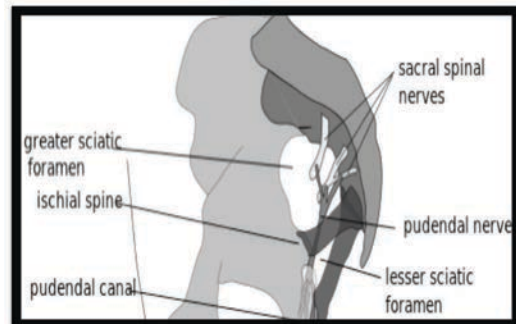


Apte, G., et al., *Chronic female pelvic pain—part 1: clinical pathoanatomy and examination of the pelvic region. Pain Pract*, 2012. 12(2): p. 88-110

**PainWeek**

## Pudendal Nerve

- Dorsal nerve of the penis/clitoris
- Perineal branch: motor to external anal sphincter and perineal muscles, sensory to vaginal tissues and vestibule, motor to external urethral sphincter
- Inferior rectal branch: motor to external anal sphincter, sensory to perineal skin
- Converges on dorsal horn structures shared with cervix, uterosacral, vulvovaginal region



Apte, G., et al., *Chronic female pelvic pain—part 1: clinical pathoanatomy and examination of the pelvic region. Pain Pract*, 2012. 12(2): p. 88-110

**PainWeek**

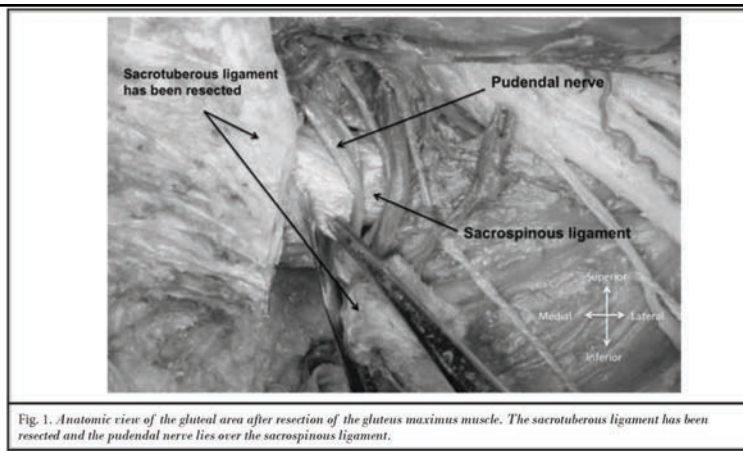
## Pudendal Neuralgia

- Prolonged 2nd stage of labor, 3rd degree tear through perineal body, high neonatal birth weight
- Sacrospinous vaginal vault suspension, laser to vulva/perineum
- Vaginal laceration repairs, episiotomies
- Straddle injuries, motorcycle or bicycle riding, repeated squatting, constipation



Apte, G., et al., *Chronic female pelvic pain--part 1: clinical pathoanatomy and examination of the pelvic region*  
*Pain Pract*, 2012. 12(2): p. 88-110

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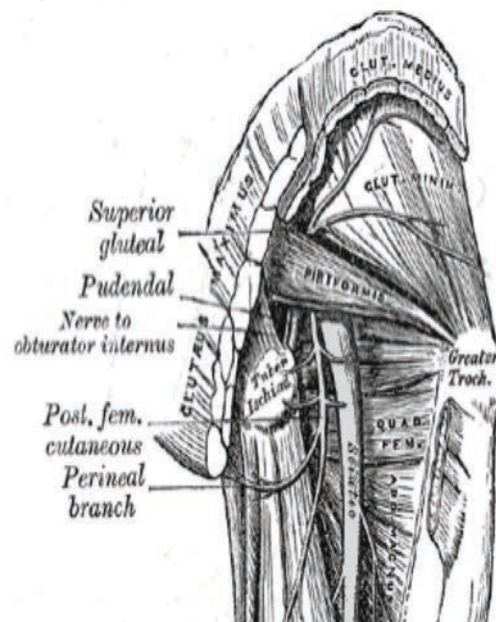


Ploteau S, Perrouin-Verbe MA, Labat JJ, Riant T, Levesque A, Robert R. Anatomical Variants of the Pudendal Nerve Observed during a Transgluteal Surgical Approach in a Population of Patients with Pudendal Neuralgia. *Pain Physician*. 2017;20(1):E137-E143.

Table 1. Sites of entrapment.

|                            | n   | %  |
|----------------------------|-----|----|
| Infrapiriform foramen (E1) | 15  | 10 |
| Ischial spine (E2)         | 101 | 70 |
| Alcock's canal (E3)        | 36  | 25 |
| Falciform process          | 58  | 40 |

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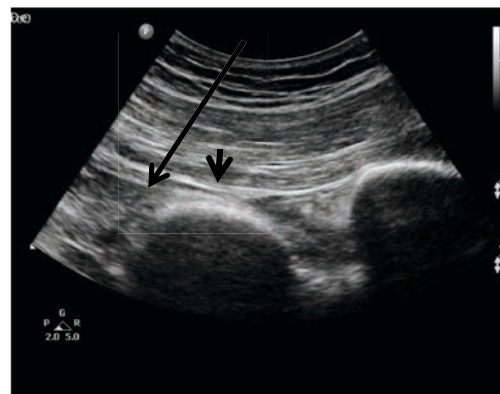
**PainWeek**

## Piriformis Syndrome

- Symptoms: Pain in the buttock, hip, and leg
- Mean age (38 years-old)
- Etiology: gluteal trauma, anatomic variants, myofascial trigger points
- Conservative Treatment: PT, lifestyle modifications, NSAIDs

Jankovic, D., P. Peng, and A. van Zundert, Brief review: piriformis syndrome: etiology, diagnosis, and management  
*Can J Anaesth*, 2013. 60(10): p. 1003-12

Fowler, I.M., et al., A randomized comparison of the efficacy of 2 techniques for piriformis muscle injection: ultrasound-guided versus nerve stimulator with fluoroscopic guidance.  
*Reg Anesth Pain Med*, 2014. 39(2): p. 126-32



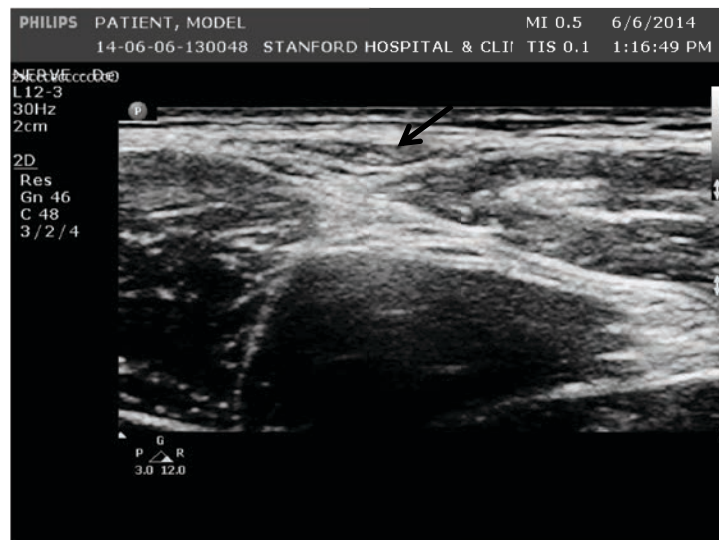
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## Lateral Femoral Cutaneous Nerve

- L2-L3
- Converge on dorsal horn structures shared with uterine fundus and lower uterus
- Meralgia paresthetica- pain and numbness in upper outer thigh
  - Post-surgical abdominal scars, iliac bone graft harvest, ascites, abdominal/pelvic mass

Apte, G., et al., Chronic female pelvic pain--part 1: clinical pathoanatomy and examination of the pelvic region. *Pain Pract*, 2012. 12(2): p. 88-110

**PainWeek**



**PainWeek**



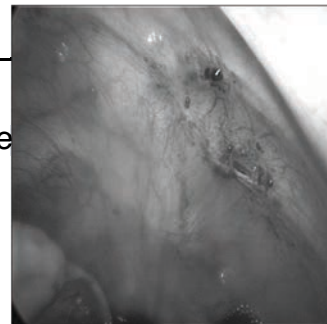
## Case

- Physical Exam: Decreased sensation to cold over the right inguinal ligament and a portion of the upper inner thigh, no tactile allodynia over laparoscopic scars of pfannenstiel incision, deep aching pain with palpation of the suprapubic region, tenderness to intravaginal palpation of pelvic floor muscles with minimal contraction strength
- Next steps from the pain specialist's perspective?

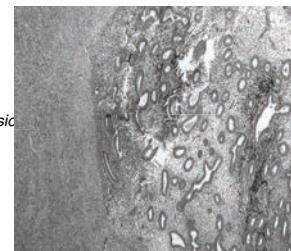
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## Endometriosis

- Affects 5-10% of women of reproductive age
- Growth of endometrial glands and stroma outside the uterus
- Severe pelvic pain
- Reduced fertility
- Histologic diagnosis



Bruner-Tran, K.L., et al., *Medical management of endometriosis: emerging evidence linking inflammation to disease pathophysiology*, *Obstetrics and Gynecology*, 2016, 127(2): p. 199-213



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## Endometriosis

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- Retrograde menstrual flow (site in the pelvis)
- Coelomic (peritoneal) metaplastic change of undifferentiated tissue outside uterine cavity
- Adult stem cells, which play a role in endometrial self-renewal, may contribute to the pathogenesis of ectopic sites of endometrial growth
- Lymphatic or vascular factors (endometrial tissue in brain, lung, skin, and eye)
- Genetic Factors
- Environmental Factors

*Bruner-Tran, K.L., et al., Medical management of endometriosis: emerging evidence linking inflammation to disease pathophysiology. Minerva Ginecol, 2013. 65(2): p. 199-213*



## Endometriosis

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- Dysmenorrhea
- Dyspareunia
- Heavy menstrual bleeding
- Non-menstrual pelvic pain
- Pain at ovulation
- Dyschezia
- Dysuria
- Chronic fatigue

*Bruner-Tran, K.L., et al., Medical management of endometriosis: emerging evidence linking inflammation to disease pathophysiology. Minerva Ginecol, 2013. 65(2): p. 199-213*



## Endometriosis

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- Medications: NSAIDs, combined OCP, GNRH agonists, progestins
- Surgery:
  - Laparoscopic surgical removal of endometriosis
  - Laparoscopic uterine nerve ablation in addition to surgical removal does not improve pain relief
- Superior hypogastric plexus block

Johnson, N.P., L. Hummelshoj, and C. World Endometriosis Society Montpellier, Consensus on current management of endometriosis. Hum Reprod, 2013. 28(6): p. 1552-68  
 Kanazi, G.E., et al., New technique for superior hypogastric plexus block. Reg Anesth Pain Med, 1999. 24(5): p. 473-6



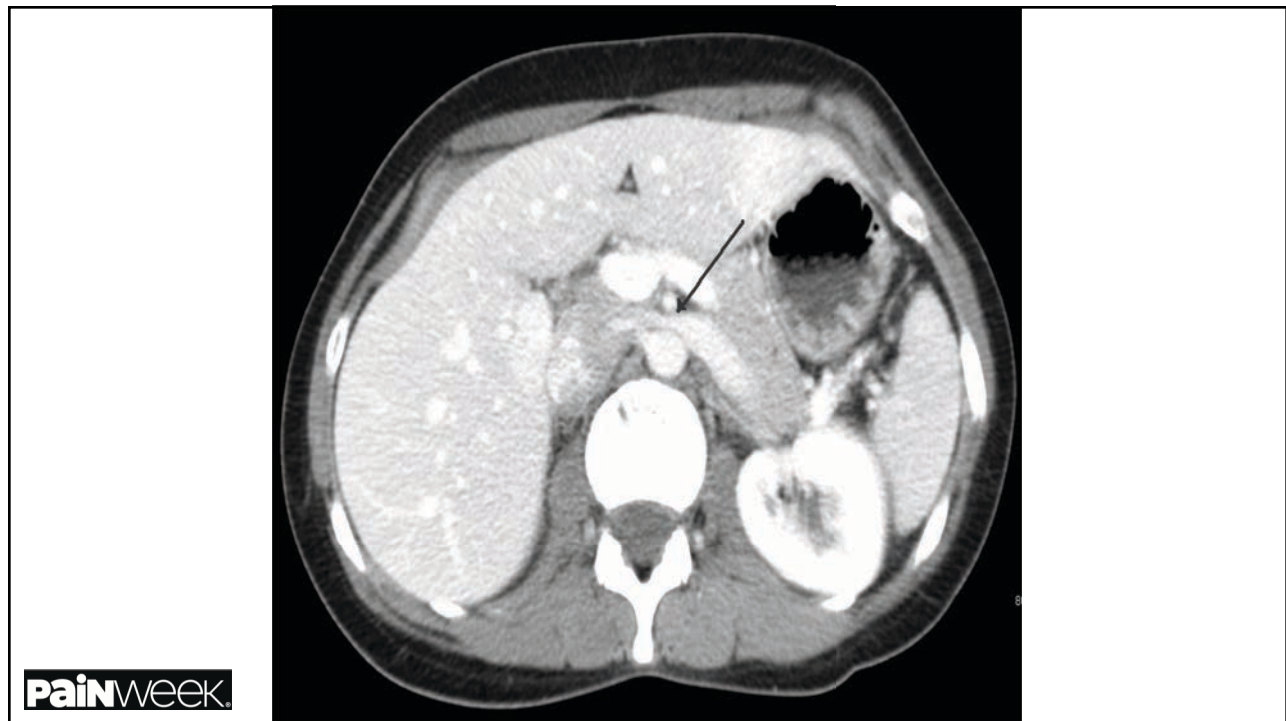
## Pelvic Congestion Syndrome

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- Enlarged venous complexes of reproductive tissue (impaired circulation and drainage)
- Etiology: Anatomic dysfunction, Orgasmic dysfunction, Psychosomatic, Hormonal dysfunction, Iatrogenic
- Dull ache exacerbated by ↑ venous pressure
- Deep dyspareunia (78%)
- Postcoital aching (65%)
- Dysmenorrhea (89%) up to one week before menses

Perry, C.P., Current concepts of pelvic congestion and chronic pelvic pain. JSLS, 2001. 5(2): p. 105-10





## Pelvic Congestion Syndrome

- Pelvic venography-gold standard for diagnosis
- Treatment
  - Medroxyprogesterone acetate
  - PT with manual lymph drainage techniques
  - Ovarian vein ligation
  - Uterine suspension (retroverted uterus)
  - Ovarian and pelvic vein embolization

*Perry, C.P., Current concepts of pelvic congestion and chronic pelvic pain. JSLs, 2001. 5(2): p. 105-10*

*Nelson, P., et al., Chronic female pelvic pain--part 2: differential diagnosis and management. Pain Pract, 2012. 12(2): p. 111-41*

## Vulvodynia

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- Chronic pain or discomfort involving the vulva for more than 3 months and for which no obvious etiology can be found
- “itching, burning, stinging, irritation, stabbing, rawness”
- Lifetime prevalence: 8% up to age 70
- PVD: most common cause of sexual pain in women < age 30
- Typically affects women ages 20-40

*Sadownik, L.A., Etiology, diagnosis, and clinical management of vulvodynia. Int J Womens Health, 2014. 6: p. 437-49*



## Vulvodynia

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- Initial trigger of inflammation/injury leading to altered pain processing
- Possibly from stretch injury of the nerve to the levator ani or the pudendal nerve during prolonged 2nd-stage labor or pelvic floor descent, episiotomy, straddle injury
- Hormonal changes, cysts, surgical side effect, steroids, antivirals
- Women with a history of anxiety/depression are 4 times more likely to develop PVD



## Vulvodynia

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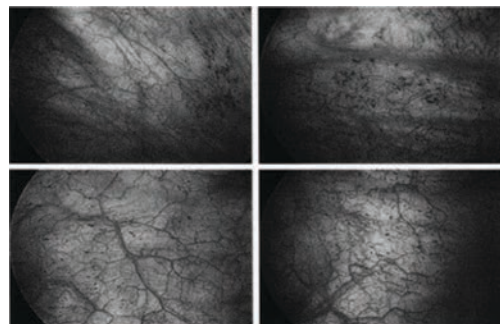
- Biofeedback (decreased pelvic floor hypertonicity)
- Manual or electrotherapeutic input to thoraco-lumbar and sacral areas
- Lidocaine gel or estrogen cream(perimenopausal/postmenopausal)
- TCAs, gabapentin, pregabalin, lamotrigine, carbamazepine
- Supportive psychotherapy, CBT, sexological counseling
- Vestibuloplasty, vestibulectomy, perineoplasty

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## Urologic Pelvic Pain

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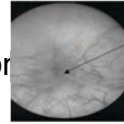
- Interstitial Cystitis
- Painful Bladder Syndrome
- Bladder Pain Syndrome



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## NIDDK Criteria (1990)

- (1) Bladder pain or urinary urgency
- (2) Glomerulations or Hunner's ulcer during cystoscopy/hydrodistension
- (3) None of the exclusions listed below:
  - Awake cystometric capacity >350 mL, Absence of intense urge to void with bladder filling during cystometry, Involuntary bladder contractions on cystometry, Urinary frequency < 8 voids per day, Absence of nocturia, Symptoms < 9 months, Age <18 years, Cystitis (bacterial, chemical, infectious, radiation) or prostatitis, vulvitis (herpes) or vaginitis, Bladder/uterine/cervical/vaginal/urethral cancer, Bladder or ureteral calculi, Urethral diverticulum, Bladder tumors



Hanno, P.M., Interstitial cystitis-epidemiology, diagnostic criteria, clinical markers. *Rev Urol*, 2002. 4 Suppl 1: p. S3-8

**PainWeek**

## AUA Guideline for the Diagnosis and Treatment of Interstitial Cystitis/Bladder Pain Syndrome

Philip M. Hanno,\* David Allen Burks, J. Quentin Clemens, Roger R. Dmochowski, Deborah Erickson, Mary Pat FitzGerald, John B. Forrest, Barbara Gordon, Mikel Gray, Robert Dale Mayer, Diane Newman, Leroy Nyberg, Jr., Christopher K. Payne, Ursula Wesselmann and Martha M. Faraday

*From the American Urological Association Education and Research, Inc., Linthicum, Maryland*

### Diagnosis and Treatment of Interstitial Cystitis/Bladder Pain Syndrome: AUA Guideline Amendment

Philip M. Hanno, Deborah Erickson, Robert Moldwin\* and Martha M. Faraday

An unpleasant sensation (pain, pressure, discomfort) perceived to be related to the urinary bladder, associated with lower urinary tract symptom(s) of more than 6 weeks duration, in the absence of infection or other identifiable causes

Hanno, P.M., et al., AUA guideline for the diagnosis and treatment of interstitial cystitis/bladder pain syndrome. *J Urol*, 2011. **185**(6): p. 2162-70

Hanno PM, Erickson D, Moldwin R, Faraday MM. Diagnosis and Treatment of Interstitial Cystitis/Bladder Pain Syndrome: AUA Guideline Amendment. *The Journal of urology* 2015

**PainWeek**

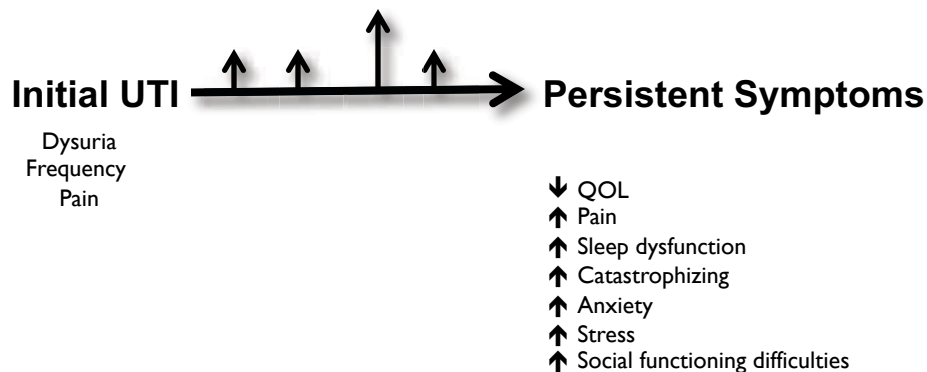
## Epidemiology

- Prevalence: 2.7-6.53% of women, 2.9-4.2% of men
- F>M
- Age at presentation: 42 years-old
- Activity avoidance (shopping, travel, exercise, sexual relationships)
- Associated with fibromyalgia, chronic fatigue syndrome, irritable bowel syndrome, temporomandibular disorder, migraine, chronic pelvic pain, vulvodynia, low back pain, allergies, asthma, depression and anxiety
- Risk factors: caffeine, anorectal disease, smoking

Warren, J.W., D.J. Clauw, and P. Langenberg. Prognostic factors for recent-onset interstitial cystitis/painful bladder syndrome. *BJU Int*, 2013. 111(3 Pt B): p. E92-7  
 Bullones Rodriguez, M.A., et al., Evidence for overlap between urological and nonurological unexplained clinical conditions. *J Urol*, 2013. 189(1 Suppl): p. S66-74  
 Offiah, I., S.B. McMahon, and B.A. O'Reilly, Interstitial cystitis/bladder pain syndrome: diagnosis and management. *Int Urogynecol J*, 2013. 24(8): p. 1243-56  
 Hanno, P., et al., Bladder Pain Syndrome Committee of the International Consultation on Incontinence. *NeuroUrol Urodyn*, 2010. 29(1): p. 191-8

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## Clinical Presentation



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## Associated Psychosocial Conditions

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- Depression
- Sexual dysfunction
- Sexual abuse
- Emotional abuse/neglect
- Physical abuse/neglect

*Offiah, I., S.B. McMahon, and B.A. O'Reilly, Interstitial cystitis/bladder pain syndrome: diagnosis and management. Int Urogynecol J, 2013. 24(8): p. 1243-56*



## Case

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- How do we consider this patient's psychosocial history in the ongoing management of her pain conditions?





## Adverse Childhood Experiences

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- Adverse Childhood Experience (ACE) Study
  - CDC/Kaiser Permanente collaboration
  - Co-PIs: Robert Anda, MD, Vincent Felitti, MD
  - Examining relationship between ACEs and health/behavioral outcomes later in life
  - Data gathered from 17K individuals between 1995-97



## Adverse Childhood Experiences

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- Physical/emotional neglect
- Recurrent emotional abuse
- Recurrent physical abuse
- Sexual abuse (contact)
- Household substance abuse
- Incarceration of household member
- Chronic mental illness
- Mother treated violently
- One or no parents



## Adverse Childhood Experiences

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- Higher ACE scores increase risk for developing
  - Medical/psychiatric disease
  - CD/SA issues
  - Health-related QOL issues
  - Partner violence
  - Sexual activity
  - Suicidality



## Adverse Childhood Experiences

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- Abuse and Somatic Disorders
- Systematic review & meta-analysis of literature from 1/1980 – 12/2008 (Paras et al. 2009)
- 23 studies, 4640 subjects
- Significant association between sexual abuse and a lifetime diagnosis of:
  - Functional GI disorders
  - Non-specific chronic pain
  - Psychogenic seizures
  - Chronic pelvic pain

*Paras et al. (2009). Sexual Abuse and Lifetime Diagnosis of Somatic Disorders. JAMA 302(5): 550-561*



## Abuse, Pain, and Depression

---

- n = 273 females evaluated for CPP
- Assessed:
  - History of physical abuse
  - History of sexual abuse
  - Pain severity
  - Pain disability
  - Depression

As-Sanie S, Clevenger LA, Geisser ME, Williams DA, Roth RS. History of abuse and its relationship to pain experience and depression in women with chronic pelvic pain. *Am J Obstet Gynecol*. 2014 Apr;210(4):317.e1-8. doi: 10.1016/j.ajog.2013.12.048. Epub 2014 Jan 8



## Abuse, Pain, and Depression

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- Logistic regression analyses:
  - Abuse categories not associated with pain severity
  - Sexual abuse predictive of pain-related disability
  - Physical & sexual abuse associated with higher levels of depression

As-Sanie S, Clevenger LA, Geisser ME, Williams DA, Roth RS. History of abuse and its relationship to pain experience and depression in women with chronic pelvic pain. *Am J Obstet Gynecol*. 2014 Apr;210(4):317.e1-8. doi: 10.1016/j.ajog.2013.12.048. Epub 2014 Jan 8



## Abuse, Pain, and Depression

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- Conclusion:

- Pelvic pain is always a sign of an underlying abuse history
- Depression in a person with pelvic pain is more related to the abuse history



## Abuse, Pain, and Depression

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- Conclusion:

- Pelvic pain is always a sign of an underlying abuse history
- Depression in a person with pelvic pain is more related to the abuse history



## Evolution of Depression

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**LIFE**

**Pain**week.

## Evolution of Depression

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**LIFE**

Family Friends Work School  
Sports Leisure Self-care Music  
Vacations Hobbies Dining  
Entertainment Socializing  
Cooking Cleaning Errands

**Pain**week.

## Evolution of Depression

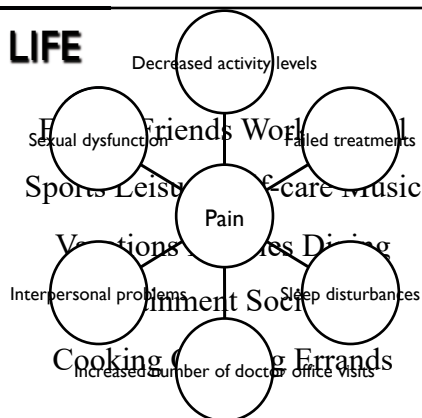
### LIFE

Family Friends Work School  
Sports Leisure Self-care Music  
Vacation Hobbies Dining  
Entertainment Socializing  
Cooking Cleaning Errands

**Pain**week.

## Evolution of Depression

### LIFE



**Pain**week.

## Psychological Factors and Pain

- Untreated/undertreated psychiatric distress adversely affects treatment outcome
- Necessitates an interdisciplinary approach to care



Kwon JK, Chang IH. Pain, Catastrophizing, and Depression in Chronic Prostatitis/Chronic Pelvic Pain Syndrome  
*International Neurourology Journal.* 2013;17(2):48-58. doi:10.5213/inj.2013.17.2.48

**Pain**week.

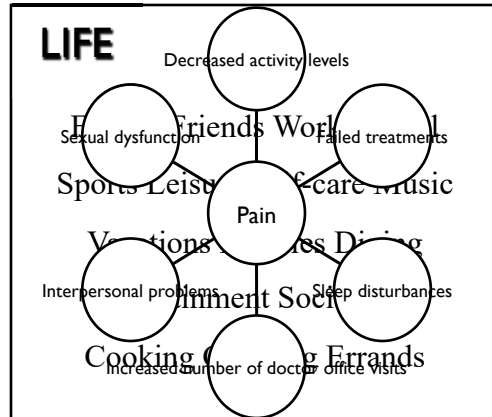
## Interdisciplinary Pain Management

|           | Acute           | Chronic               |
|-----------|-----------------|-----------------------|
| Meaning   | Hurt = Harm     | Hurt ≠ Harm           |
| Etiology  | Clear, singular | Vague, multifactorial |
| Treatment | Unimodal        | Interdisciplinary     |

- Pain management similar to approach used with other chronic health conditions
- Education focuses on QOL, improving functionality

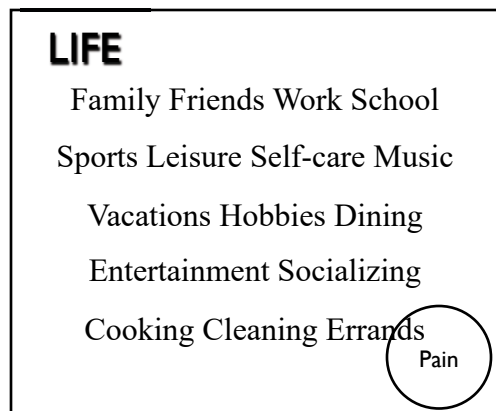
**Pain**week.

## Interdisciplinary Management



**Pain**week

## Interdisciplinary Management



**Pain**week



## Summary: Role of Psychology in Pain Etiology

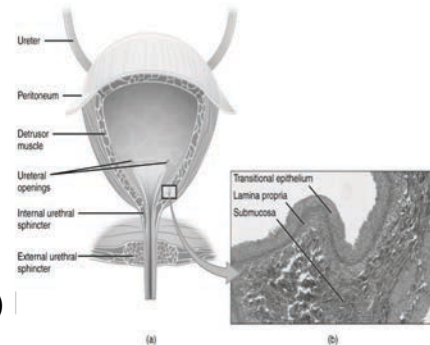
- Some pain conditions are primarily due to psychogenic factors but virtually all can be influenced by psychological factors
- Employing an interdisciplinary approach can maximize outcomes



**PainWeek**

## Etiology

- Epithelial dysfunction
- Subclinical infection
- Mast cell and vascular abnormalities
- Neurogenic inflammation
- Autoimmune
- Central sensitization
- Altered integrity of the glycosaminoglycan (GAG)



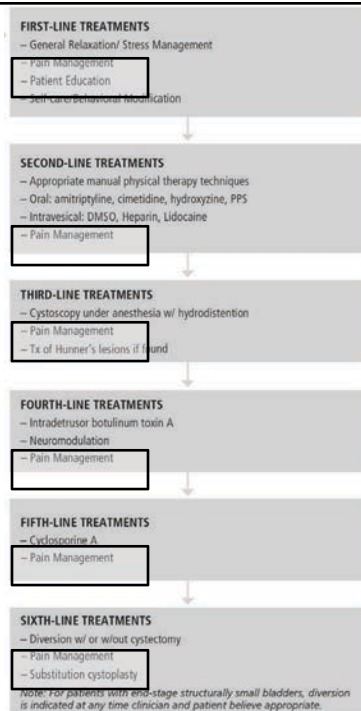
Offiah, I., S.B. McMahon, and B.A. O'Reilly, Interstitial cystitis/bladder pain syndrome: diagnosis and management. *Int Urogynecol J*, 2013. 24(8): p. 1243-56

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“Pain management should be considered throughout the course of therapy with goal of maximizing function and minimizing pain and side effects.”

Hanno PM, Erickson D, Moldwin R, Faraday MM. Diagnosis and Treatment of Interstitial Cystitis/Bladder Pain Syndrome: AUA Guideline Amendment. *The Journal of urology* 2015

**PainWeek**



## Treatment

1. Patient education and support, Self-care/Behavioral modification
2. Appropriate PT, amitriptyline, cimetidine, hydroxyzine, PPS, intravesical instillations
3. Cystoscopy and hydrodistention, Tx of Hunner's lesions
4. Intradetrusor onabotulinumtoxinA, Neuromodulation
5. Cyclosporine A
6. Surgery, substitution cystoplasty

Hanno, P.M., et al., AUA guideline for the diagnosis and treatment of interstitial cystitis/bladder pain syndrome. *J Urol*, 2011. 185(6): p. 2162-70  
Hanno PM, Erickson D, Moldwin R, Faraday MM. Diagnosis and Treatment of Interstitial Cystitis/Bladder Pain Syndrome: AUA Guideline Amendment. *The Journal of urology* 2015

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## Intravesical Dimethyl Sulfoxide

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- FDA-approved for IC in 1997
- anti-inflammatory, analgesic, smooth muscle relaxing, and mast cell inhibiting effects
- bladder catheterization with instillation of 50 mL DMSO weekly for 6-8 weeks, followed by 50 mL every 2 weeks for 3 to 12 months
- pain and significant exacerbation of symptoms (10%)
- garlic-odor, headache side effects

*Vij M, Srikrishna S, Cardozo L. Interstitial cystitis: diagnosis and management. European journal of obstetrics, gynecology, and reproductive biology 2012;161:1-7*

**PainWeek**

## Pentosan Polysulfate Sodium

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- FDA approved (1996) for IC treatment
- 100mg TID with water 1 hr. before or 2hrs. after meals
- Filtered by the kidneys and appears in the urine to reconstitute the deficient glycosaminoglycan (GAG) layer over the urothelium
- Only 3-6% of active drug reaches the bladder
- Full effect may not be seen for 6-9 months
- Contraindicated with allergy to LMWHs and heparin or HIT

*Vij M, Srikrishna S, Cardozo L. Interstitial cystitis: diagnosis and management. European journal of obstetrics, gynecology, and reproductive biology 2012;161:1-7*

**PainWeek**

## Cimetidine

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- Mast cell degranulation postulated to initiate inflammation
- H<sub>2</sub> antagonist
- 2<sup>nd</sup> line agent
- 300mg BID for or 200mg TID

*Seshadri, P., L. Emerson, and A. Morales, Cimetidine in the treatment of interstitial cystitis. Urology, 1994, 44(4): p. 614-6*

*Dasgupta, P., et al., Cimetidine in painful bladder syndrome: a histopathological study. BJU Int, 2001, 88(3): p. 183-6*

*Thilagarajah R, Witherow RO, Walker MM. Oral cimetidine gives effective symptom relief in painful bladder disease: a prospective, randomized, double-blind placebo-controlled trial. BJU international 2001;87:207-12*



## Amitriptyline

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- 50 subjects with IC randomized to amitriptyline or placebo
- 4 months with a self-titration protocol, escalate drug dosage by 25 mg increments weekly to a maximum of 100 mg
- Greater improvement in O'Leary-Sant Interstitial Cystitis Symptom Index than placebo
- 42% of patients in the amitriptyline group experienced greater than 30 percent decrease in symptom score, suggesting that benefits are modest

*van Ophoven A, Pokupic S, Heinecke A, Hertle L. A prospective, randomized, placebo controlled, double-blind study of amitriptyline for the treatment of interstitial cystitis. The Journal of urology 2004;172:533-6*



### Effect of Amitriptyline on Symptoms in Treatment Naïve Patients With Interstitial Cystitis/Painful Bladder Syndrome

Harris E. Foster, Jr.,\* Philip M. Hanno, J. Curtis Nickel, Christopher K. Payne, Robert D. Mayer, David A. Burks, Claire C. Yang, Toby C. Chai, Karl J. Kreder, Kenneth M. Peters, Emily S. Lukacz, Mary P. Fitzgerald, Liyi Cen, J. Richard Landis, Kathleen J. Probert, Wei Yang, John W. Kusek, Leroy M. Nyberg and the Interstitial Cystitis Collaborative Research Network

*J Urol. Vol. 183, 1853-1858, May 2010*

- multicenter, randomized, double-blind, placebo controlled trial (N=271)
- 6-week titration from 10 -75 mg daily
- Evaluated after 12 weeks of treatment
- No difference in GRA (moderate or marked improvement)
- Subgroup reaching 50 mg daily (N=207): GRA in the amitriptyline group (66%) compared to placebo (47%) (p=0.01)

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## Gabapentin

- Prospective study of 38 patients with BPS, administered etodolac (600mg), gabapentin (300-900mg), and amitriptyline (5-75mg) at bedtime over 6 months
- 70% improvement in VAS scores, and 60-70% improvement in ICSI and ICPI scores

Lee JW, Han DY, Jeong HJ. Bladder pain syndrome treated with triple therapy with gabapentin, amitriptyline, and a nonsteroidal anti-inflammatory drug. *International neurology journal* 2010;14:256-60

**PainWeek**

## Nerve Stimulation

### Sacral Neuromodulation

- FDA-approved for urinary urge incontinence, refractory voiding dysfunction, urgency-frequency syndrome, and idiopathic non-obstructive urinary retention
- implanted lead that lies along a sacral nerve root (usually at S3 level)

### Posterior Tibial Nerve Stimulation

- Needle inserted 5 cm cephalad to medial malleolus at the site of the posterior tibial nerve
- Usually weekly, 30 minute sessions for 10-12 weeks

Zhao J, Bai J, Zhou Y, Qi G, Du L. Posterior tibial nerve stimulation twice a week in patients with interstitial cystitis. *Urology* 2008;71:1080-4  
Tirlapur SA, Vlismas A, Ball E, Khan KS. Nerve stimulation for chronic pelvic pain and bladder pain syndrome: a systematic review. *Acta obstetrica et gynecologica Scandinavica* 2013;92:881-7

**PainWeek**

## Spinal Cord Stimulation

- Not studied in large trials
- Potential efficacy in case series

Hunter, C., et al., *Neuromodulation of pelvic visceral pain: review of the literature and case series of potential novel targets for treatment* 13(1): p. 3-17



**PainWeek**

## Conclusions

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- A wide range of disorders encompass pelvic pain
- The definition of BPS/IC has evolved to describe a chronic pain condition with a variety of associated lower urinary tract symptoms, and unpleasant sensations perceived to be related to the urinary bladder
- It is important to understand the psychosocial factors associated with chronic urologic pelvic pain syndromes, the interdisciplinary approach to management, and the role of pain management throughout the course of treatment