When Pain is Real, but Opioids are Contraindicated: Pediatric Primary Pain Disorders in Head, Abdomen, Muscles & Joints

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WALDO E. NELSON, MD, 1898 – 1997

Dr. Nelson’s distinguished career spanned nearly seven decades, during which he changed the course of treatment of childhood disorders and improved health care for the world's children. He served as the editor and senior editor of the Textbook of Pediatrics for more than 50 years and as editor of the Journal of Pediatrics from 1958 to 1977. He retired in 1984 after being the medical director of St. Christopher's Hospital for Children for 24 years.

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Stefan J. Friedrichsdorf, MD, FAAP (USA)
Learning Objectives

- Explore obstacles to treat "chronic-on-acute" pain through a rehabilitative pediatric pain program
- Discuss successful interdisciplinary approaches in managing primary pain disorders in children with underlying recurrent acute pain episodes
- Explore treatment choices and appreciated low importance of pharmacotherapy

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Minneapolis / St. Paul, Minnesota

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Learning Objectives

- Explore how primary headaches, centrally mediated abdominal pain syndromes, and chronic musculoskeletal pain are considered to be symptoms of the same underlying pain vulnerability
- Discuss successful interdisciplinary approaches in managing primary pain disorders in children using a rehabilitative pediatric pain approach
- Appreciate the low importance of pharmacotherapy to effectively treat chronic pain in children
Case Example: Barbette Payn

- (not a real case): 14-year-old with 4-year history of periumbilical abdominal pain (in remission following ALL treatment age 5)
- 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 where non-helpful, some causing odd side effects
- Has trouble falling asleep - usually sleeps with mum in bed, with dad now sleeping downstairs

Barbette Payn

- Mum very well organized (color coded folder)
- Mother 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, now 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 bi-frontal headache developed 8 months ago with her eyes going blurry, occasionally “blackening out”: workup 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
- One out of city clinic diagnosed her with “POTS”, another with “autonomic dysfunction”, a third with Chronic 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 an exploratory laparoscopy.
- 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 / Online school.
- She herself has been diagnosed with Fibromyalgia and quit her job to stay home with her daughter to care for her.
- Barbette has stopped meeting with friends and attending social activities and sports activity (competitive dancing).

Case Example

What now?

???

Pain Assessment

(1) Nociceptive Pain: arises from the activation of peripheral nerve endings (nociceptors) that respond to noxious stimulation
- Somatic (for example, muscles, joints)
- Chronic somatic pain typically well localized & often results from degenerative processes (such as arthritis)
- Visceral (internal organs)

(2) Neuropathic Pain: resulting from injury to, or dysfunction of, the somatosensory system.
- Central pain: caused by a lesion or disease of the central somatosensory nervous system

(3) Psycho-social-spiritual-emotional Pain / Total Pain

(4) Chronic Pain
Chronic Pain in Children

- Pain lasting > 3-6 months: Time definition arbitrary
- Pain that extends beyond the expected period of healing and hence lacks the acute warning function of physiological nociception
- Chronic Pain in children is the result of a dynamic integration of biological processes, psychological factors, and sociocultural factors considered within a developmental trajectory. (Pediatric Chronic Pain Task Force, 2012 American Pain Society)

Pain versus Disability

- Chronic pain is a significant problem in the pediatric population, conservatively estimated to affect 15% to 20% of children. (Goodman, J.E., & McGrath, P.J. (1991). The epidemiology of pain in children and adolescents. A review. Pain, 46, 247-264)
- However, majority of Children reporting chronic pain are not greatly disabled by them. (Huguet A, Miro J. The severity of chronic pediatric pain: an epidemiological study. The journal of pain : official journal of the American Pain Society. 2008 Mar;9(3):226-36)

Metaanalysis 2011 (King et al.)

- 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%
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.
  - **Rumination**: Parent anxious preoccupation with pain
  - **Magnification**: Parent amplification of the significance of pain

- Significant link between child and parent catastrophizing

- Kids have higher pain ratings, if either child or mother displays high pain catastrophizing

- 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

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”

- considerable treatment response

- shared biological sensitivity

- considerable treatment response

- considered treatment response
Chronic Pain Pathophysiology

- **Biological**
  - Genetics
  - Microtrauma
  - Infection
  - Injury

- **Psychological**
  - Pain Processing
  - Anxiety
  - Depression
  - Stress Sensitivity

- **Social**
  - School
  - Adverse Events

- **Disordered Pain**

- **Functional Primary Pain Disorder**

Functional Primary Pain Disorder

- 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.

Primary Pain Disorders

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

The Porcupine

“I Guess That Explains The Abdominal Pains”
Gary Larson, The Far Side

Primary Pain Disorder

Pain Problem

Medical Workup

Positive

Assume manifestations of underlying vulnerability

Negative

Chronic-on-acute

Medical Treatment

Referral to:
Integrative Medicine
Mental Health Therapist
Pain Clinic
(1) Headaches / Migraines

**“Bi-modal” Headache Construct**

**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

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Primary Headache = Severity Continuum?

- “Migraine” and “Tension-type” headache are not separate diagnostic disease entities, but rather points on a severity continuum for children, teenagers, and young adults who experience headaches more than 3-4 days per week

- Headache symptomatology obtained from 3449 individuals with headache from 2 large-scale cross-sectional studies

- high headache frequency (>15 d/mo) and younger age (<24 years old) were associated with unimodal distributions suggestive of dimensional construct of primary headache
- lower headache frequency and older age were associated with bimodal distributions characteristic of discrete diagnostic entities

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)
  - Rule out: CO; Obstructive Sleep Apnea

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**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

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**Meta-analyses: Migraine in Kids**


  - **Placebo** were observed in all trials, with pain relief at 2 hours ranging from 53% to 57.5%.

Meta-analyses: Pharmacology Headaches


- Drugs more effective than placebo for episodic migraines: topiramate (difference in headaches per month, -0.71; 95% CI, -1.19 to -0.24); trazodone (-0.60; 95% CI, -1.09 to -0.11).

- Other commonly used drugs have no evidence supporting their use in children and adolescents.

- Ineffective drugs: clonidine, flunarizine, pizotifen, propranolol, and valproate; single trial of fluoxetine for chronic daily headaches

- 10 comparator trials, flunarizine more effective than piracetam, but no better than aspirin, dihydroergotamine, or propranolol. Propranolol compared with valproate, behavioral treatment, & 2 studies compared different doses of topiramate; none showed significant differences.

- **Placebo**: 5.6 -> 2.9 headaches/month [Cochrane Q=8.14]

(2) Dys-Functional Abdominal Pain

Rome III-Criteria (2006)

- 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

Centrally mediated abdominal pain syndrome (2016)
Abdominal Pain

• Constipation most common diagnosis in children presenting with abdominal pain in ED (& no racial difference)

• Endogenous inhibition of somatic pain is impaired in 7-12 year old girls with irritable bowel syndrome compared with healthy peers.

• Mothers with children chronic abdominal pain show pain bias when interpreting ambiguous emotional expressions (possibly contributes to maintenance of the condition via specific parenting behavior?)

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

(3) Chronic Musculoskeletal Pain
Chronic Musculoskeletal Pain

Warning signals requiring further work-up:

• Asthralgia: 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

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


“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

Excerpt from "Little Stars" by Moonshine Movies (58Min; 2014)
https://www.youtube.com/watch?v=3Bbb785JH64

Who do we need?
Physical Therapy

- **Physical activity** reduces risk for depression in female adolescents

- Adolescents with chronic pain: lower physical activity level
Who do we need?

**Psychology**


**Psychological Treatments** significantly reduce pain intensity reported by children and adolescents with headache, abdominal pain, and fibromyalgia. - Eksteen C, Palermo TM, Williams AECC. (2016) Pain in adolescence: impact on functional disability and health-related quality of life. Pain Medicine 17(suppl 1):S1-17


- CBT led to significant improvements in pain coping, catastrophizing, and efficacy that were sustained over time in adolescents with juvenile fibromyalgia. - Kudler-Scott L, S. Li, et al. (2013) Changes in pain coping, catastrophizing, and coping efficacy after cognitive-behavioral therapy for adolescents with juvenile fibromyalgia. J Pediatr. 163(4):493-97

Psychological Treatments


- However, none of these Internet interventions are publicly available. Costly to develop and out of date quickly!


Integrative Medicine


- **Iyengar Yoga:** n=5 adolescents; rheumatoid arthritis. 6-week, bi-weekly: 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(5):814-15

The Exit Interview

- **Pain is real!**
- Positive Expectation = Self-fulfilling prophecy!

- Chronic-on-acute: **Close collaboration** with specialist of underlying acute condition to ensure no injury will be caused by rehab treatment
  - Pediatrics
  - Rheumatology
  - Gastroenterology
  - Hematology/Oncology
  - Cardiology
  - etc.

Exit Interview:

What is the Hard Work...and non-negotiable...?
**Sleep & Chronic Pain**

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.

**School & Chronic Pain**

- 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


**Exit Interview**

↑ ↑ Pain

↑ ↑ Stress × Grumpy × Anxiety

Attending School
Exit Interview:
What is the Hard Work...and non-negotiable...?

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

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**Medications?**

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**Opioids & Chronic Pain**

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

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Opioids & Chronic Pain


Cannabis
San Diego, CA

AAP Handout for parents "Despite relaxed regulations, marijuana harms developing brain": [Link](http://aapnews.aappublications.org/content/36/3/4.full.pdf+html)

Updated AAP policy opposes marijuana use, citing potential harms, lack of research. [Link](https://aapnews.aappublications.org/content/early/2015/01/26/aapnews.20150126-1)
1. Low-dose 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 not indicated!

Exit Interview

Further Reading

HarperResource

$ 14.95

PainBytes

Persistent (Chronic Pain)

Clinicians have historically considered most chronic pain to be largely from peripheral nociceptive input (i.e. damage or inflammation), and now data increasingly suggest this is simply not the case. 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! The importance of rehabilitative, interdisciplinary team approach.

Conclusion

- Clinicians have historically considered most chronic pain to be largely from peripheral nociceptive input (i.e. damage or inflammation), and now data increasingly suggest this is simply not the case.
- 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 Links

- Video: Kiran Stordalen and Horst Rechelbacher Pediatric Pain, Palliative and Integrative Medicine Clinic Tour [Link](https://vimeo.com/122654881)
- Short Movie: Meet the Interdisciplinary Chronic Pain Clinic Team at Children’s Minnesota: LittleStars TV [Link](https://www.youtube.com/watch?v=13kxv8i9l6p)
- Video: Tour of the Kiran Stordalen and Horst Rechelbacher Pediatric Pain, Palliative and Integrative Medicine Clinic at Children’s Hospitals and Clinics of Minnesota and an overview of the three programs that are offered at Children’s under this clinic. [Link](https://vimeo.com/12397279)
- Short Movie: LittleStarsFilm Kali’s Story - Beyond the NICU This amazing pediatric palliative care short movie (7 min) features 12-year-old Kali’s journey at Children’s Hospitals and Clinics of Minnesota from NICU to today receiving care by the Pain & Palliative & Integrative Medicine program while inpatient, in the clinic, and at home (Jan 22, 2015) [Link](http://www.littlestars.nichols-films/beyond-the-nicu)
Further Training

10th Annual Pediatric Pain Master Class
- Minneapolis, Minnesota, USA | June 17-23, 2017

Education in Palliative & End-of-life Care [EPEC]: Become an EPEC-Pediatrics Trainer
- Montréal, Québec, Canada | April 29-30, 2017 (Professional Development Workshop: 04/28/17)

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