



# Complex Child E-Magazine

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## The Importance of Early and Aggressive Pain Treatment in Children with Complex Medical Issues

*Kristi is an adorable and happy three-year-old who was deprived of oxygen at birth and is now diagnosed with severe cerebral palsy. While she was an infant, Kristi was incredibly irritable and struggled with reflux and vomiting, but she eventually progressed to 25% oral feeding and 75% G-tube feeding. Six months ago she had a virus that caused vomiting and diarrhea. Since that time, she has become irritable again, appears to have nearly constant abdominal pain, vomits frequently, and has only been able to tolerate slow G-tube feeds.*

*Frankie is a vibrant six-year-old who is diagnosed with a maternally-linked mitochondrial myopathy. While he is reasonably healthy, he does experience difficult-to-treat constipation, intolerance to heat, migraine headaches, and occasional bouts of severe vomiting. Four months ago he fell off his bicycle and fractured his left leg. His fracture has healed, but he continues to have tingling and stabbing pain in his leg, along with color and temperature changes in his foot. At times, the pain also affects his other leg.*

These two children are representative examples of the large number of children with both chronic pain and complex medical issues, particularly those whose conditions are neurological or neuromuscular in origin. In addition, the type of pain these children experience is often atypical or non-specific, making it difficult to treat. Many children like Kristi and Frankie experience neuropathic or nerve pain, visceral or internal pain, or functional pain without clear organic cause.

A previous article outlined the frequency and intensity of pain experienced by children with neurological disorders, as well as the undeniable fact that this pain is rarely appreciated or treated by medical professionals. While that article makes an argument for treating pre-existent pain, this one has an entirely different focus. This article addresses the physiological need for early and aggressive treatment of pain, postulating that untreated pain in this population can lead to profound and ongoing physical, medical, and psychological consequences.

## **A Predisposition to Pain from Early Painful or Stressful Experiences**

While somewhat difficult to understand, there is clear evidence mounting that early pain experiences and stresses may cause a child to later develop severe pain, given a trigger such as surgery, trauma, or illness.

The neonatal period is a time of profound brain development, and the brain is considered to have great "plasticity," or the ability to make new and unique connections between neurons. If the brain is exposed to a great deal of stress or pain during this critical period, it may be fundamentally altered, thereby predisposing an individual to be more sensitive to pain later on in childhood or adulthood.<sup>1</sup> Common experiences that may contribute to these alterations include early intensive care stays where the baby is separated from the mother, surgeries done during infancy, and painful or uncomfortable procedures such as IV and NG placements or frequent blood draws.

While the mechanism by which this happens is poorly understood and even more challenging to explain in layman's terms, it can be summed up as a combination of sensitization of nerves, impaired responses to stress, and an altered "pain gate" that may open or close too readily, meaning the brain does not respond to pain appropriately.<sup>2</sup> These changes may be permanent and are thought to last for many years and potentially into adulthood.

These types of early stresses and pain seem to particularly predispose children to visceral pain and hypersensitivity, such as abdominal pain with no physical cause that seems to be out of proportion to what would be expected. Commonly called visceral hyperalgesia, this condition frequently affects children with multiple medical issues. One child may feel extreme pain as the stretchy part of his stomach, the fundus, is filled with food or formula. Another child may have constant pain in the abdomen. Still another may experience vomiting whenever anything enters the stomach, because the body perceives formula or food as a painful toxin instead of nutrition. Others may experience gas and bloating, as well as pain in the lower gastrointestinal tract.

Studies in rats have shown that baby rats who were separated from their mothers during their first two weeks later had severe visceral pain when their colons were distended.<sup>3</sup> Another study linked oral suctioning of baby rats to later visceral pain and hyperalgesia in adulthood. There is strong evidence that conditions such as irritable bowel syndrome and functional abdominal pain (without anatomic cause) in older children and adults are more common in individuals who have experienced greater amounts of pain or stress in infancy or childhood.

These types of responses are not limited to visceral pain or hypersensitivity. A study of infants with a history of an early surgical procedure showed that repeated surgery, especially to the same area, caused increased pain.<sup>4</sup> These children, who were neurologically typical, required more pain medication during surgery and greater comfort measures during recovery.

Most children who have complex medical issues have a long history of hospitalizations, procedures, and surgeries during infancy, all of which induce both pain and stress. In many cases, infants did not receive proper pain control or analgesia. It is still very common, for example, to circumcise infant boys without any anesthetic. Based on science's current understanding of pain, these large number of early stresses may predispose children with complex medical issues to pain and pain syndromes later on in childhood and adulthood.

### **A Predisposition to Pain from an Impaired Autonomic Nervous System**

While early life experiences may shape the development and function of the central and peripheral nervous system, many children with complex medical issues also have underlying neurological issues that contribute to pain perception and response. These children commonly suffer from dysregulation of their autonomic nervous systems, the part of the nervous system that is "automatic" and controls body processes like heart rate, blood pressure, body temperature, and the "fight or flight" response.

Children with certain disorders, such as mitochondrial diseases, spinal injuries, or multiple sclerosis, are commonly recognized as having autonomic dysfunction or impaired autonomic system function, also called dysautonomia. But autonomic dysfunction is also extremely prevalent in children with brain injuries, encephalopathy, and cerebral palsy. This autonomic dysfunction is rarely recognized or treated by medical professionals, and even detailed textbooks on cerebral palsy management rarely include more than a page or two on autonomic symptoms beyond temperature regulation or bowel and bladder problems.

Nonetheless, symptoms from autonomic dysfunction can be frustrating for families and may severely impact quality of life for many children. In general, the more severe the neurological issues or disease, the more likely a child is to have autonomic dysfunction. Many of these children suffer from milder forms of the condition, including symptoms such as constipation and heat intolerance. Some children, however, may be profoundly affected, with most bodily functions ranging from digestion to urination and maintenance of vital signs impacted.

How does autonomic dysfunction relate to pain? In many of these children, the brain and central nervous system do not transmit messages appropriately to and from nerves that control both sensation and motion. So, for example, a child with autonomic issues may have motility issues of the gut and bladder, such as abdominal pain, slow motility, stomach and intestinal spasms, constipation, or bladder spasms, all of which may cause significant discomfort and visceral or neuropathic pain.

Sensation may also be impaired in either direction, and oftentimes both increased and decreased sensation is found in the same child. Children may develop hyperalgesia, or increased sensitivity to pain, as well as allodynia, or a pain response to non-painful

stimuli, such as touch. Neuropathic pain, or burning, numbness, or shooting pain, is also common. Some children may feel pain on the "inside," in the forms of both visceral and neuropathic pain, while actually having decreased sensation to pain on the skin and within muscles and bones.

In many children, both sensation and motility are impaired to some degree, causing increased perception of pain, as well as secondary discomfort from spasms, headaches, gut, and bladder problems. These types of pain tend to feed on each other, with impaired sensation making motility worse, and impaired motility making the sensation of pain more dramatic.

### **Why Early and Aggressive Treatment is Critical**

Simply put, pain begets pain. When a child struggles with pain, especially visceral or neuropathic pain, that pain will increasingly affect the body's ability to perceive and respond to pain, especially when the autonomic nervous system is impaired. The earlier the pain is treated, the more likely the child will have a better outcome, with resolution of pain and other symptoms. Left untreated, the pain is likely to feed on itself, affecting autonomic nervous system function even more, and potentially shutting down body processes such as motility.

This pain is treatable, although it often takes a lot of trial and error. Unfortunately, many doctors do not feel comfortable treating pain in children with complex medical issues, especially when the autonomic nervous system is heavily involved. Children are often left to suffer for months or years, with their pain explained as "neuro-irritability" or simply part of their disease process.

For example, the case of Kristi related above describes a child who spent much of her first year irritable and uncomfortable. A recent study showed that children with unexplained irritability and her level of neurological impairment are actually suffering from visceral hyperalgesia.<sup>5</sup> When treated with neuropathic/visceral pain medications like Neurontin (Gabapentin) or Elavil (Amitriptyline), these children improved dramatically.

Kristi's case also points out the susceptibility of these children to later insults. In her case, a simple virus wreaked havoc on her gastrointestinal tract, leading to increased pain and gastrointestinal symptoms that most likely represent increased visceral hyperalgesia. Without treatment, Kristi is likely to continue losing weight, being in pain, and experiencing negative symptoms like vomiting. If Kristi instead receives aggressive and early intervention for this new pain, she will likely begin to thrive once again. She may need to rest her stomach for awhile to allow her perception of sensation to calm back down, and she may need additional or increased neuropathic or visceral pain medication.

It is common for children with complex medical issues to have unusual and seemingly out-of-proportion side effects to stresses such as illness, surgery, or trauma. Another

study on children with mild/moderate cerebral palsy who underwent orthopedic surgery showed that 6 out of 40 (15%) children had serious neuropathic pain in the affected limb(s) after surgery.<sup>6</sup> While the authors posit that this may be a side effect of stretching the nerves during surgery, the hyperalgesia and allodynia experienced by these children suggests that they may also have a predisposition to pain related to the nervous system due to underlying neurological issues or early stresses. These children were treated with neuropathic pain medications and other supportive measures and most recovered completely.

Two of the children who did not receive early and aggressive pain management ultimately took much longer to become pain-free, roughly two and four years, while those children with quick interventions more typically were pain-free in less than a year. The authors are careful to note that early treatment is absolutely necessary to prevent a continued decline in functioning, continually increasing pain, and psychological issues.

The second case above describes a child with a mitochondrial disorder, Frankie, who clearly has underlying autonomic issues, including gut problems, impaired temperature regulation, and headaches. Once again, a simple event such as a leg fracture triggered a cascade of events, ultimately leading to severe pain. Frankie most likely has Complex Regional Pain Syndrome Type 1, a pain syndrome that is functional and not anatomic in nature, and has strong links to the autonomic system, including clear autonomic symptoms. A study on eight children with this type of pain syndrome and pre-existing other autonomic issues, as in the case of Frankie, showed that these children actually had mitochondrial disorders predisposing them to this pain syndrome.<sup>7</sup> When these children were treated appropriately with physical therapy and visceral pain medication, most recovered quite well.

These cases show that pain can be controlled and symptoms improved if early and aggressive intervention is provided. It is exceptionally important for children, especially those children who cannot communicate easily, to undergo a thorough analysis for pain and be treated appropriately. Interventions may include visceral or neuropathic pain medications, physical therapy, and other supportive measures, and usually prove quite effective when initiated quickly and comprehensively.

Parents need to be vigilant advocates for their children, especially when they are in pain or discomfort. It may take a visit to a pain specialist or other physician to get appropriate care for certain children. But pain management is possible, and the earlier it is begun, the better the outcome.

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<sup>1</sup> Adrian Miranda, "Early Life Events and the Development of Visceral Hyperalgesia." *Journal of Pediatric Gastroenterology and Nutrition* 2008;47(5), 682-4; Jeroen W.B. Peters, *et al.*, "Does neonatal surgery lead to increased pain sensitivity in later childhood?" *Pain* 2005;114(3):444-54.

<sup>2</sup> Jackie D. Wood, "Functional Abdominal Pain: The Basic Science." *Journal of Pediatric Gastroenterology and Nutrition* 2008;47(5), 688-93.

<sup>3</sup> Miranda, 683.

<sup>4</sup> Peters, 444-54.

<sup>5</sup> Julie M. Hauer, *et al.* "Gabapentin Successfully Manages Chronic Unexplained Irritability in Children with Severe Neurologic Impairment." *Pediatrics* 2007;119(2):e519-22.

<sup>6</sup> G.R. Lauder and M.C. White. "Neuropathic pain following multilevel surgery in children with cerebral palsy: a case series and review." *Pediatric Anesthesia* 2005;15:412-20.

<sup>7</sup> T. Higashimoto, *et al.* "Reflex Sympathetic Dystrophy: Complex Regional Pain Syndrome Type 1 in Children with Mitochondrial Disease and Maternal Inheritance." *Archives of Disease in Children* 2008;93:390-7.