Overview of Patho-Physiology and Assessment of Acute Post Operative Pain in Pediatrics Undergoing Inguinal Hernia Repair

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ABSTRACT

Children may suffer mild to severe pain from a vast array of encounters during the perioperative or postoperative period. Pain is a protective sensation that acts as an early warning system designed to minimize tissue damage, which is the positive aspect of pain. On the other end of the spectrum, negative characteristics have both an immediate impact on the well-being of a child and may result in long term detrimental consequences. Nevertheless, latter results in prolonged stimulation and pathological alterations to the peripheral or central nervous system (CNS) is brought about by untreated or inadequately managed pain. In spite of the known presence of pain in children, epidemiological studies demonstrate the continued lack of adequate pain management in this population. Gaining an understanding of the pathophysiology of pain and how to apply age-appropriate pain assessment tools will help to create targeted pain treatment plans that promote the implementation of successful pain management strategies and improved pain control in children. The aim of the current study to review the patho-physiology and assessment of acute post-operative pain in children undergoing inguinal hernia repair.

Keywords: Post-operative Pain; Patho-Physiology; Inguinal Hernia Repair; Children

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Introduction

The International Association for the Study of Pain (IASP) defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage" **(1)**.

Such an expansive definition of pain emphasizes the subjective nature of pain and how psychosocial, developmental, ethnic, genetic, and cultural factors impact its experience. Defining pain in this manner gives explanation to the pain experienced by a fearful child waiting for intravenous cannulation, as well as an infant undergoing a circumcision; however, pain can occur

and exist in the absence of tissue damage. Furthermore, a caregiver is urged to address both the psychological and physical aspects of pain in order to effectively and reliably treat it **(2)**.

Somatic pain is described as acute, well localized and sharp in nature. Children also encounter episodes of visceral or neuropathic pain. Visceral pain is characterized as diffuse and aching, whereas neuropathic pain associated with nerve damage is burning in nature. Acute pain from minor and major procedures is associated with acute illness or an acute exacerbation of a chronic illness as in sickle cell anemia **(3)**.

Neuroscience of Pain

Transduction, transmission, modulation, and perception are processes that define pain. Pain is distinguished from nociception in that pain is a perception, while nociception is the biophysical process that encodes noxious stimuli that often, but not always, leads to the expression of pain **(4)**.

Several types of pain are produced by noxious mechanical, thermal, or chemical injury (nociceptive pain, inflammatory pain, and neuropathic pain), and whatever the type of pain, it passes through the following pathway **(5)**.

Specialized pain receptors, nociceptors, on the afferent somatosensory A-δ and C neurons transduce noxious stimuli into electrical activity. These encoded nociceptive signals are transmitted through sensory neurons traveling through the dorsal horn of the spinal cord **(6)**.

Sensory neurons synapse on secondary neurons that cross the midline of the spinal cord and transmit the nociceptive signals, usually through specific ascending "pain tracts" that include the spinothalamic, spinomesencephalic, and spinoreticular tracts **(7)**.

The signals from the periphery project into a "neuromatrix" that includes the thalamus, hypothalamus, anterior cingulate cortex, somatosensory cortex, brain stem, periaqueductal gray-matter (PAG), brain stem reticular nuclei, and locus ceruleus **(4)**. These tracts spread to a wide variety of sites in the brain that are involved with nociceptive processing **(Fig. 1)**. Signals reaching the somatosensory cortex are perceived as pain, on the other hand, other signals project into the midbrain and areas that are involved with the affective (emotional) components of pain **(5)**.

Pain modulation occurs through neuronal projections from the PAG area and the nucleus raphe magnus, which form descending pathways that inhibit or facilitate pain signals at lower levels of the central nervous system (CNS), including the substantia gelatinosa (the Rexed lamina II) **(8)**.

Current research proved that the neuro-anatomic and neuroendocrine systems necessary to perceive pain are present by the 25th week of gestation, but the descending inhibitory systems are not completely developed until sometimes after birth. Tissue injury produces a neuroendocrine stress response and inflammatory immunologic changes that modulate pain. Local inflammatory reaction induced by mast cells, macrophages, and neutrophils produces leakage of plasma, increased capillary wall permeability, and the release of mediators like kinins,

amines, arachidonic acid derivatives, tumor necrosis factor (TNF), purines, potassium ions, hydrogen ions, serotonin, afferent amines, proteases, and nerve growth factor **(9)**.

This inflammatory reaction decreases the threshold for neuronal activation, and results in hyper-algesia, leading to chronic pain, moreover, the intracellular changes alter the properties of the pain neurons making pain cells to be more excitable and reactive to harmless stimuli, producing central sensitization or "wind-up". With central sensitization, pain becomes self-sustaining and very difficult to treat. Even non-noxious sensations can evoke pain if wind-up is present; examples of which are complex regional pain syndrome type 1 and allodynia **(10)**.

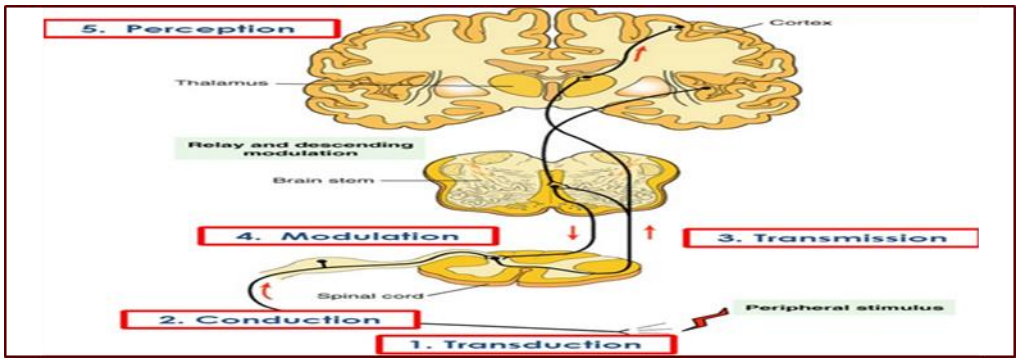

Figure (1): Overview of the basic nociceptive circuit (5 Polaner and Anderson., 2016)

Endogenous Substances Modulating Nerve Function

Peripheral activation of the nociceptors (transduction) is modulated by a number of chemical substances, which are produced or released when there is cellular damage **(Tab. 1)**. These mediators influence the degree of nerve activity and, hence, the intensity of the pain sensation. Repeated stimulation typically causes sensitization of peripheral nerve fibers, causing lowering of pain thresholds and spontaneous pain, a mechanism that can be experienced as cutaneous hypersensitivity **(11).**

Table (1): Selected chemical substances released with stimuli sufficient to cause tissue damage:

Substance	Source
Potassium	Damaged cells
Serotonin	Platelets
Bradykinin	Plasma
Histamine	Mast cells
Prostaglandins	Damaged cells
Leukotrienes	Damaged cells
Substance P	Primary nerve afferents

Modulation of pain perception:

There are many mechanisms that modulate pain perception: segmental inhibition, the endogenous opioid system, and the descending inhibitory nerve system **(11)**. Segmental inhibition is the noxious impulse that crosses the synapse between the Ad and C nerve fibers and the cells in the dorsal horn of the spinal cord can be blocked by stimulation of inhibitory nerve in the spinal cord that result from stimulation of the Aß fibers (carry impulses from low-threshold mechano- receptors such as touch). Endogenous opioid system: Three compounds (Enkephalin, Endorphin, and Dynorphin) were found to bind to the opium receptors that are located in the peri-aqueductal gray matter, ventral medulla, and spinal cord. Descending inhibitory system: Certain brain-stem areas (periaqueductal gray-matter and rostral medulla) can control the ascent of noxious impulse to the brain, serotonin and noradrenaline are the main neuro-transmitters of this pathway **(12)**.

Protective function of pain:

Local release of chemicals such as substance P causes vasodilation, swelling and release of histamine from the mast cells that further increase vasodilation. This complex chemical signaling protects the injured area by producing behaviors that keep that area away from stimuli. Promotion of healing and protection against infection are aided by the increased blood flow and inflammation **(13).**

Adverse Pathophysiological effects of acute postoperative pain:

Acute postoperative pain after inguinal hernia repair surgeries in pediatrics can activate a neuro-humoral and an immune response to injury **(Fig. 2)**, and the injury responses have a major influence on acute pain mechanisms, so acute postoperative pain and injury of various types are inter-related and if it was severe and prolonged **(Tab. 2)**, the injury response becomes counter-productive and can have adverse effects on outcome **(14)**.

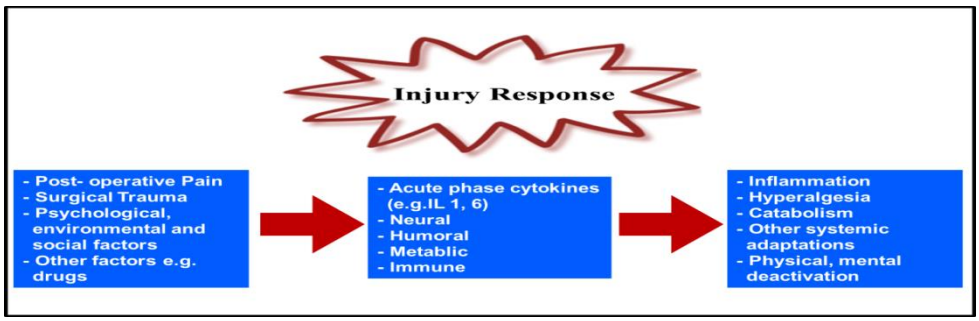

Figure (2): The post-operative injury response **(14).**

The cytokine cascade activated in response to surgical trauma consists of a complex biochemical network with diverse effects on the injured host. Whereas elements of the immune system are stimulated to an excessive degree following major surgery, other functions such as that of cell-mediated immunity are dramatically paralyzed. Cytokines are immune mediators that direct the inflammatory response to sites of injury and infection and are essential for wound healing **(15).**

An exaggerated production of proinflammatory cytokines from the primary site of injury, however, can manifest systemically as hemodynamic instability or metabolic derangements.

Proinflammatory cytokine production in the intraoperative and early postoperative periods is initiated by macrophages and monocytes at the initial site of injury as part of the acute-phase response. These cytokines include tumor necrosis factor and interleukin 1 which are primarily responsible for the non-hepatic manifestations of the acute-phase response, including fever and tachycardia. In turn, TNF and IL-1stimulate the production and release of other cytokines, including IL-6. Interleukin 6 primarily regulates the hepatic component of the acute-phase response resulting in the generation of acute-phase proteins, including C-reactive proteins. Circulating levels of several other acute-phase proteins, including serum amyloid A,7 pro calcitonin,8 C3 complement, and haptaglobin, have also been shown to increase after traumatic insult, providing further evidence of a systemic host response**(16)**

Table (2): Metabolic and endocrine responses to injury (14).

Endocrine	↑ Catabolic hormones	↑ ACTH, Cortisol, ADH, Growth hormone, Catecholamines, angiotensin II, aldosterone, glucagons, IL-l, TNF, lL-6.
	↓ Anabolic hormones	↓ Insulin, testosterone
Metabolic		
Carbohydrates	Hyperglycemia, glucose intolerance, insulin resistance.	↑ Glycogenolysis, gluconeogenesis (cortisol, glucagon, growth hormone, adrenaline, free fatty acids). ↓ Insulin secretion activation.
Proteins	Muscle protein catabolism. ↑ synthesis of acute phase proteins	↑ Cortisol, adrenaline, glucagons, IL-l. IL-6, TNF.
Lipids	↑ Lipolysis and oxidation	↑ catecholamines, cortisol, glucagon, growth hormone.
Water and Electrolyte	Retention of water and sodium. ↑ excretion of potassium and ↓ functional ECF with shifts to ICF	↑ catecholamines, aldosterone, cortisol, ADH, angiotensin II, prostaglandins and other factors.

ACTH: Adreno Cortico Trophic Hormone. **ADH**: Anti Diuretic Hormone. **IL**: Interleukin. **TNF**: Tumor Necrosis Factor. **ECF**: Extra Cellular Fluid. **ICF**: Intra Cellular Fluid.

Assessment of post-operative pain in Pediatrics

The distinction between measurement and assessment in pain research has not always been clarified. Measurement refers to the application of some metric to a specific element; usually intensity of pain, However assessment is much broader, as it measures the impact of different

factors on the experience of pain. These factors might include the affective response to noxious stimuli, the role of family style on the perception of pain, the impact on families of having a child in pain, and the meaning of pain to the child and to the family **(17)**.

Multidimensional Pain Assessment Physiologic pain measures in conjunction with carefully applied behavioral scales have proven to be the best tools for measuring pain in this group. Multi-dimensional assessments are more accurate than single parameters. Composite pain measures use more than one parameter in assessing pain experience. Measures for older children often include self-report in addition to behavioral or physiologic indicators **(18)**.

Assessments that use multiple measures (behavioral and physiologic) and that assess different aspects of the pain experience (e.g. intensity, location, pattern, and meaning) may result in more accurate evaluation of children's pain experiences **(19)**.

One of the challenges of pediatric pain management is the assessment and treatment of pain in preverbal children and patients with neurologic or cognitive impairment who cannot communicate their experience of pain **(20)**.

In children under 3 years, one must rely on a combination of behavioral clues and physiologic signs. Many of these signs are also seen in conditions other than pain, such as parental separation, hunger, fear, and anxiety. Thus misinterpretation is common. Parents can often determine whether their child is in pain by learning specific behaviors in their child that distinguish pain from distress or anxiety **(21)**.

We primarily rely on five different types of pain scales that are used in different age groups. For the neonatal population2 (up to approximately3 months of age), we use the neonatal infant pain scale **(Tab. 3)**. It is primarily used to assess pain associated with medical procedures and includes assessment of facial expression, severity of crying, breathing patterns, movement of arms and legs, and state of arousal **(22)**.

The CRIES score is also used in infants and uses five parameters: severity of crying, oxygen requirement, increased heart rate and blood pressure, facial expression, and degree of sleeplessness **(Tab. 4)**, each of which are graded from zero to two; this gives a total between zero and 10 A score over four indicates that additional analgesics are required **(23).**

Table (3): Neonatal Infant Pain Scale. (22).

Parameter	Finding	Points
Facial Expression	Relaxed	0
	Grimace	1
Cry	No cry	0
	Whimper	1
	Vigorous crying	2

Breathing Patterns	Relaxed	0
	Change in breathing	1
Arms	Restrained	0
	Relaxed	0
	Flexed	1
	Extended	1
Legs	Retrained	0
	Relaxed	0
	Flexed	1
	Extended	1
State of Arousal	Sleeping	0
	Awake	0
	Fussy	1

Table (4): The CRIES Scale (23)

	0	**1**	**2**
Crying	None	High-pitched	Inconsolable
Requires O_2	None	<30% FiO_2 needed	>30% FiO_2 needed
Increased vital signs	Normal HR & BP	Increased HR & BP < 20%	Increased HR & BP > 20%
Expression	Normal	Grimace	Grimace & grunt
Sleeplessness	None	Wakes frequently	Awake constantly

The second Piaget developmental stage is the preoperational stage (approximately 2 to 7 years), in which children acquire some language ability and can localize pain, differentiate "a little" and "a lot," and can use simple terms to describe their pain such as "boo-boo," "ouch," "hurt," and "ow-ee." For this age group, we commonly use the Wong-Baker FACES scale or the FLACC scale This FACES scale has recently been updated to include more realistic facial expressions. Mature children in this stage may be able to use patient-controlled analgesia **(23)**.

Faces scale:

The Wong-Baker FACES Pain Rating Scale (WBS) is preferred by parents and patients for reporting pain severity **(Fig. 3)**. However, it is speculated that the "no hurt" and "hurts worst" anchors confound pain measurement with nonnociceptive states **(24)**.

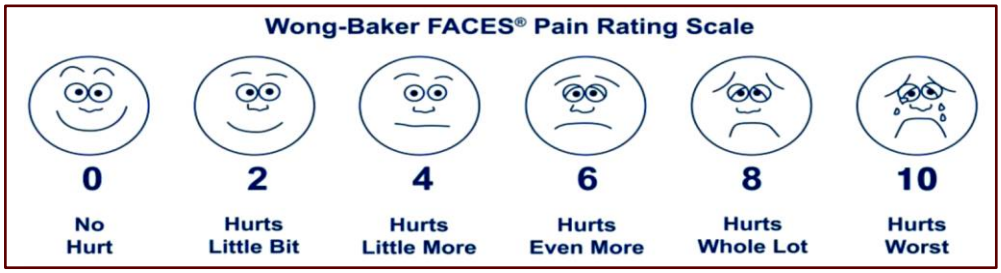

Figure (3): FACES scale (24)

Flacc scale:

The FLACC scale or Face, Legs, Activity, Cry, and Consolability scale is one of the most commonly and widely used behavioral observation pain scales to assess pain for children between the ages of 2 months and 7 years or individuals that are unable to communicate their pain. The level of response for each observation is given a numerical value rating from "0" to "2," with "0" being the most comfortable with no pain and "2" being the most painful, which results in a total score between "0" and "10." **(24)**.

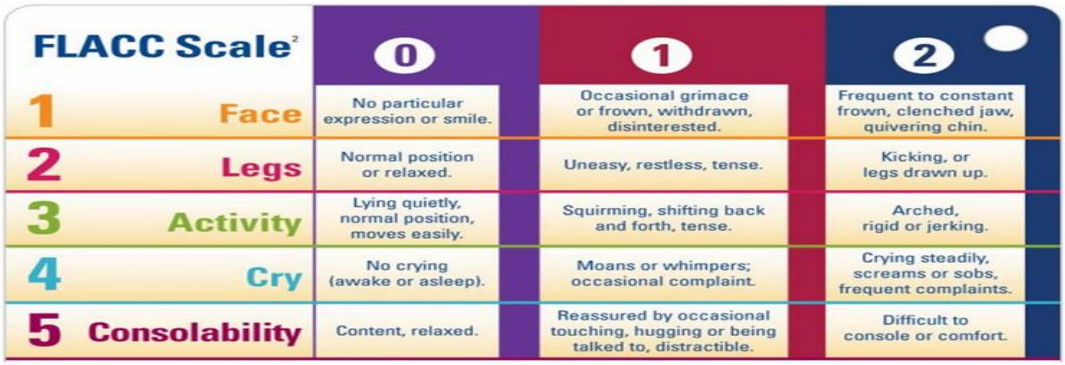

Figure (4): FLACC scale (24)

The FLACC scale has also been found to be accurate for use with adults in intensive-care units (ICU) who are unable to speak due to intubation. The FLACC scale offered the same evaluation of pain as did the Checklist of Nonverbal Pain Indicators scale which is used in ICUs **(24)**.

Also commonly used is the Revised-FLACC (rFLACC) scale, which is a modification of the FLACC scale aimed to better evaluate pain in pediatric patients with cognitive impairments, in addition to those who are unable to report their pain score because of age or have difficulty with oratory or motor skills. As such, rFLACC was modified to include several additionalbehavioral descriptors, including: verbal outbursts, tremors, increased spasticity, jerking movements, and respiratory pattern changes, such as breath holding or grunting **(25)**.

Table (5): The revised FLACC SCALE (25)

(REVISED) FLACC Scale SCORING			
Categories	**0**	**1**	**2**
Face	No particular expression or smile.	Occasional grimace or frown, withdrawn, disinterested, **Sad, appears worried.**	Frequent to constant quivering chin, clenched jaw, **distressed looking face, expression of fright/ panic.**
Legs	Normal position or relaxed; **usual tone and motion to limbs.**	Uneasy, restless, tense, **occasional tremors.**	Kicking, or legs drawn up, **marked increase in spasticity, constant tremors, jerking.**
Activity	Lying quietly, normal position, moves easily, **regular, rhythmic respirations.**	Squirming, shifting back and forth, tense, **tense/guarded movements, mildly agitated, shallow/ splinting respirations, intermittent sighs**	Arched, rigid or jerking, **severe agitation, head banging, shivering, breath holding, gasping, severe splinting.**
Cry	No cry (awake or asleep)	Moans or whimpers: occasional complaint, **occasional verbal outbursts, constant grunting**	Crying steadily, screams or sobs, frequent complaints, **repeated outbursts, constant grunting.**
Consolability	Content, relaxed	Reassured by occasional touching, hugging, or being talked to: distractible	Difficult to console or comfort, **pushing caregiver away, resisting care or comfort measures.**

Each of the five categories (**F**) Face; (**L**) Legs; (**A**) Activity; (**C**) Cry; (**C**) Consolability is scored from 0-2, which results in a total score between zero and ten.

During Piaget's concrete operations stage (approximately8 to 12 years), children think logically and can be taught methods of cognitive and behavioral pain control such as distraction, relaxation, guided imagery, and hypnosis. They can relate details about their pain such as how the pain varies with activity or time of day. For children in this age range, we use FACES, or a simple verbal numeric 11-point scale0–10) on which 0 represents no pain and 10 represents the worst pain imaginable. Patient-controlled analgesia is often used during this developmental stage **(22)**.

Pre-emptive and preventive analgesia:

It is well documented that although general anesthesia may attenuate synaptic transmission of afferent injury discharge from the periphery to the spinal cord and brain, it does not completely block it. Moreover, systemic opioids may not provide a sufficiently effective blockade of the neuro-transmission of spinal nociceptive neurons to prevent central sensitization **(26)**.

The idea that surgical incision is the trigger of central sensitization has been broadened to include the sensitizing effects of preoperative noxious inputs and pain, also other noxious stimuli include intraoperative stimuli, postoperative peripheral and central inflammatory mediators and ectopic neural activity **(27)**.

Recent meta-analysis provides support for pre-emptive epidural analgesia. The efficacy of different pre-emptive analgesic interventions (epidural analgesia, local anesthetic wound infiltration, systemic opioids, and systemic NSAIDs) was analyzed in relation to different analgesic outcomes. Improvements were found in all outcomes, but the most effective was epidural analgesia **(28)**.

Another study demonstrated a clear preventive effect on the development of residual pain up to 1 year after surgery with continuous peri-operative epidural analgesia **(29)**.

Many acute pain services use techniques of concurrent or co-analgesia based on four classes of analgesics, namely local anesthetics, opioids, nonsteroidal anti-inflammatory drugs (NSAIDs), and acetaminophen (paracetamol) **(30).**

Conclusion:

Inguinal hernias are common in infants and children. Assessment of pain and its impact on the patient is the most important first step in managing pain.

Pain assessment is most accurate when the child can describe its location, nature, and severity.

Prevention of pain whenever possible, using multi-modal analgesia, has been shown to work well for nearly all cases and can be adapted for day cases, major cases, the critically ill child, or the very young.

In particular, a local/regional analgesic technique should be used in all cases unless there is a specific contra-indication.

No Conflict of interest.

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