Rethinking Back Pain
based on
Epidemiology and Basic Science Discoveries

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Disclosure

• Up-to-Date author – Royalties
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Spine Care Report Card

- Medical Expenditure Panel Survey
  - ICD-9 codes to capture spine conditions
  - 1997 to 2006
  - Utilization, expenditures and health status

Increase in self-reported disability because of back pain

Martin BI, Deyo RA, et al. JAMA 2008; 299: 656-64

Slide courtesy of Richard Deyo, MD
From 1997 through 2006...

- No changes in reported back pain within the population
Changes in *Adjusted* Expenditures between 1997 and 2006

<table>
<thead>
<tr>
<th></th>
<th>Change</th>
<th>Description</th>
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<tbody>
<tr>
<td>Inpatient</td>
<td>↑ 53 %</td>
<td>29% of total expenditures</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ 85 % cost / fusion</td>
</tr>
<tr>
<td>Outpatient</td>
<td>↑ 77 %</td>
<td>↑ 60 % total visit</td>
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<tr>
<td></td>
<td></td>
<td>↑ 7 % visits / pt</td>
</tr>
<tr>
<td>Medications</td>
<td>↑ 232 %</td>
<td>↑ 33 % # prescriptions / pt</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No ∆ in % with prescriptions</td>
</tr>
<tr>
<td>Opioids</td>
<td>↑ 660 %</td>
<td>↑ 84 % Cost / visit</td>
</tr>
<tr>
<td>ER Visits</td>
<td>↑ 132 %</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>↑ 82 %</td>
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* Adjusted for age, sex, co-morbidities and inflation
Disability was *chosen* by more people
Back pain related disability is a choice!
Choices that result in disability are influenced by what people believe about back pain.....
....altering beliefs about back pain could alter choices about disability!
....altering beliefs about back pain could alter choices about disability!

How?

Offer patients “alternative facts!”
Science- the systematic study of the structure and behavior of the physical and natural world through observation and experiment.

- Epidemiology - the study and analysis of the patterns, causes, and effects of health and disease conditions in defined populations.
- Basic science - the sciences such as anatomy, physiology, pathology, or biochemistry fundamental to the study of medicine.
- Clinical research - science that determines the safety and effectiveness (efficacy) of medications, devices, diagnostic products and treatment regimens intended for human use. These may be used for prevention, treatment, diagnosis or for relieving symptoms of a disease.
Important Beliefs that Affect Choices Resulting in Disability

- Spinal degeneration
Important Beliefs that Affect Choices Resulting in Disability

• Spinal degeneration

• Relationship between degeneration and pain
Important Beliefs that Affect Choices Resulting in Disability

- Spinal degeneration
- Relationship between degeneration and pain
- Back pain
Important Beliefs that Affect Choices Resulting in Disability

• Spinal degeneration

• Relationship between degeneration and pain

• Back Pain

• Recovery
Important Beliefs that Affect Choices Resulting in Disability

- What do patients believe caused their spinal degeneration....
What do patients believe caused their spinal degeneration....

.....physical activities!
“Cumulative Injury Model” of Disc Degeneration

• Abnormal or awkward stresses, strains and repetitive movements damage spine structures

• “Cumulative Injury Model” is engrained in our societal wisdom about the spine
Risk of Disc Degeneration

• Serial lumbar MRIs over 5 years on 41 asymptomatic adults
  – Lack of sports activities predicted progression of disc degeneration (OR 2.71; CI 1.04-7.07)

• Disc degeneration more prevalent in sedentary than ambulatory workers
Epidemiology
Disc Degeneration – Twin Studies

• Predictors of disc degeneration

  — **Heritability** - 74%

  — Occupational exposures – 1%

Epidemiology

Genetic factors drive disc degeneration

• Apoptosis

• Disc matrix
  - Etc........................................................................................................................................
Basic Science

Pathology of Disc Degeneration

- Disk degeneration is driven by diminishing cell function
  - Apoptosis, senescence, changes in cell phenotype
  - Decreased number of viable cells capable of synthesizing correct matrix components along with increased catabolism of existing matrix
Pathophysiology

Consequence of Loss of Cell Function

• Nucleus pulposus
  – Loss of proteoglycans
  – Loss of water content
  – Fissures develop
  – Loss of disc volume and height

  • Anderson DG, Tannoury C. Molecular pathogenic factors in symptomatic disc degeneration. Spine J 2005;5:260S-266S
Pathophysicsology

Consequence of Loss of Cell Function

- **Annulus Fibrosis**
  - Breakdown of collagen fibrils
  - Weakening of lamellae of annulus
  - Lamellae will fail when their ability to maintain tension is less than intradiscal pressure
Pathophysiology
Consequence of Loss of Cell Function

- **Annulus Fibrosis**
  - Breakdown of collagen fibrils
  - Weakening of lamellae of annulus
  - Lamellae will fail when their ability to maintain tension is less than intradiscal pressure

- **Annular Tears**
  - Noted as early as age 10
  - By age 30 everyone has annular tears
What do patients believe caused their spinal degeneration....

Degeneration is driven by diminished cell function (aging) that is largely determined by genetics.
Important Beliefs that Affect Choices Resulting in Disability

- Spinal degeneration

- **Relationship between degeneration and pain**
Relationship between degeneration and pain...

... spinal degeneration is the cause of their pain
Basic Science
Back Pain in Mice

- SPARC (secreted protein acidic and rich in cysteine) deficient mice have an error in collagen production
- Demonstrate premature disc degeneration
- Behavioral signs of back and radicular pain
Basic Science

Disc damage and pain

- Chemical disc injury ➔ hind paw allodynia
Relationship between degeneration and pain...

... spinal degeneration is could be the cause of their pain

Slide courtesy of Aage Indahl, MD
Epidemiology
Disc Degeneration and Back Pain in Adolescents

• Early disc degeneration increases risk of recurrent back pain episodes
Epidemiology
Disc Degeneration and Back Pain in Adults

• Weak association between severity of disc degeneration and the frequency of back pain episodes
Epidemiology
Disc Degeneration and Back Pain

- Twin studies confirm that disc degeneration increases risk for low back pain, though the risk is small.
Relationship between degeneration and pain...

... spinal degeneration is the cause of their pain may have something to do with back pain.

Slide courtesy of Aage Indahl, MD
Epidemiology
Disc Degeneration and Back Pain in the Elderly

• No association
Epidemiology

Back Pain is Common

• Lifetime prevalence 80%
Natural history of back pain

• 75% of back pain episodes resolve

• Degeneration did not resolve!

• It is irreversible!
Epidemiology
Back Pain

• 20-25% of population denies ever experiencing low back pain
Epidemiology
Back pain and Disc Degeneration

• Asymptomatic people have all stages of disc degeneration
Epidemiology and Basic Science

• Genetically predetermined insensitivity to the processes that induce back pain
  
Epidemiology
Back Pain

- 20-25% of population denies ever experiencing low back pain
Important Beliefs that Affect Choice of Disability

• Relationship between degeneration and pain...

...spinal degeneration is the cause of their pain may have something to do with back pain

• The *presence* of degeneration is not the cause of back pain
Important Beliefs that Affect Choice of Disability

• Relationship between degeneration and pain...

... spinal degeneration is the cause of their pain may have something to do with back pain

• The *presence* of degeneration is not the cause of pain

• Could some process associated with degeneration cause back pain?
Pathophysiology
Consequence of Loss of Cell Function

• **Structural Failure of the Annulus Fibrosis**
  - Breakdown of collagen fibrils
  - Weakening of lamellae of annulus
  - Lamellae fail when their ability to maintain tension is less than intradiscal pressure
Pathophysiology
Consequence of Loss of Cell Function

- Structural Failure of the Annulus Fibrosis
  - Breakdown of collagen fibrils
  - Weakening of lamellae of annulus
  - Lamellae fail when their ability to maintain tension is less than intradiscal pressure

- Annulus is always in tension
Best Theory (according to me)

- Annular tears may occur spontaneously, with incidental movements, or with significant stresses on the spine.
- Progression of annular tears may induce back pain.

Epidemiology
Onset of Back Pain

• 2/3 episodes – spontaneous onset
• Inciting events are often trivial
Discs herniation – when nucleus pulposus material extends through the annular tear
Inciting Event 37.7%
Spontaneous 62.3%
Heavy lifting 6.5%
Light lifting 2%
Non-lifting activity 26%
Non-exertion Occurrences 2%
Physical trauma (1.3%)

Epidemiology and Basic Science

• Genetically predetermined insensitivity to the processes that induce back pain

• Insensitivity to annular tears?
Relationship between Degeneration and Pain

- Relationship between degeneration and pain...

  ...spinal degeneration is the cause of their pain may have something to do with back pain

- The presence of degeneration is not the cause of back pain

- Events (annular tears) associated with the degenerative process may initiate back pain
Important Beliefs that Affect Choices Resulting in Disability

• Spinal degeneration

• Relationship between degeneration and pain

• Back pain
Beliefs about back pain

- Biologically important indicator of tissue damage in the back

"Good news. The test results show it's a metaphor."
Epidemiology and Basic Science

• Genetically predetermined insensitivity to the processes that induce back pain
  
Epidemiology and Basic Science

• Genetically predetermined insensitivity to the processes that induce back pain
  

• No alteration of activities in response to degenerative events
Epidemiology and Basic Science

• Genetically predetermined insensitivity to the processes that induce back pain

• No alteration of activities in response to degenerative events

• No evidence that this insensitivity harms the back
Beliefs about Back Pain

- Biologically *useless* important indicator of tissue damage in the back
Epidemiology
Genetics as risk factor for back pain

• Twin Studies
  – Monozygotic co-twins – Odds Ratio 6.0
  – Dizygotic co-twins – Odds Ratio 2.2

Epidemiology
Genetics as risk factor for back pain

- Familial clusters have been noted in population bases studies of back pain disorders requiring treatments
Genetics as risk factor for back pain

• Back Pain risk is independent of inherited propensity to develop spine degeneration

• Gene polymorphisms that influence pain neuron function may predispose to (or protect from) musculoskeletal pain
  • Omair A. Genetic contribution of catechol-O-methyltransferase variants in treatment outcome of low back pain. BMC Musculoskeletal Disord 2012;3:76.
Beliefs about Back Pain

• It is important!

• Biologically *useless* useful indicator of tissue damage in the back

• Largely a consequence of genetic misfortunes
The pain system, not the back, is the primary determinant of symptoms.
Basic Science

Back Pain in Mice

- **Dorsal Ganglia, Spinal Cord**
  - Upregulation of
    - brain-derived neurotrophic factor
    - nerve growth factors
  - Disregulation of ion transport
  - Induces astrocyte and microglia hyperactivity

Basic Science

Back Pain in Mice

- **Brainstem**
  - Decreased serotonin (5-HT) metabolism
  - Increase inflammatory cytokines, tumor necrosis factor-alpha, and interleukin-1 beta
  - Mu-opioid receptors altered in brain stem and spinal cord shifting balance of pain modulation to facilitation.
Neuroscience
Descending Pain Modulation

- Descending pathways from the brainstem have a facilitatory and inhibitory function on the pain neurons in the spinal cord and thereby determine the threshold for sensory processing.
  
  "On Cells" – facilitate pain
  "Off Cells" – inhibit pain

- Injury boosts pain facilitation, thereby lowering pain stimulus threshold
Not all rats are created equal!

- Some rats have faulty pain modulation, increasing their risk of developing chronic pain after injury.
  - Exercise induced hypoalgesia (EIH)
    - Rats can be classified as low, medium or high EIH
    - Sciatic nerve injury
  - Low EIH rats developed more severe and more diffuse pain findings after sciatic nerve injury.
Neuroscience
Descending Pain Modulation

• Not all rats are created equal!
  – 30% of Sprague-Dawley rats did not develop pain after spinal nerve ligation.
  – They have enhanced function of “off cells” and reduced function of “on cells”
  – This enhances pain inhibition
Neuroscience

• Genetically predetermined insensitivity to the processes that induce back pain

• Favorable descending pain modulation – enhanced pain inhibition?
Meaning of Back Pain

- Back pain reflects dynamic alterations in pain neuron function resulting in *low threshold pain*
Meaning of Back Pain

• Back pain reflects dynamic alterations in pain neuron function resulting in **low threshold pain**

• "**Low threshold pain is not low pain tolerance**"
Higher brain functions, including emotions and cognition affect descending pain modulation, thereby influencing pain.

Epidemiology – Psychosocial risk factors

- Low educational status, worry, anxiety, depression, high psychological stress, poor self-rated health, frequent use of health or social services, and concurrent pain in other areas
Epidemiology – Psychosocial risk factors

- Work factors - job dissatisfaction, low levels of social support in the workplace and lack of control over job tasks

Chronic Spinal pain

- Persistence of low threshold pain state
- Predominantly a neurological phenomena
Beliefs about Back Pain

• It is important!
• Biologically *useless* useful indicator of tissue damage in the back
• Largely a consequence of genetic misfortunes
• Reflects changes in pain neuron function – *low threshold pain*
Important Beliefs that Affect Choices Resulting in Disability

• Spinal degeneration

• Relationship between degeneration and pain

• Back Pain

• Recovery
Beliefs about Recovery

- Healing!
Epidemiology

• Recovery from acute back pain is highly variable

• More variable than acute musculoskeletal problems in general
Beliefs about Recovery (Chronic)

• Healing (not straightforward)
• Correction of the problem or process that caused the pain
Clinical Trials – Lumbar Fusion

1/3 Reduction of Pain

Beliefs about Recovery (Chronic)

- Healing *(not straightforward)*
- Correction of the structural problem that caused the pain *(Plausible)*
Beliefs about Recovery (Chronic)

• Healing (not straightforward)
• Correction of the structural problem that caused the pain (Plausible)
• Correct the processes that cause the pain
Natural history of back pain

• 75% of acute back pain episodes resolve quickly

• 25% of episodes persist long beyond times typical of tissue healing
Exercise
Neuroscience
Effects of Exercise on Pain

- **Aerobic** exercise for 5 weeks

- **Results of exercise**
  - Reversed mechanical sensitivity of limb
  - Normalized injury induced changes in dorsal ganglia and spinal cord
    - peripheral nerve growth factors (NGF)
    - brain-derived neurotrophic factor (BDNF)
    - phosphorylation status of PLCI-1
    - astrocyte and microglia hyperactivity

Neuroscience

Effects of Exercise on Pain

- **Low intensity exercise**

- **Results of exercise**
  - Reduced pain behaviors
  - **Brainstem**
    - Increased serotonin (5-HT) production
    - Decreased 5-HT transport
    - Increased 5-HT receptors
    - Reduced inflammatory cytokines, tumor necrosis factor-alpha, and interleukin-1 beta
    - (These factors are known to modulate pain)

Effects of Exercise on Pain

• High intensity exercise

• **Results of exercise**
  
  – Reduced withdrawal reflex
  – Mu-opioid receptors
    
    • Altered expression of **mu-opioid receptors in brain stem and spinal cord** shifting balance of pain modulation to inhibition.

    • This effect is **blocked by opioid receptor antagonist** naloxone.


Effects of Exercise on Pain

- **Graded exercise**

- **Results of exercise**
  - Reduced hyperalgesia in the skin
  - Neurological changes
    - Prevented nerve fiber sprouting in the skin
    - Lowers neurotrophic factors in the sciatic nerve
    - Reduced NGF and BDNF in sensory neurons and spinal cord
    - Normalized pain disregulated ion transport in dorsal ganglia and spinal cord
    - Reduce microglia cell proliferation in spinal cord


Neuroscience

The stimulus from exercise reverses pain sensitizing changes in the brainstem, spinal cord, dorsal ganglia and peripheral nerves.

Neuroscience

• The stimulus from exercise **reverses pain sensitizing changes** in the brainstem, spinal cord, dorsal ganglia and peripheral nerves.
• These effects may be non-specific.

The stimulus from exercise reverses pain sensitizing changes in the brainstem, spinal cord, dorsal ganglia and peripheral nerves.

These effects may be non-specific.

Mechanisms?

Neuroscience

Effects of Exercise on Pain

- Exercised muscles release neural active proteins
  - Insulin-like growth factor 1 (IGF-1)
  - Muscle secretory factor – cathepsin B protein

- These proteins penetrate the brain and enhance neurogenesis and brain function

- Do exercise release neuroactive proteins that normalize pain neuron function?

Beliefs about Recovery

- Healing *(not straightforward)*
- Correction of the problem that caused the pain *(plausible)*
- Correct the processes that cause the pain by normalization of pain neuron function
Human studies of exercise
Exercise as a Modality to Reduce Chronic Low Back Pain

– 84 subjects with CLBP

– Tested physical performance levels pre- and post-treatment

– Measured pain experience during testing

Pain induced by lifting

Pain

3.7
Improved lifting
Improved pain induced by lifting
Improved Global Back Pain

Change in Induced Pain correlate with changes in Global Pain $r = 0.52$
Human Studies of Exercise
Exercise effect may be non-specific
Clinical Trials – Exercise

Spinal stabilization

General exercise

Improvements in pain and disability similar in both groups.

Clinical Trials – Exercise

Pilates exercise

General exercise

Improvements in pain and disability similar in both groups.

Clinical Trials – Exercise

Motor control impairment

General exercise

Improvements in pain and disability similar in both groups.

Clinical Trials – Exercise

High load lifting

Low load motor control

Improvements in pain and disability similar in both groups.

Supervised walking

Fitness training

Improvements in pain and disability similar in both groups.

The neurological effects of exercise are rather non-specific!

• Specific exercise techniques may be less important than reaching a certain threshold of exercise needed to induce neurological changes that reduce pain stimulus threshold
Beliefs about Recovery

- Healing (not straightforward)
- Correction of the problem or process that caused the pain (Possible)
- Correct the processes that cause the pain by normalization of pain neuron function
- Movement, physical activities (exercise) promote this process
Important Beliefs that Affect Choices Resulting in Disability

- Spinal degeneration
- Relationship between degeneration and pain
- Back Pain
- Recovery
“We are not responsible for what patients believes before they come to our office.”

“We are responsible for what they believe when they leave.”

Aage Indahl, Spine 1995
Thank you!