

CHRONIC PAIN AND INTERSTITIAL CYSTITIS

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CHRONIC PAIN AND INTERSTITIAL CYSTITIS

- **Pain definition and basic pathophysiology**
- **Causes of Interstitial Cystitis pain**
- **Pain Assessment and Conclusion**

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Defining Pain

“An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.”



International Association for the Study of Pain (IASP)

International Association for the Study of Pain Web site. Available at: <http://www.iasp-pain.org/terms-p.html>, Accessed September 30, 2004.

PHYSIOLOGICAL PAIN



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Pain Perception: A Necessity

- **Pain is an essential protective mechanism**
- **The inability to perceive strong stimuli may lead to severe injury:**
 - **Children born without the perception of pain**
 - » **usually die young**

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Classifying Pain

Duration




Acute

vs

Chronic

Pathophysiology



Nociceptive

vs

Neuropathic

Acute vs. Chronic Pain

Acute pain	Chronic Pain
<ul style="list-style-type: none"> • Associated with tissue damage • Increases autonomic activities • Resolves with healing • Has a protective function 	<ul style="list-style-type: none"> • Continues after the projected period of healing • Mostly non protective functions • Decreases health and functioning • Contributes to depression

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Nociceptive Vs. Neuropathic Pain

Nociceptive	Neuropathic
<ul style="list-style-type: none"> • Stimulus originate outside the nervous system • Proportional to the receptor stimulation • May have protective functions 	<ul style="list-style-type: none"> • Originates from injury or changes in the nervous system • No stimulation of nociceptors required • Pain disproportioned to the stimulus • No protective functions

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Descartes (1596-1650) Pain Perception

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1965 Melzack and Wall The Gate Control Theory

INTERNATIONAL ASSOCIATION FOR THE STUDY OF PAIN

Row Melzack Patrick D Wall

PHYSIOLOGICAL NOCICEPTION

Excitability in dorsal horn neurons is determined by balance between excitatory inputs from primary afferents and inhibitory inputs (local and descending)

Local Descending
Dorsal horn neuron
To brain

Excitatory synapse
Inhibitory synapse

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Normal Pain Pathways

TRANSMISSION MODULATION

Key:
 RVM = rostroventral medulla
 PAG = periaqueductal grey
 C = cingulate cortex
 F = frontal cortex
 SS = somatosensory cortex
 A = amygdala
 H = hypothalamus
 — Ascending pathway
 — Descending pathway

Injury

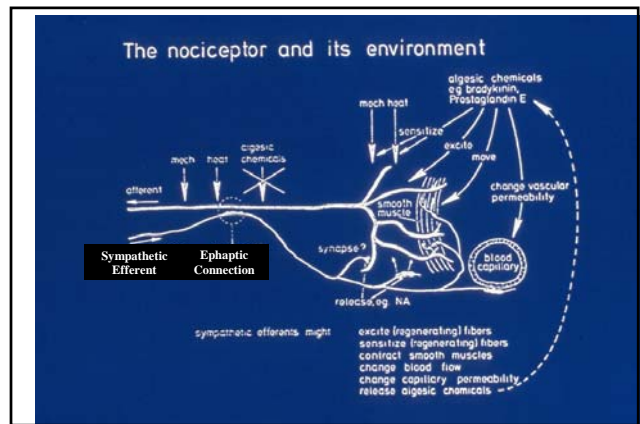
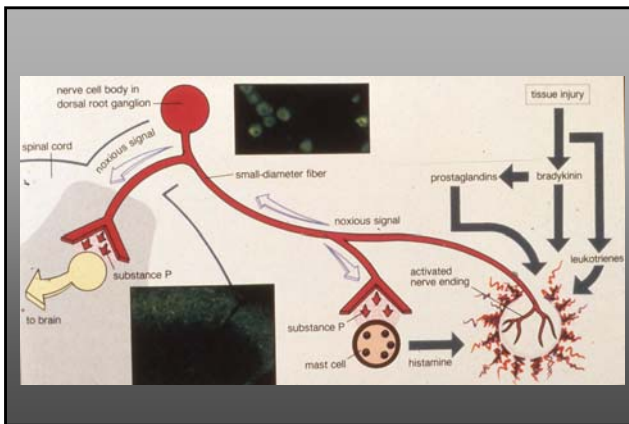
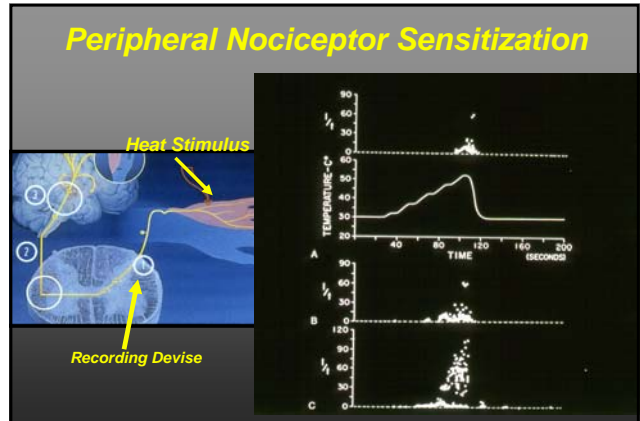
Adapted with permission, from Fields. In: *The Placebo Effect: An Interdisciplinary Exploration*, 1997.

CLINICAL PAIN: A System Gone Awry

Most clinical pain syndromes are caused by an abnormal nociceptive system:

- A series of strong stimuli or inflammation
 - Lowers the threshold of peripheral nociceptors
- Injury or alteration of peripheral nerves
- Repeated nociceptive impulses reaching the CNS
 - lead to CNS' alteration
 - » gradual expansion of the area with a lower nociceptive threshold.

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Changes in the Dorsal Horn Post- Herpetic Neuralgia

Watson C.P.N. et al. *Pain* 44 (1991) pp.105-117

NEUROPATHIC PAIN MECHANISMS (I) INCREASE EXCITABILITY OF DORSAL HORN NEURONES

Nerve injury reduces inhibitory input, increasing excitability in dorsal horn neurones. Primary afferent inputs now evoke a much greater response, and dorsal horn neurones may fire spontaneously

The diagram illustrates the mechanism of neuropathic pain. It shows a primary afferent input to a dorsal horn neuron, which then projects to the brain. The diagram shows that nerve injury reduces inhibitory input, leading to an exaggerated pain response. The diagram also shows that nerve injury leads to the release of algogenic chemicals, which further sensitize the primary afferent input.

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NEUROPATHIC PAIN MECHANISMS (IV) Spontaneous Firing Dorsal Root Ganglion

Sensory function after nerve injury with spontaneous firing along axon

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NEUROPATHIC PAIN MECHANISMS SPONTANEOUS FIRING OF DORSAL HORN NEURONES

Sensory function after nerve injury with spontaneous firing of dorsal horn neurons in spinal cord

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Spontaneous activity in primary afferents can produce peripheral sensitisation in injured and uninjured adjacent neurons. Partial denervation increases relative concentrations of neuron growth factor for intact cells

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A BETA FIBERS NORMAL SENSORY FUNCTIONS

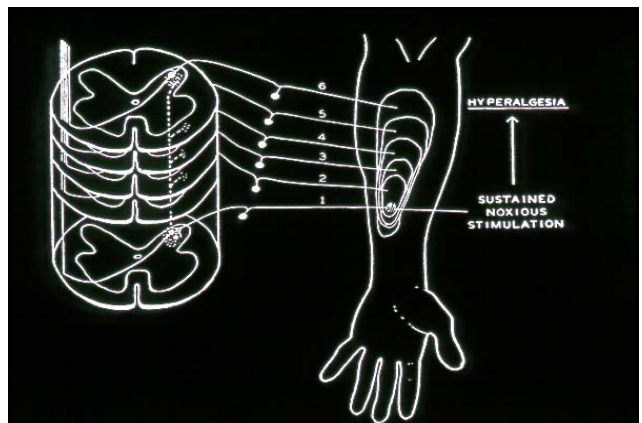
Normal sensory function. Activation of Aβ fibre by low threshold stimuli is unable to activate dorsal horn pain pathways

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NEUROPATHIC PAIN MECHANISMS CENTRAL SENSITIZATION

Increased nociceptor drive leads to central sensitisation of dorsal horn neurons. Aβ fibre input is now sufficient to activate spinal cord pain pathways

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THERAPEUTIC IMPLICATIONS

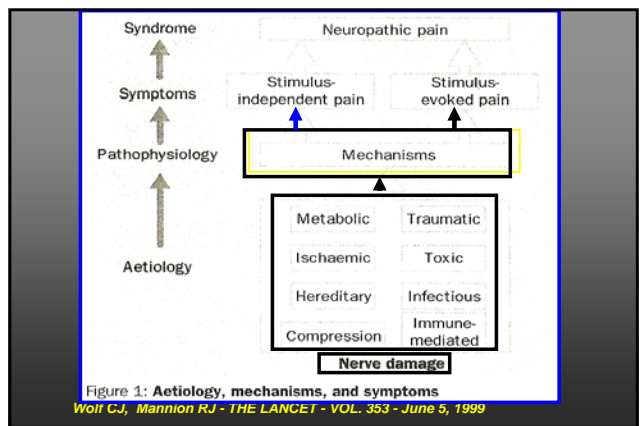
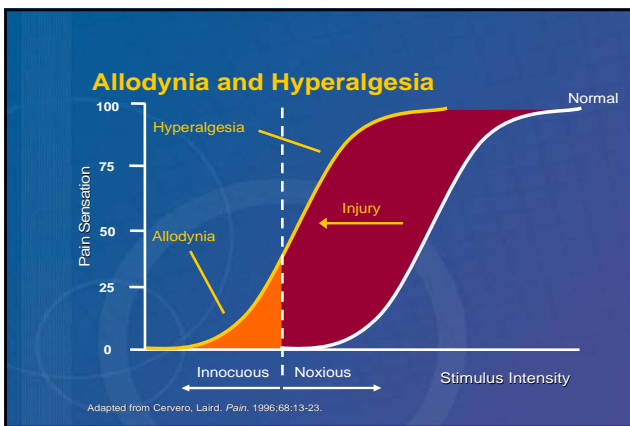
Any drug that:
decreases or blocks transmission of neural impulses from the first to the second neurons or impairs neuroplasticity

Opioids
Local anesthetics
NMDA receptor antagonists

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Effects of Opioids on Transmission of Noxious Impulses

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Stimulus-Evoked Symptoms

Allodynia	Pain caused by a normally non painful stimulus
Hyperalgesia	Increased pain experience caused by a normally painful stimulus
Hyperpathia	Explosive response to a normally painful stimulus

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Spontaneous Symptoms

Spontaneous Pain	Persistent burning, shooting –like pain
Dysesthesia	Abnormal unpleasant sensation (shooting, lancinating, burning)
Paresthesia	Abnormal but not unpleasant sensation (tingling)

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INTERSTITIAL CYSTITIS

Interstitial cystitis
Painful bladder syndrome
Complex visceral pain syndrome
Reflex sympathetic dystrophy of the bladder
Complex regional pain syndrome type I of the pelvis

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INTERSTITIAL CYSTITIS

IC closely resemble:
Chronic abacterial prostatitis now renamed by NIH chronic pelvic pain syndrome
Pelvic floor dysfunction
Frequency-urgency syndrome

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EXPERIMENTAL CYSTITIS IN RATS (I)

Infection of rat tail with pseudorabies virus causes tail necrosis and the virus travels in the spinal neurons causing an infection. These of neurons are close to those that innervate the bladder.

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EXPERIMENTAL CYSTITIS IN RATS (II)

The infection causes an immune response which activates the bladder neurons causing a cystitis.
Section of the bladder's innervation prevents the cystitis
There are no viruses in the bladder
The cystitis is neurogenic

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INTERSTITIAL CYSTITIS

*Neurologic generators
of
nociception*

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INTERSTITIAL CYSTITIS

- **Hypersensitivity of urinary bladder**
– Exaggerated abnormal sensory and motor reactions to the presence of urine in the bladder\
 - » Can cause debilitating hyperalgesia and allodynia
 - Urgency to urinate
 - Small volumes

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Interstitial Cystitis Symptoms

Daily (or constant) pain	55%
Dysparunia	50–75%
Dysuria	60%
Hematuria	22%
Nocturia	50%
Pelvic pain	70%
Perineal discomfort (scrotal/vaginal/groin)	
Prolonged pain after intercourse (i.e., days)	37%
Urge Incontinence	Rare
Urinary frequency	91%
Urinary urgency	92%

INTERSTITIAL CYSTITIS

- **Pelvic pain often triggered or increased by:**
 - stress,
 - use of acid foods,
 - food with high potassium concentration (apple and orange juice),
 - alcohol.

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INTERSTITIAL CYSTITIS

IC frequently associated with pelvic nerve injury / surgery:
 Prolonged post-partum urge-incontinence -> very high risk of prolonged symptoms
 44% had hysterectomy several months before onset vs. 17%
 Majority of men had transurethral prostatectomy 6 months before diagnosis but some may have had the symptoms before the surgery

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INTERSTITIAL CYSTITIS

Pelvic pain in IC may be due to pelvic floor muscle dysfunction
 Myofascial trigger points in pelvic floor muscles may generate bladder pain and voiding symptoms
 Hypertonus of the pelvic floor muscles may initiate neurogenic inflammation of the bladder.

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INTERSTITIAL CYSTITIS

Chronic neurogenic inflammation of the bladder can cause vulvar vestibulitis
 Strong association between chronic pelvic pain, irritable bowel syndrome and fibromyalgia
 Patients with IC are 100 x more likely to suffer from inflammatory bowel disease and 30 x more likely to have systemic lupus

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NEUROPATHIC PAIN CHARACTERISTICS

- Background dull-aching pain
- Allodynia, hyperalgesia
- Electric-like shock - shooting pain
- Exacerbation with strange unpleasantness and radiating character
- Worms or ants under skin
- Dysesthesia (uncomfortable sensation with great unpleasantness caused by slightest stimulus but not by firm pressure)

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Measurement of Pain Intensity

Numeric Scale 0 -10 (0 No Pain-10 Worst Pain)

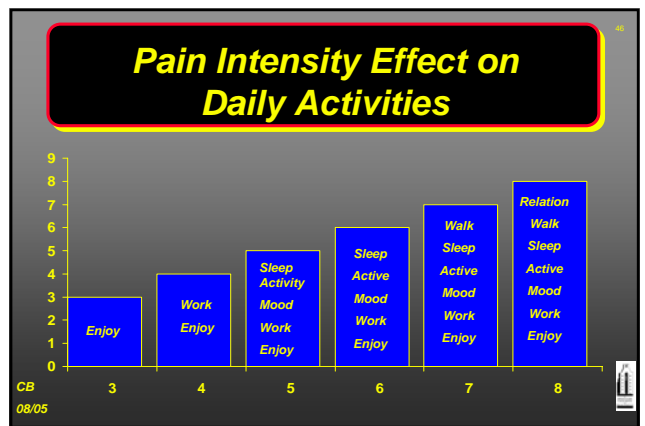
Descriptor (Mild-Moder.-Severe-Excruciating)

Bearable - Unbearable

Distractible - Distracting

Satisfied - Unsatisfied

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Neuropathic Pain Therapeutic Modalities

Opioids are not as effective in controlling neuropathic pain as they are in controlling nociceptive pain

Poly-pharmacy often needed

- Opioids
- Anticonvulsant
- Tricyclic Antidepressant
- Trigger Points Stimulation
- Biofeedback, Relaxation, imaging

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Interstitial Cystitis Challenges to Consider

- To know what we know
- To know what we don't know
- To know that we do not know
 - what we don't know

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