Chronic, Complex, Complicated? From Functional Abdominal Pain, Tension Headaches, Musculoskeletal Pain & CRPS

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Disclosure

- Consultant for Purdue Pharma Ltd., Stamford, CT
- The views presented in this lecture are my own. NO conflict of interest exists with my presentation
- I do intend to discuss unapproved or investigative use of commercial products or devices (= off-label).
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Learning Objectives

- Define chronic versus acute pain in children
- Review prevalence of chronic pain in children
- Discuss successful interdisciplinary approaches in managing functional pain syndromes in children
- Appreciate low importance of pharmacotherapy
Case Example: Barbette Payn

- (not a real case): 14-year-old with 4-year history of periumbilical abdominal pain
- Worsened in early September of last year (coinciding with attending new school)
- Previous work-up: Several endoscopies, repeated laboratory investigations, and imagery (CT, MRI, ultrasound) - all normal/negative
- Was prescribed numerous medications, all of which were non-helpful, some causing odd side effects
- Has trouble falling asleep - usually sleeps with mum in bed, with dad now sleeping downstairs

Thanks to Neil Schechter

Barbette Payn

- Mum attends to her until she falls asleep, or when waking up at night
- Often too much headache and too tired in the morning to go to school, frequently sleeps until 11:30 am and takes naps in afternoon
- Missed > 35 days at school last school year, usually goes to school nurse x1-2/day
- Constant bilateral headache developed 8 months ago with her eyes going blurry, occasionally just being able to see black and white: work-up by ophthalmologist and neurologist, incl. CT, MRI, EEG normal

Barbette Payn

- Constant neck, shoulder and bilateral knee, ankle pain for > 5 months: work-up by rheumatologist, orthopedic surgeon incl. X-rays, exhaustive laboratory investigations, all negative/normal
- Barbette has been in Emergency Rooms a total of 5 times in last 12 months, resulting in 2 hospital admissions at Mrs. Payn’s request
- One out of city clinic diagnosed her with POTS, another with autonomic dysfunction, a third with Lyme disease (despite negative titers x3)
- Chiropractor found yeast in stool (prescribed antifungals), clots behind the eyes (-> blood thinner), and heavy metal toxicity (-> chelation therapy) and performed several adjustments
Barbette Payn

Mrs. Payn is worried that a terrible disease is missed by the physicians and is requesting a exploratory laparoscopy

She herself has been diagnosed with Fibromyalgia and quit her job to stay home with her daughter to care for her

Three months ago the overwhelming pain and fatigue resulted in Barbette’s inability to attend school anymore and Mrs. Payn has arranged with school for home tutoring

Barbette has stopped meeting with friends and attending social activities and sports activity (competitive dancing)

Case Example

What now?

What now?

Persistent (Chronic Pain)

Most muscles, bones, ligaments and discs are healed by 3 to 6 months

http://www.youtube.com/watch?v=4b8dF737tKc&feature=player_embedded
Chronic Pain in Children

- **Acute Pain**
  - Tissue injury, inflammation or infection
  - Typically brief, ends when healed

- **Subacute Pain**
  - Ongoing course (arthritis, muscle spasms, nerve damage, chronic infection)

- **Chronic Pain** (not associated with a disease) vast majority of pediatric patients
  - Persist, after initial injury
  - Not ongoing (no tissue damage nor chronic disease)

- **Acute on Chronic?**
  - Status post episodes of recurrent disease process (such as inflammatory bowel, sickle cell disease)

IASP: pain lasting > 3 months
- Time definition arbitrary

Pain that extends beyond the expected period of healing.


Metaanalysis 2011 (King et al.)

- Chronic and recurrent pain prevalent in children and adolescents

  - girls > boys
  - increasing with age
  - psychosocial variables impacting prevalence: anxiety, depression, low-self-esteem, other chronic health problems, lower socio-economic status

- **Range**
  - Headaches: 8-83 %
  - abdominal pain 4-53% 
  - musculoskeletal (incl. back) pain 4-49%
  - pain combinations 4-49%

- **Mean prevalence**
  - Headaches: 23%
  - abdominal pain, musculoskeletal pain, and pain combinations: 11-38%
**Chronic Pain**

Using Most Conservative Estimates:

**Recurrent headaches (tension/migraines) [8 %]**
USA: 5.9 Million children (age 0-17)

**Chronic daily headaches**
USA: 146,000 children (age 0-17)

**Severe Recurrent Abdominal Pain [4 %]**
USA: 2.9 Million children (age 0-17)

**Musculoskeletal Pain [4 %]**
USA: 2.9 Million children (age 0-17)

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**Impact on Family**

* Family Life
* Financial Burden (direct medical & indirect)
* Emotional


- Families of children with chronic pain generally have poorer family functioning
- Pain-related disability is more consistent related to family functioning than pain intensity

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**Chronic Pain Patients: Adults**

* Early-life stress produces muscle hyperalgesia and nociceptor sensitization in adult rat

* 25% of American population has chronic or recurrent pain of those, 40% pain has moderate or severe degrading impact
Chronic Pain: Survivors of Childhood Cancer


- Prevalence of pain conditions (12% pain/abnormal sensation; 15.5% migraines; 20.5% other headaches) and using prescription analgesics higher among survivors than siblings. (3) Miser AW, Dothage JA, Wesley RA, Miser JS. The prevalence of pain in a pediatric and young adult cancer population. Pain. 1987 Apr;29(1):73-83.

- Risk factors:
  - Younger age at diagnosis
  - Pain: non-Hodgkin lymphoma, Wilms tumor, neuroblastoma (vs leukemia)
  - Prescription: bone cancer, soft tissue sarcoma
  - Female gender, lower educational attainment, minority status, unemployment, being single


Catastrophizing [“Awfulizing”]

- A set of negative emotional/cognitive processes such as magnification, rumination, and pessimism about pain sensations and feelings of helplessness when in pain.


- Parent catastrophizing was associated with greater pain in children with IBD. Sicard M, Campbell CM, Quintana C, Blum H,入场 M, Haythornthwaite J. The role of parent and child catastrophizing in pediatric inflammatory bowel disease pain and functioning. (Poster) 29th Annual Scientific Meeting of the American Pain Society, Baltimore, May 6-8, 2010


Catastrophizing & Chronic Pain

- When exposed to pain, persons who are high catastrophizers are less likely to experience the immediate pain reducing effects of distraction. (1) Relation between attachment (Adolescent Relationship Scale Questionnaire) and pain severity/depression
  - (2) Catastrophizing and anxiety play a role in mediating the relation between attachment and pain severity/depression

Catastrophizing & Chronic Pain

- Parental catastrophic thoughts about child’s pain
  - ↑ parental distress, but did not ↑ feelings of sympathy
  - ↑ tendency to stop their child to performing pain-inducing activity
  - parental feeling of distress (not sympathy)
  mediated relationship between catastrophic thoughts and parental stop tendency


Fear of Pain

- Plays a significant role in relation to functional disability and depressive symptoms in the context of pediatric chronic pain

- Appears to play both a facilitative and inhibitory role in relation to treatment response:
  - may hinder improvements in disability & depressive symptoms
  - declines are strongly associated with positive functional outcomes

Parents

  - there was an increased risk of symptoms of anxiety and depression in teens
  - Girls had an increased risk of conduct problems in school if their mothers had chronic pain
Adolescent Chronic Pain (n=222)

- Highly anxious adolescents were functioning poorly regardless of level of pain

At low anxiety: higher pain predicted greater disability

Chronic Pain Pathophysiology

- Many different chronic and recurrent pain syndromes, in both adult and pediatric populations, are now considered manifestations of an underlying vulnerability rather than separate disorders


- Considerable evidence, especially from twin studies, points to a role of shared biological sensitivity: “pain vulnerability”, “pain sensitivity”, or “central sensitivity syndrome”

Majority of children with chronic pain have sleep difficulties; problems with:
- Sleep initiation
- Maintaining sleep
- Early morning awakening

Insomnia: 12-18 years with chronic pain: 54% (vs 20% control)

Sleep problems are persistent (50% vs 20%) and associated with negative impact for youths with chronic pain

Treatment of insomnia in youths with chronic pain may lead to improvements in QoL and reduction in healthcare cost.

Long-term school impairment -> poorer academic and occupational achievement, increase educational costs, development of psychiatric disorders

Parental pain catastrophizing and parental protective response to child pain each individually predict school attendance rates and reports of overall school impairment
A summary of key points from the document:

**Trajectory**


- **Two birth cohorts**: 1946 Medical Research Council and 1958 National Child Development Study showed that children with persistent abdominal pain and headaches go on to suffer more physical symptoms in adult life, more anxiety, and more depression than healthy children.

- **Pain in adolescents**: Trajectory over 3 years (general population, 11-14 years, n=1336)

**44% painful trajectory (12% persistent pain)**
- 25% Headaches (5% persistent)
- 22% Back pain
- 21% Abdominal Pain
- 10% Facial Pain (1% persistent)


**When adolescents with chronic pain do not perceive friends as providing support, they may avoid these social situations.** Forgeron PA, McGrath P, Stevens B, Evans J, Dick B, Finley GA, et al. Social information processing in adolescents with chronic pain: my friends don't really understand me. Pain. 2011 Dec;152(12):2773-80.

**Children’s of MN Pain Clinic: Our Patient Population Includes**

- Tension headaches (plus/minus mixed migraines)
- Functional abdominal pain
- Musculoskeletal pain [formerly “juvenile fibromyalgia”]
- CRPS (Complex Regional Pain Syndrome) [formerly “RDS”]
- Avascular Necrosis
- Irritable Bowel Syndrome
- Conversion disorders
- Cerebral palsy / spasticity
- Neurodegenerative / metabolic conditions
- Muscular dystrophy
- Cancer related pain
- Posttraumatic / phantom pain
- JRA
Chronic pain disorder that after appropriate medical assessment cannot be explained in terms of conventionally defined medical disease based on biochemical or structural abnormalities.

Associated with significant disruption of everyday life and often incapacitation.

Not typically responsive to conventional medical therapy but responsible for the consumption of enormous medical resources.

Often pejorative implication, i.e. pain is not organic and therefore not real or serious.


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Functional Pain Syndromes

- Chronic daily headache
- Functional abdominal pain
- Chronic musculoskeletal pain ("fibromyalgia")
- Majority of children experience pain at multiple sites

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The Porcupine

*I Guess That Explains The Abdominal Pains*
Functional Pain Syndromes

Pain Problem

Medical Workup

Positive

Assume manifestations of underlying vulnerability

Negative

Referral to:
Integrative Medicine
Mental Health Therapist
Pain Clinic

Medical Treatment

Headaches

*Tension-type headache
* Infrequent episodic
  * At least 10 episodes occurring on <1 day/month on average (<12 days/year)
* Frequent episodic
  * At least 10 episodes occurring on >1 but <15 days/month for ≥3 months (>12 and <180 days/year)
* Chronic

• Migraine: No aura / aura
  • 1/2:
    • Nausea and/or vomiting
    • Photophobia
  • 2/4:
    • Unilateral
    • Pulsating
    • Aggravation by/avoidance of physical activity
    • Medium-severe pain

Headaches

Inkas
Headaches

Warning signals requiring further work-up (incl. neuroimaging):

- Focal or abnormal neurological signs, ataxia
- Papilledema (r/o pseudotumor cerebri)
- Age < 3 years
- “Worst headache of my life”
- Progressive worsening headaches
- VP-shunt
- Neurocutaneous syndrome
- Immunocompromized -> CSF? (check with ID)
- CO
- Obstructive Sleep Apnea

Medication Overuse Headaches (MOH)

International Headache society [ICHD-II] Criteria, 2006
- headache > 15 days/month > 3 months
- ergotamine, triptans, or combination analgesics on > 10 days
- or, simple analgesics or any combination of ergotamine, triptans, analgesics, and opioids on > 15 days/month
- MOH can be caused by most, if not all acute headache drug therapies
- Treatment duration?
  - Triptans: 1.7 yrs
  - Ergots: 2.7 years

- analgesics: 4.8 years


- Therapy: Rapid (or slow?) discontinuation of medication
  EA MacGregor, TJ Stein; PTG Davies: Guidelines for All Healthcare Professionals in the Diagnosis and Management of Migraine, Tension-Type, Cluster and Medication-Overuse Headache. 3rd edition (1st revision), September 2010

Functional Abdominal Pain

Rome III-Criteria (2006)

At least x1/week for > 2 months:
- Episodic or continuous abdominal pain
- Insufficient criteria for other functional GI disorders (cyclic vomiting, functional dyspepsia, IBS, abdominal migraine, functional constipation etc.)

- No evidence of an inflammatory, anatomic, metabolic, or neoplastic process that explains the patient’s symptoms
Abdominal Pain

Warning signals requiring further work-up:

- Persistent right upper or right lower quadrant pain
- Pain that wakes child from sleep
- Dysphagia
- Arthritis
- Persistent vomiting
- Perirectal disease
- Gastrointestinal blood loss
- Involuntary weight loss
- Nocturnal diarrhea
- Deceleration of linear growth
- Unexplained fever

Abdominal Pain


Abdominal Pain


Abdominal Pain

- Functional abdominal pain in childhood and adolescence increases risk for chronic pain in adulthood (prospective study, n=155)
  - 65% resolved
  - 35% abdominal pain:
    - most in addition migraine/tension headache
    - Significant higher risk of chronic musculoskeletal pain


Chronic Musculoskeletal Pain

- Demystifying problem: Pain has lost warning signal
- Often de-conditioned
- Frequently tension at trapezius / paraspinal muscles
- Treatment Goal:
  - (1) Return to function
  - (2) Pain decrease

Chronic Musculoskeletal Pain

Warning signals requiring further work-up:

- Athralgia: Rubor, Calor, Edema
- Pain, stiffness in the morning
- Abnormal radiographic findings
- Pain at rest, relieved by activity
- Pain at night: Worsened by massage, analgesics ineffective
- Bony tenderness
- Poor growth
- Weight loss
- Abnormal CBC, CRP, ESR
Low grade in physical education for adolescent girls significantly associated with increased risk of musculoskeletal diagnosis, especially chronic soft tissue pain, 30 years later.


Ginger (raw = heat-treated) results in reduction of muscle pain following exercise-induced muscle injury.


Chronic Musculoskeletal Pain

Adults (> 16 yr) with Ehlers-Danlos-Syndrome

• (clinically & genetically heterogeneous group of inherited connective tissue disorders, caused by mutations in genes encoding various types of collagen or collagen-modifying enzymes [collagen I, III, and V; tenascin X or lysyl hydroxylase-1]: joint hypermobility, skin hyperextensibility, and tissue fragility.

Chronic pain highly prevalent (90 %), severity: hypermobile type > classic type.


Fibromyalgia

• Diagnostic criteria not (!) validated in children and teenagers

• Animal Model: Rats exposed to unpredictable sound stress develop

  • mechanical hyperalgesia in muscle and skin
  • increased anxiety
  • temporomandibular disorder
  • irritable bowel syndrome

Complex Regional Pain Syndrome (CRPS)

(Formerly RSD)

Regional pain & sensory changes after noxious event:
IASP Definition
(1) Chronic neuropathic pain (at least 2)
- Burning
- Dysesthesia
- Paresthesia
- Mechanical allodynia
- Hyperalgesia to cold

AND

(2) Signs & symptoms of autonomic dysfunction (at least 2)
- Cyanosis
- Mottling
- Hyperhidrosis
- Extremity cooler than contralateral by 3 degrees Celsius
- Edema

Budapest Clinical Diagnostic Criteria for CRPS

(1) Continuing pain, which is disproportionate to any inciting event
(2) Must report at least one symptom in 3 of the 4 following categories
- Sensory: Reports of hyperesthesia and/or allodynia
- Vasomotor: Reports of temperature asymmetry and/or skin color changes and/or skin color asymmetry
- Sudomotor/Edema: Reports of edema and/or sweating changes and/or sweating asymmetry
- Motor/Trophic: Reports of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)

(3) Must display at least one sign* at time of evaluation in 2 or more of the following categories:
- Sensory: Evidence of hyperalgesia (to pinprick) and/or allodynia (to light touch and/or deep somatic pressure and/or joint movement)
- Vasomotor: Evidence of temperature asymmetry and/or skin color changes and/or asymmetry
- Sudomotor/Edema: Evidence of edema and/or sweating changes and/or sweating asymmetry
- Motor/Trophic: Evidence of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)

(4) There is no other diagnosis that better explains the signs and symptoms


Complex Regional Pain Syndrome (CRPS)

Several pathological mechanisms
- Oxidative stress
- Classic inflammation
- Neurogenic inflammation
- Autonomic & sensory nerve system alterations
- In animal model NFκB is involved in development of allodynia after physical injury (ischemia and reperfusion) without direct nerve trauma


Complex Regional Pain Syndrome (CRPS)

- **CRPS Type I**: (RCT, n= 23 adults) Standard therapy plus 10 daily sessions of high-frequency repetitive transcranial magnetic stimulation (rTMS) of motor cortex (precentral gyrus) decreased pain (VAS reduction 4.6 vs 2.2) Picarelli H, Teixeira MJ, de Andrade DC, Myczkowski ML, Lavrinova TR, Yeng LT et al. Repetitive transcranial magnetic stimulation is efficacious as an add-on to pharmacological therapy in complex regional pain syndrome (CRPS) type I. The journal of pain. 2010 Nov;11(11):1203-10.


- **Parental insulation**: CRPS patients were often highly stressed adolescent

- **Male:Female = 1:6**

- **Lower:Upper extremity = 5:1**

- **Competitive sport, often from early age**


- **No data to support that sympathetic and somatic nerve blocks (or spinal cord stimulators) are superior to...**
Intervention for CRPS in adults

- Very common use of sympathetic blocks, spinal cord stimulators, and implant pumps
- Widespread belief that nerve blocks should be done very early in the treatment
- Recent interest in “IV ketamine sedation or coma”

However, the evidence for any of these interventions is very weak

Berde C. USA. Pharmacological and Interventional Management of Pain. 8th International Symposium on Pediatric Pain, Education Day. March 7, 2010

Complex Regional Pain Syndrome (CRPS)

CRPS in children and adolescents

- Very good response to rehabilitative treatment (PT, OT, CBT)
- Longer cumulative risks from stimulators and implanted pumps
- Dr. Berde’s team (Boston Children’s) “Over the years, we are doing fewer and fewer blocks for these patients”
- “If we do blocks, we favor placement of indwelling peripheral, plexus, or epidural catheters for inpatient rehabilitation”

Berde C. USA. Pharmacological and Interventional Management of Pain. 8th International Symposium on Pediatric Pain, Education Day. March 7, 2010

Conversion Disorder

- Condition in which a person has blindness, paralysis, or other nervous system (neurologic) symptoms that cannot be explained by medical evaluation
- Symptoms
  - Blindness
  - Inability to speak
  - Numbness
  - Paralysis
  - Diagnostic testing does not find any physical cause for the symptoms
- Signs
  - Debilitating symptom that begins suddenly
  - History of a psychological problem that gets better after the symptom appears
  - Lack of concern that usually occurs with a severe symptom

How long can we wait?

- Unknown at what point clinical deterioration begins
- Wait-times for chronic pain treatment of 6 months or longer are medically unacceptable: significant decrease in health related quality of life and psychological well being (metanalysis, 24 studies)


- 2/3 of US pediatricians felt it was not their primary responsibility to treat chronic pain


Who do we need …?

- Psychological Treatments can significantly reduce pain intensity reported by children and adolescents with headache, abdominal pain, and fibromyalgia.


- Physical activity reduces risk for depression in female adolescents


- Adolescents with chronic pain: lower physical activity level


CBT led to significant improvements in pain coping, catastrophizing, and efficacy that were sustained over time in adolescents with juvenile fibromyalgia. Clinicians treating adolescents with JFM should focus on teaching a variety of adaptive coping strategies to help patients simultaneously regain functioning and improve mood.

Interdisciplinary Pain Clinic


* n=5 adolescents with rheumatoid arthritis, 6-week, bi-weekly Iyengar Yoga: improvements in pain, pain disability, depression, mental health, vitality, self-efficacy. Iyengar Yoga for Young Adults with Rheumatoid Arthritis: Results From a Mixed-Methods Pilot Study. J Pain Symptom Manage 2010 May. 39:904-13

Interdisciplinary Pain Clinic

Children’s Hospitals and Clinics of Minnesota
Minneapolis

Team:
• Nurse Clinic Coordinator
• Physical Therapist
• Psychologist
• Social Worker/Family Therapist
• Pediatrician

Pediatric US Pain Clinics

* http://www.americanpainsociety.org/membership/content/specialinterestgroups/painininfantchildandadolescents.html
Exit Interview: What is the Hard Work...and non-negotiable...? 

1. Physical Therapy
   - Daily home exercise, TENS
2. Integrative Medicine
   - Self-Hypnosis
   - Biofeedback
   - Progressive Muscle relaxation
   - Daily home exercise
     - Passive: Massage, Acupuncture
3. Psychology (only, if missing school)
4. Normalize Life
   - Sports/Exercise
   - Sleep-hygiene
   - Social: Having daily fun
   - School: Attending full-time (or school-re-entry plan)
5. Family Coaching

Medications?

Medication

- Adolescents with chronic pain: higher income and greater level of depressive symptoms predicted higher number of prescribed medications
Exit Interview

1. Amitriptyline (stimulates)
2. Gabapentin (inhibits)
3. Acetaminophen
4. Ibuprofen (Celecoxib?)
5. Lidocain 5% patch
6. Melatonin
7. Vitamin D?
8. SSRI?
9. Co-Q10, Fish-Oil/Omega 3000, Peppermint oil (coated) [for abdo pain]?

Opioids in the absence of tissue injury or inflammation are contraindicated!

Opioids & Chronic Pain

- Lack of evidence supporting long-term effectiveness
- Escalating misuse of prescription opioids including abuse and diversion
- Uncertainty about incidence of adverse drug events
  - endocrine dysfunction (androgen deficiency)
- Immunosuppression & infectious disease
- Opioid-induced hyperalgesia
- Xerostomia
- Overdose
- Falls & fractures
- Psychosocial complications

Opioids & Chronic Pain

- 109 patients with chronic pain over 7 years: NO relation between opioid dose change and clinical pain score
Further Reading

HarperResource
$ 14.95

Conclusion

* Many different chronic and recurrent pain syndromes, in both adult and pediatric populations, are now considered manifestations of an underlying vulnerability rather than separate disorders

* Opioids in the absence of tissue injury or inflammation are contraindicated!

* Importance of rehabilitative, interdisciplinary team approach

Further Training

7th Annual Pediatric Pain Master Class | Minneapolis, MN | June 7-13, 2014

Center to Advance Palliative Care (CAPC) - Pediatric Palliative Care Leadership Center (PCLC) Training | 2014


Pediatric Integrative Medicine Master Class | Minneapolis, MN | Sept 21-26, 2014