Chronic Pelvic Pain—A new Paradigm

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CPP Substantially Impacts Quality of Life

Effect of CPP

- Pain During/After Intercourse: 88%
- Impacted Energy: 82%
- Reduced Activity: 58%
- Interfered With Mood: 56%
- Felt “Downhearted and Blue”: 47%
- Stayed in Bed: 26%

CPP Is a Significant and Common Disorder in Women

• Magnitude of CPP
  – >9 million women in the United States¹
  – 20% of women had pelvic pain >1 year in duration²

• CPP accounts for
  – 10% of referrals for OB/Gyn visits³
  – Over 40% of laparoscopies⁴
  – 18% of hysterectomies⁵

• Patients with CPP have significantly lower general health scores compared with patients without CPP¹

• CPP is associated with painful intercourse (dyspareunia)

Majority of Women With CPP Have No Obvious Etiology

61% Undefined Etiology

39% Confirmed Diagnosis

“The Pelvic Theatre”

- There is more in the pelvis than gynecologic organs
- Need to see and examine the entire pelvis
- Consider all systems
Muscles of the Perineum
(female, inferior view)

- Clitoris
- Urethral orifice
- Vaginal orifice
- Ischiocavernosus
- Bulbospongiosus
- Superficial transverse perineus
- Levator ani:
  - Pubococcygeus
  - Iliococcygeus
- Gluteus maximus
- External anal sphincter

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Pelvis and Ligaments, Rear View, Female
Nerve Supply

- Autonomic nervous system
  - Parasympathetic vs Sympathetic
  - Hypogastric plexus: T10-L2 sympathetic
  - Pelvic nerve: S2- S4 parasympathetic
  - Pelvic plexus: joining of hypogastric and pelvic nerves lateral to rectum
Somatic Nerves

- Iliohypogastric
  - L1
  - Innervates skin above pubic bone, lower abdominal muscles, posterior lateral gluteal region

- Ilioinguinal
  - L1
  - Innervates mons pubis, external genitalia, upper medial thigh

- Genitofemoral
  - L1, 2
  - Innervates upper anterior thigh and mons pubis
Somatic nerves cont

- **Lateral femoral cutaneous**
  - L2, 3
  - Innervates lateral and anterior thigh to knee

- **Femoral**
  - L2, 3, 4
  - Quadratus lumborum, sartorius, pectineus, psoas, iliacus, medial ant thigh and lower leg (cutaneous), knee joint

- **Obturator**
  - L2, 3, 4
  - Adductor muscles, medial thigh cutaneous
Pudendal nerve

- S2, 3,4
- Out greater sciatic notch between piriformis and coccygeus
- Hooks around sacrospinous ligament, Enters back into pelvis though lesser sciatic notch, continues medial to ischial tubersity through alcocks canal
- Inferior rectal branch innervates posterior perineum
- Finally braches into perineal branch (middle perineum) and dorsal nerve to the clitoris or penis
Pudendal nerve continued

- Innervates superficial and perineal membrane muscles, external anal sphincter: inferior rectal branch, cutaneous perineal area and clitoris
- Damage may occur during vaginal delivery, prolonged increased intra-abdominal pressure (lifting, coughing, vomiting, exercising), surgery
Direct efferents from $S_2-S_4$
(nerve to levator ani m.)

Pudendal n.

Levator ani m.

Puborectalis m.
Female Pudendal Nerve

- Clitoris
- Urethral orifice
- Ischiocavernosus muscle
- Vaginal orifice
- Bulbospongiosus muscle
- Perineal membrane
- Superficial transverse perineus muscle
- Dorsal nerve of clitoris
- Posterior labial nerve
- Deep perineal nerve
- Superficial perineal nerve
- Perineal nerve
- Pudendal nerve
- Levator ani muscles
- External anal sphincter
- Inferior anal nerve

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Source of CPP in Female Patients

Visceral Sources of Pelvic Pain

- Reproductive causes are the source of CPP in only 20% of patients

Chronic Pelvic Pain Is Characterized by Overlapping Disease Conditions

- Interstitial Cystitis
- Endometriosis
- GI Disorders
- Recurrent UTI
- Vulvodynia
- Pelvic Infection and Adhesions
Associated Medical Conditions

• IC/Bladder Pain Syndrome
• Vulvodynia
• Endometriosis
• IBS
• Tension Headaches
• Fibromyalgia
• Chronic Fatigue Syndrome
• Temporomandibular Joint Disorder
Gynecologic causes

- Endometriosis
- Adenomyosis
- Ovarian Remnant Syndrome
- Adhesions?
Vulvar Causes of Chronic Pelvic Pain

- Vulvodynia
- Lichens Sclerosis
- Lichens Planus
- Vaginal/vulvar Atrophy
- HPV
Functional Bowel Disorder as Cause of Chronic Pelvic Pain

• Irritable Bowel Syndrome (IBS)
• Functional GI disorder characterized by abdominal pain or discomfort associated with changes in bowel habit and features of disordered defecation
• ROME III Criteria—recurrent abdominal pain or discomfort at least 3 days/month in the last 3 months
NeuroMuscular Pain as Cause for Chronic Pelvic Pain

- Pelvic Myalgias/muscle spasms
- Neuropathic pain

Causes of neuromuscular pain

--Trauma
--Obstetrical
--Surgery
--Medical conditions
Spectrum of IC Symptom Severity OverTime

- IC symptoms range from mild to severe and may be attributed to other conditions in the early stages

Endometriosis/Vulvodynia “Misdiagnosis”
Chronic Pelvic Pain (CPP) Syndrome
Advanced CPP Syndrome—Multiorgan disease

Increasing Severity

- UTI “Misdiagnosis”
- Urge/Freq Failed OAB Tx
- Urethral Syndrome
- NIDDK IC
- Advanced IC

NIDDK = National Institute of Diabetes and Digestive and Kidney Diseases.
“The classical view that pain is due to altered neuronal responses only is not the case”
—Ihssane Zouikr, PhD, RIKEN Brain Science Institute

“To understand pain, we need to understand the interaction between the immune, endocrine and nervous systems and how alteration in one system will lead to alteration in the whole ‘mutisystem' network,” Ihssane Zouikr, PhD, RIKEN Brain Science Institute in Waco, Japan
The Neuroendocrine-Immune Link

There are numerous possible mechanisms underlying the link between hyperalgesia and

In recent years, the role of the immune system in pain has become well-established.

“Pain is by nature inflammatory, so there is activation of immune cells at the peripheral level.

“When these immune cells are activated, they release pro-inflammatory cytokines—such as

Interleukin IL-1 was found to directly activate the HPA axis and promote the release of glu
Early Adverse Events & the HPA Axis

The hypothalamic-pituitary-adrenal (HPA) axis is a primary mediator of the stress response.

“The HPA axis goes through a period of significant change and development during the period of pregnancy.”

Dr Zouikr and colleagues from the University of Newcastle in Australia, who examined early adverse events on the HPA axis, report:

*In utero* exposure to stress, for instance, has been associated with impaired endocrine function.
Considering the sum of the evidence, the authors believe there is multisystem interaction in

“Instead of targeting only the neuronal component of pain, we need to target the inflamm

“But also clinicians need to consider the early life history of their patients when treating chron
A negative pain mindset – catastrophizing

» Undermines pain treatment effectiveness and facilitates structural brain changes that serve to maintain pain and distress.

» In short, catastrophizing makes pain more painful, last longer, and much harder to treat.

» Pain catastrophizing is the negative expectation of actual or anticipated pain, and is comprised of persistent rumination on pain, mental magnification of pain, and feelings of helplessness.
The Persistent Pain Cycle

Persistent Pain

Time off work, money worries, relationship concerns

Negative thinking, fear of the future, depression/mood swings

Sometimes the arrows can also go anti-clockwise as well. For example - time off work can lead to negative thinking fear of the future - can lead to stress, fear etc.

Loss of fitness, weak muscles and joint stiffness

Create ‘no go’ lists of things you cannot do

Sleep problems/tiredness/fatigue

Stress/fear/anxiety/anger/frustration

Weight gain/loss

Being less active
Opioid-induced Hyperalgesia

Though the long-term use of opioids for chronic pain treatment has increased significantly, there is a lack of evidence supporting this approach. As a result, experts are concerned that it may be ineffective or even harmful because of the paradoxical opioid-induced hyperalgesia (OIH) that has been observed.

Following peripheral nerve injury, spinal release of danger-associated molecular patterns (DAMPs) activates the Toll-like receptor 4 (TLR4) signaling pathway, resulting in spinal microglial reactivity.

Opioids also activate TLR4, leading to release of pro-inflammatory mediators (including Interleukin 1β [II-1β] and Nuclear Factor NF-κB).

Previous research has described a “two-hit hypothesis of microglial priming” in which the neuroinflammatory response is enhanced upon secondary challenge. In this model, peripheral nerve injury-related neuropathic pain is considered 'hit 1;' this pain can be exacerbated by opioid treatment (hit 2).
Evaluation

• Consider all potential causes of pain
• Thorough History
• Thorough Exam
  --examine vulva, vagina, pelvic muscles, bladder, rectum, pelvic organs
• Assess the emotional/psychological needs
• Supplemental labs as needed
• Testing as needed—ultrasound, cystoscopy, awake pain mapping, traditional laparoscopy
“How I See It”

• Need to understand all causes of pt’s pain
• Evaluate all the organ systems in the pelvis—The Pelvic Theatre
• Concept—Stage the CPP
• Develop treatment regimen that addresses every aspect of pt’s pain
• Multiorgan Pelvic Pain Syndrome (“MOPPS”)
Conceptual Staging for CPP—“MOPPS”

- Stage 1—duration ≥ 6 months in < 1 year organ system(s) affected - 1
- Stage 2—duration ≥ 6 months < 2 years organ systems affected - 2
- Stage 3—duration ≥ 6 months < 5 years organ systems affected - 3
- Stage 4—duration ≥ 5 years organ systems affected > 3
Conceptual Staging of CPP

- Pre-CPP—an “in situ” stage
  duration ≥ 1 month < 6 months
  organ system affected - 1

Organ Systems Considered

Bladder                  Psychiatric
Reproductive             Nervous system
GI                        Epidermal/skin
Musculoskeletal          Immune
Conceptual Staging of CPP Summary

• CPP “in situ”/pre CPP-<6 months
• Stage 1-< 1 year/1 organ
• Stage 2-<2 years/2 organs
• Stage 3-<5 years/3 organs
• Stage 4->5 years/> 3 organs

Hypothesis—Treatment—the higher the stage, the more intensive treatment required to resolve the pain
Goals of Therapy

• Address underlying pathology(s) of CPP
• Set expectations
  – Time to response
• Establish long-term treatment plan
  – Lifestyle change
Goals of Therapy

• Develop an individualized treatment plan for the particular patient
• Treatment plan must address all of patient’s causes of pain
• Multidisciplinary approach to address all areas contributing to pain
Collaborative Effort

• MD and NP—
  – Evaluate the patient
  – Develop the treatment plan
  – Medications as indicated
  – Office/outpt treatments as indicated
    • Trigger point injections/pudendal/scope(s)

• Physical Therapist
  – Pelvic Floor PT

• Psychiatric Nurse Practitioner
  – Counseling
  – Assist in medication therapy
Collaborative Effort

- Surgical Options
  - Cystoscopy
  - Awake Pain Mapping
  - Laparoscopy
    - Excision of endometriosis
    - Appendectomy
    - Lysis of Adhesions
  - Interstim
  - Trigger point injections/pudendal nerve injections
Pharmacologic Therapy-adjuvant considerations

- Amitriptyline/imipramine
- Antihistamines—ex. Atarax
- Elmiron/Intravesical treatments
- Antispasmodics
- SSRI’s
- Gabapentin/Lyrica
- Gabapentin/lidocaine ointments
- NSAID’s—PO, patches, creams
- GNRH Agonist
- Hormonal considerations
- “Holistic” considerations—fish oil, hyaluronic acid, Chondroitin, other
- Allograft/stem cell technology
- Vaginal suppositories
Collaborative Effort

- Gastroenterologists
- Interventional radiology
- Pain specialty
- Neurology
- Rheumatologist
- Accupuncturist
- Dietician
- Massage therapist
- Physical Therapist
- Psychological support
Therapy continued

• Begin multidisciplinary therapy
  – Diet modification
  – Behavioral changes
  – Medication
  – Trigger point injections
  – PT
  – Counseling
  – Surgery as indicated
Pain Catastrophizing—Therapy

» Cognitive behavioral therapy (CBT) effectively reduces pain catastrophizing

» Changing mental focus (cognitive restructuring)

» Apply mind-body relaxation response skills

» Shaping a positive mindset is an active process

» Mindfulness-based stress reduction

» Yoga
Therapy continued

• Reevaluate after institution of therapy
  – What’s working? What’s not?
• Adjust therapy based on progression
• Add additional therapy as needed
• Add additional therapists as needed—
  – Interventional radiology—CT guided injections
  – Pain specialists—other injections
  – Other specialists
Therapy continued

• Continue to reassess
• Continue to adjust
• Begin to withdraw therapies as patient responds
• Educate patient that she can have recurrence
Summary

• CPP is a common condition that affects millions of women
• CPP is a multiorgan, multisystem disease
• CPP is a complex disorder
• CPP requires a multidisciplinary approach to adequately address all of the conditions that contribute to the syndrome
Summary

• Therapy may include medical therapy, physical therapy, surgical therapy
• Therapy requires a team approach
• By addressing all of the causes of the pain, most women can achieve improved quality of life with proper therapy
Don’t Lose......
...sight of the big picture
Thank you

• Questions??