Aims of course/workshop
This workshop aims to discuss the importance of a multimodal approach in the treatment of patients diagnosed with chronic pelvic pain syndrome. There is emphasis on a multimodal approach while recognizing the unitary psycho-physiologic nature of both illness and healing. Discussion of neuromodulation and neuroplasticity in the treatment of chronic pelvic pain will be undertaken. Specific consideration will be given not only the symptoms as guidelines to treatment but also the patient as a whole including the environment he or she is living and functioning. New information on the importance to evaluate gut microbiome and possibility of auto-vaccinationin in the treatment of IC. Another talking point involves the degree of patient willingness.
Pain is an unpleasant sensory and emotional experience associated with actual and potential tissue damage, or described in terms of such damage.

**Definition of Pain by IASP and APS**

Pain is a more terrible lord of mankind than even death itself.

*Albert Schweitzer, 1931*
Pain is generated in the brain. It is physical and it is mental. It is physical in the sense that the nerve cells and their activity are physical. It is mental pain in the sense that it is subjectively experienced in what is generally called the mind.

Pain (like the mind) occupies a strange position between biology and culture.

What is Pain exactly?
What is its relation to suffering?
How many sorts of pain are there?
Can "physical" pain be separated from "mental" or "spiritual" pain?
Is pain private and incommunicable?

The Dynamics Between Stress, Disease and Pain

To understand the relationship between stress and disease and pain, one needs to understand that several factors act in unison to create a pathological outcome including:

- Cognitive perceptions of a threatening stimulus (Perception: conscious view of the external world. Shaped by beliefs, values and expectation)
- Activation of the sympathetic nervous system
- Engagement of the endocrine system
- Engagement of the immune system
Conditioned immunomodulation: research needs and directions

- It is now clear that immune function is influenced by autonomic nervous system activity and by the release of neuroendocrine substances from the pituitary.
- Conversely, cytokines and hormones released by an activated immune system influence neural and endocrine processes.
- Regulatory peptides and receptors are expressed by both the nervous and immune systems enabling each system to monitor and modulate the activities of the other.
- It is hardly surprising that immunologic reactivity can be conditioned in response to stressful life experiences or by Pavlovian conditioning.

Do Words hurt?

- Processing of pain-related words leads to activations within regions of the pain matrix.
- “This job is a real headache.”
- You are a “pain in the neck”
- “This makes me feel bad”
- “This is sickening”
- “My IC”
- “My Headache”
Biofeedback

Biofeedback is a technique that trains to improve health by controlling certain bodily processes that normally happen involuntarily, such as heart rate, blood pressure, muscle tension, and skin temperature.

Autogenic Training

- Hyperventilation
- Asthma
- Constipation and diarrhea
- Pain
- Ulcers and gastritis
- Tachycardia, arrhythmia
- Hypertension
- Raynaud Syndrome
- Headache
- Thyroid problems

Biofeedback Improves Relaxation Therapy’s Effects

- Biofeedback, when used in conjunction with other forms of relaxation therapies such as music, and autogenic and imagery training significantly improved physiological components including respiratory and heart rate and athletic performance in college students.

Our brain changes automatically, instantly, efficiently, seamlessly and constantly in response to changes in our body.

The messengers are our senses, thoughts, beliefs, memories, emotions and movement. They bring in constant brain altering data.

The brain also changes in response to injuries, disease, traumatic events and stressful situations.

Synapses form and disconnect at about the same rate.

Areas of the thinking brain have shown rates of 7% per week of making and breaking connections.

Hippocampus (memory) and olfactory bulb (scent) actually make new brain cells - 9000 per week in adult hippocampus.
Stopping Persistent Pain

- To decrease pain we must increase other regional functions
- What gets fired gets wired. What you don’t use you lose. During pain spikes - pain nerve cells fire and wire
- If this is countered by the firing of other regional nerve cells during pain spikes, then the population of firing pain nerves is decreased
- Eventually the brain rewires away from pain


Access to the Brain

- We do not need to be brain surgeons
- Seven holes and the biggest organ we have: Eyes, Ears, Nose, Mouth, and the Skin
- Sensation comes from billions of receptors in skin, muscle, bones, joints, etc
- The thinking brain makes decisions based upon sensory input
- Touch, position, vibration, movement, temperature, pressure, itch, pain, vision, scent, taste, sound

How do we shrink the map?

Brain is a learning machine: Learn self-efficacy
Flood the brain with other input during pain spikes with intention of changing brain.

- **Thoughts**: Opposition to pain, feeling good, shrinking pain map
- **Images**: brain maps, brain clear of pain, pleasant imagery
- **Sensations**: touch, temperature, pressure, auditory, visual, olfactory, taste, movement (proprioception)
- **Memories**: Pleasant and strong memories other than pain
- **Calming emotions**: mindfulness, pleasure, peacefulness, serenity
- **Movement** or thoughts of movement

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**Imagery**

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**Norman Doidge**

- When we wish to perfect our senses, neuroplasticity is a blessing.
- When it works in the service of pain, plasticity can be a curse.
fMRI to control Pain

- Individuals can learn to directly control activation of localized regions within the brain.
- Control over the endogenous pain modulatory system can enable a mechanism for clinical control over pain.
- Using real-time functional MRI (rtfMRI) to guide training, subjects were able to learn to control activation in the rostral anterior cingulate cortex (rACC), a region putatively involved in pain perception and regulation. When subjects deliberately induced increases or decreases in rACC fMRI activation, there was a corresponding change in the perception of pain caused by an applied noxious thermal stimulus.
- Chronic pain patients trained to control activation in rACC reported decreases in the ongoing level of chronic pain.


Mind over Pain

- Grant and Rainville exposed 13 Zen masters and 13 comparable non-practitioners to equal degrees of painful heat while measuring their brain activity in a functional magnetic resonance imaging (fMRI) scanner.
- The meditators reported feeling less pain than the control group.
- The meditating group reported feelings of pain at levels below what their neurological output from the fMRI indicated.
- Researchers also found that compared to people who don’t meditate, meditators have thicker gray matter, specifically in an area known to influence perceptions of pain (the anterior cingulate).
- The neuroplastic differences found in the brains of meditators were the real cause of their lower sensitivity to pain.

*Grant, Courtemanche, Duerden, Duncan, Rainville. Emotion. 2010 Feb;10(1):43-53*
Mirror Therapy

- Mirror visual feedback originally devised as a therapeutic tool to relieve perceived involuntarily movements and paralysis in the phantom limb.
- Since this pioneering work was conducted in the mid-1990s, the technique has been applied to relieve pain and enhance movement in other chronic conditions such as stroke and complex regional pain syndrome (CRPS) type 1.


Learning

- If prefrontal functioning is impaired placebo responses are reduced or absent similar to dementia seen in patients suffering from Alzheimer's disease.
- The placebo effect is a learning phenomenon

Pain and the Brain

- Clinicians who specialize in treating chronic pain now recognize that it is not merely a sensation, like vision or touch, but rather chronic pain is strongly influenced by the ways in which the brain processes the pain signals.

Andrew R. Block, PhD. Chronic Pain Coping Techniques - Pain Management
Brain and the Pain

The important role the mind plays in chronic pain is clearly recognized in the medical literature, as well as in the International Association for the Study of Pain's definition of pain, which states that pain is always subjective and is defined by the person who experiences it.

Andrew R. Block, PhD, Chronic Pain Coping Techniques - Pain Management

Sistine Chapel ceiling, painted by Michelangelo 1508 - 1512 commission of Pope Julius II
### Chronic Pelvic Pain

**Duration**
- Non-cyclical pain persisting for at least 6 months

**Location**
- Pelvis
- Medial aspects of thigh
- Lower abdomen
- Inguinal Area
- Low back

**Perception of Pain**
- Sharp
- Burning
- Dull ache
- Pressure/Discomfort
- Throbbing


Lee, S et al. Urol 2008; 7: 79-84

### CPP Syndromes

The complex of CPP Syndromes:
- Lower Urinary Tract
- Male Genital Pain
- Female Genital Pain
- Gastrointestinal Pain
- Musculoskeletal Pain
- Neuropathic Pain
- Psychological overlay
- Sexual Pain
- Extra-Pelvic Co-Morbidities

### Symptoms

**LUT Pain**
- **Signs**
  - Bladder Pain
    - Pain—pain, pressure of discomfort associated with bladder filling
    - Experienced in the bladder, or referred from the abdomen, lower back and/or pelvic floor
    - Frequency — ≥ 8 daytime voids
    - Urgency — persistent urge to void without fear of pain
    - Nocturia — at least one void from state of sleep, per session
  - Urethral Pain
    - Intermittent
    - During of after voiding
    - During or after intercourse
    - Persistent

**Dyspareunia**

**Urethral Pain**
- Supra-pubic tenderness
- Bladder tenderness

**Evaluation**
- **Bladder Pain/Urethral Pain**
  - Questionnaires: Voiding Diaries, O’Leary-Sant Indices, Visual Analog Sales(VAS), FSFI, IIEF
  - Post-Void Residual, Uroflow
  - Anesthetic Challenge to identify pain generator and/or referred sites
  - UA, Culture, Cytology
  - Urodynamics, Cystoscopy
  - Ultrasound, MRI, CT Scan
  - Rule-out Confusable Diseases


Lee, S et al. Urol 2008; 7: 79-84
Female Genital Pain

**Symptoms**
- Vulvodynia (skin)
  - Vulvar, vestibular or clitoral
- Uterine/Tubal Pain
  - Dysmenorrhea, infection, endometriosis, adenomyosis
- Vaginal Pain (Dyspareunia)
  - Superficial/deep
- Pelvic Floor Pain (Musculoskeletal)
  - Childbirth injuries, POP
- Pelvic Organ Malignancy
- Pain following Pelvic Surgery
  - Mesh complications, organ or nerve injuries during surgery

**Evaluation**
- Vulvodynia
  - Q-tip touch test, Algesiometry
- Uterine/Tubal
  - Imaging, C & S, Pathology
- Dyspareunia
  - Severity and QOL questionnaires
- Pelvic Floor
  - Musculoskeletal assessment
  - POP-Q Exam for prolapse
- Pelvic Organ malignancy
  - Pathology, imaging
- Following Pelvic surgery
  - Mesh contracture
  - Imaging

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Male Genital Pain

**Signs**
- Prostate
  - Tenderness with digital exam
- Scrotal
- Testicular
- Penile
- Urethral
- Epididymal

**Evaluation**
- Prostate Pain – secretion culture, UA, CPSI questionnaire
- Scrotal Pain – ultrasound (US)
- Testicular Pain – US
- Penile Pain
- Urethral Pain
- Epididymal Pain Syndrome
- Sexual Pain – Questionnaires
  - IIEF

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GI Pelvic Pain

**GI Symptoms – Anorectal**
- Chronic proctalgia
- Levator ani syndrome
- Proctalgia fugax
- Unspecified
- Anal fissure
- Abscess
- Hemorrhoids
- Crohn’s disease

**Colorectal**
- IBS
- Colitis
- Crohn’s Disease

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Musculoskeletal Pain

**Evaluation**
- Identify pain generators
- Assess muscle strength
- SJD and Sacro-Spinous Ligament
  - assess for mobility, posture, and symmetry
- Trigger point injections
- EMG, Manometry
- Imaging
  - X-Ray, MRI

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**GI Pelvic Pain**

**GI Evaluation**
- Anorectal/Colorectal
  - Questionnaires
  - Imaging
    - Ultrasound, CT, MRI
  - Identify Pain Generators

**GI Symptoms in IBS sufferers with constipation compared with general US population**

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Female Genital Pain

**Dyspareunia**

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Neuropathic Pain

Symptoms and Signs
- Infiltration of sacral nerves
- Somatic neuropathic pain
  - Iliohypogastric neuropathy
  - Ilioinguinal neuropathy
  - Genitofemoral neuropathy
  - Lateral femoral cutaneous neuropathy
  - Pudendal neuropathy
  - Neurona formation / Maladaptive neuronal plasticity
- Complex regional pain syndrome (CRPS)
- Pain following mesh injury
- Post-herpetic neuralgia
- Tarlov’s cyst

Evaluation
- Neuropathic pain questionnaires:
  - Leeds assessment for neuropathic symptoms and signs
    - Not validated for chronic pelvic pain
  - Douleur neuropathic-4 questions
  - Neuropathic pain questionnaire
    - May have unacceptable low diagnostic accuracy
  - PainDETECT
    - Not validated for chronic pelvic pain
- Cotton swab sensory testing, quantitative sensory testing, sensory pain mapping, MRI, ultrasound, nerve block (LOE 4)

Psychological

Symptoms and Signs
- Fear
- Anxiety

Evaluation
- The chief purpose of psychological assessment is to get a complete picture of the pain syndrome with all affected dimensions: somatic, affective, cognitive, behavioral and the individual consequences for the patient.
- Early referral to a psychological healthcare provider should be considered. Patients with sexual dysfunction may need sexual counseling.

Extra-Pelvic Co-Morbidities

First-Line Therapy (for all CPP)
- Education
- Behavior modification
- Exercise and exercises (eg, relaxation, stretch)
- Avoidance of flare initiators
- Diet modification
- Support groups

Treatment of Pain Generators
Bladder (IC/BPS)
- Organ-specific therapy
  - Pentosan polysulfate (PPS)¹
  - Intravesical therapies – DMSO, GAGs, alkalized lidocaine²
  - Surgery – cautery, laser, cystectomy³
- Neuromodulation⁴
  - Amitriptyline, gabapentin, pregabalin⁵,⁶
  - Neurostimulation
  - Botulinum toxin type A
- Immunomodulation⁷
  - Hydroxyurea
  - Cyclosporine, mycophenolate mofetil
- Physiotherapy⁸
  - Specific pelvic floor physiotherapy⁹
- General physiotherapy
- Cognitive behavioral therapy¹⁰,¹¹
  - Directed at depression, maladaptive coping mechanisms, social interaction including sexual functioning

DMSP = dimethyl sulfoxide.
**Sexual Health is IMPORTANT**

- Majority of women consider sexual health an important part of their overall health
- WHO considers maintenance of sexual health a responsibility of health care professionals
- WHO defines FSD as: “the various ways in which an individual is unable to participate in a sexual relationship ... as she would wish.”

**Maverick, C. et al. JAMA, 1999;281:2173-4**

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**Does clinical practice show concern for sexual health?**

- Global Study of Sexual Attitudes and Behaviors Study
  - only 14% of Americans aged 40-80 y.o. reported that a physician inquired about their sexual health concerns within the past 3 years
- Berman et al 2003
  - On line survey of women with sexual health concerns who had consulted a physician:
    - 52% - “physician didn’t want to hear about their problems”
    - 87% - “no follow up re: the complaint at subsequent visits

**Laumann et al. Archives Sex Behav, 2006;35:145–64.
Berman et al. Fertility Sterility 2005;79:572–6**

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**Does clinical education show concern for sexual health?**

- Survey: N=125, 3rd and 4th year medical students
  - 75.2% - considered taking a sexual history as an important part of their future career
  - 57.6% - considered themselves “adequately trained” in this area
- Survey: 101 US and Canadian medical schools
  - Only 10 hours of human sexuality education in 67% of programs (including contraception, STD prevention and treatment, etc.)


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**Traditional Sexual Response Cycle:**

**Masters & Johnson
Helen Singer Kaplan**

**Sexual
Excitement/Tension**

**Orgasm (s)**

**Satisfaction**

**Time following sexual stimulation**

**Basson K. Obstet Gynecol. 2003;92:1595-2.**

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**Male vs. Female “Wiring”**

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**Female sexual response:**

**Basson Model**

- Circular model, begins with neutrality, influenced by goal of emotional intimacy
- Physical desire may be reactive, rather than spontaneous
- Satisfaction = subjective reaction to the experience
- Importance of environment and stimuli that are conducive to sexual expression

**Basson, K. Sexual Dysfunction in Medicine, 2006, p199, vol 21:11
Female sexual response: Basson Model

- SWAN 2003 – Study of Women’s Health Across the Nation
- 2400 multiethnic midlife women in 6 US cities (Hispanic, Caucasian, AA, Chinese, Japanese)
- Reported many motivations for engaging in sexual play. Primary = desire for emotional closeness
- 40% = never/rarely experience physical desire at initiation or between experiences
- 87% = satisfied with their sexual relationships

Female Sexual Function

What do we know?
Only the tip of the iceberg ....

Primary mechanisms: VASOCONGESTION
- Genital vascongestion begins within 30 sec of erotic stimuli
- Parasympathetic and Sympathetic nerves release:
  - Nitric oxide
  - Acetylcholine
  - VIP (vasoactive intestinal polypeptide)

Hormones
- 40% of women with symptomatic vaginal atrophy due to low levels of estrogen confirm “adverse effects” on sexual function
- Low estrogen levels are associated with reduced baseline vaginal vascongestion (i.e., in the nonstimulated state)

Princeton Consensus Statement on Female Androgen Insufficiency

- Female androgen insufficiency consists of a pattern of clinical symptoms in the presence of:
  - Decreased bioavailable testosterone
  - Normal estrogen status
  - Clinical symptoms include impaired sexual function, mood alterations, and diminished energy and well-being

Female sexual function

Female sexual function POSITIVELY affected by:
- Stable mental health (past and current)
- Positive emotional well being and self image
- Rewarding past sexual experiences
- Positive feelings for a partner
- Positive expectations for the relationship

Lower Estrogen Levels Are Associated With Increased Prevalence of Sexual Problems

<table>
<thead>
<tr>
<th>% Reporting Problems</th>
<th>&lt;50 pg/mL Estradiol</th>
<th>&gt;50 pg/mL Estradiol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaginal Dryness</td>
<td>Green</td>
<td>Yellow</td>
</tr>
<tr>
<td>Bothered by Problem</td>
<td>Green</td>
<td>Yellow</td>
</tr>
<tr>
<td>Dyspareunia (Intimacy)</td>
<td>Green</td>
<td>Yellow</td>
</tr>
<tr>
<td>Pain With Penetration</td>
<td>Green</td>
<td>Yellow</td>
</tr>
<tr>
<td>Burning</td>
<td>Green</td>
<td>Yellow</td>
</tr>
</tbody>
</table>

n = 90: significance not reported

Female Sexual Function

Hormones
- 40% of women with symptomatic vaginal atrophy due to low levels of estrogen confirm “adverse effects” on sexual function
- Low estrogen levels are associated with reduced baseline vaginal vascongestion (i.e., in the nonstimulated state)
  - Peak androgen production mid 20’s
    - Halved by age 60
  - Large scale study: FSD + low FAI
    - Significant decrease in desire, mood, well being
  - Premenopausal women: HSDD + A-lowest quartile
    - Significant decrease in desire, energy

**Female Sexual Function: Aging**

- Clitoral perfusion/engorgement/arousal diminished = decreased lubrication
- Decline neurophysiologic response: decreased touch, perception, vibratory sensation, and slowed reaction time = lengthened O latency time
- Decreased muscle tone = PFM/Uterine contractions diminish = decreased O amplitude


**Female Sexual Health in Urogynecology**

- National Health and Social Life Survey (1999):
  - Strong assoc between urinary tract sxs and arousal disorders (odds ratio 4.2)
  - Sexual pain disorders (odds ratio 7.6)
- Screening, identifying, and managing sexual complaints can result in significant improvement in overall QOL for women

Laumann, ED. et al. JAMA, 1999;281: 537–44
Laumann, ED. et al. Arch Sex Behav, 2006;35:145–61

**Neurotransmitters and Mood**

- Neurotransmitters regulate mood, cognition, and behavior, including sexual motivation and reward seeking

**FSD definitions**

- **Hypoactive sexual desire disorder**
  - The persistent or recurrent lack of sexual fantasies, thoughts, desires and receptivity to sexual contact.
- **Sexual aversion disorder**
  - The persistent or recurrent fear or aversion of sexual contact.
- **Sexual arousal disorder**
  - The persistent or recurrent inability to become sexually aroused, often characterized by inadequate vaginal lubrication for penetration.
- **Orgasmic disorder**
  - The persistent or recurrent inability to orgasm.
- **Dyspareunia**
  - Pain during sexual intercourse.

**Must cause personal and/or interpersonal distress**


**FSD is complex: Physiologic & Psychological Components**

- Sexual function based primarily on **intimacy**
  - Important to understand and quantify genital responses, but also consider how sexual stimuli are "processed"

Important to assess if sexual symptoms are:
- reflecting normative changes across the lifespan
- adaptations to a particular situation
- related to her medical illness
- of unexplained etiology

Important to assess if patient is experiencing **distress** as a result of sexual changes, or simply reporting that they occur

**FSD: Diagnostic Inventories**

**The Female Sexual Function Index (FSFI)**
- 19 items, internal consistency, test-retest reliability
- Discriminates FSD in 5 domains:
  - desire, arousal, orgasm, satisfaction and pain

**The Sexual Function Questionnaire (SFQ)**
- 31 items, reliability and validity established
- Discriminates FSD in 7 domains, including partner satisfaction

*Kuway, B. et al. Sex and Mental Therapy, 2016, 36:310–28
Most common sexual complaints in urology:

Dyspareunia
Lack of arousal

- Women may be unable to separate these two
- Dyspareunia leads to fear of more pain and altered arousal (psychological and physical)
- Poor arousal can lead to poor lubrication, which can lead to dyspareunia


Dyspareunia

Affects ALL aspects of the female sexual response (eg: desire, arousal, orgasm, satisfaction)

Dyspareunia : 2 types

- Superficial (entry) :
  - often due to inflammation at the introitus associated with: UTI, urethritis, vaginitis, provoked vestibulodynia
- Deep (thrusting) :
  - often occurs in women with CPP related to bladder, uterine, ovarian, bowel or pelvic floor muscle pathology

Hypersensitivity disorders can cause or complicate FSD symptoms in urogynecology
  - CPP/IC/BPS, HTPFD, PVD, etc


Features of Dyspareunia

- Localized or generalized (or both)
- Superficial or deep (or both)
- Aggravated by penetration or thrusting (or both)
- Primary or Secondary
- Constant or Episodic
- May or may not have a clearly discernible sentinel event
- Mean time to dx=4.4 yrs

Descriptions of Dyspareunia

- Ripping
- Tearing
- Burning
- Friction
- Irritation
- Itching
- “Deep” pain
- Feeling of need to urinate during vaginal intercourse
- Feeling that something is “hitting” or “blocking”

Examination for sexual pain

- Inspection of external genitalia
  - Muscle tone, skin color/texture/turgor/thickness, pubic hair
  - Cotton swab test (pain mapping): vulva, vestibule, hymenal ring.
  - Bartholin’s and Skene’s glands
  - Vulvar atrophy, vulvar dystrophy, vulvar vestibulitis, HPV infection
  - Retract clitoral hood and expose clitoris
  - Examine posterior fourchette and hymenal ring

- Bimanual vaginal examination
  - Palpate rectovaginal surface, levator muscles, vaginismus, bladder/urethra
  - Episiotomy scars, strictures, vaginal adhesions, vaginal atrophy, vaginal pH
  - Speculum examination and Pap smear
  - Evaluate for prolapse, vaginal length, vaginal mobility
  - Perform uterus, adnexa, rectal examination
  - Rectal disease, vaginismus, levator ani myalgia, IC, UTI
  - Postoperative or post-radiation changes, stricture
  - Fibroids, endometriosis, masses, cysts


Important Points about Sexual Pain

- The pain is REAL!
- Impacts QOL
- History taking/accurate diagnosis: KEY
- Realistic expectations
- Multi-disciplinary approach is necessary