Nonprescription therapies for fever & pain management in children

Welcome
We will begin shortly.

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Pfizer Consumer Healthcare

Today's Speaker (s)

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Disclosure(s)

I received an honorarium from CPhA for this presentation.

Relationships with commercial interests:

Speakers Bureau/Honoraria: J&J, Pfizer, GSK, P&G

Advisory Boards/Consulting Fees: Apotex, Allergan, J&J, Pfizer, WN Pharmaceuticals

Learning Objectives

1. Dispel common myths & misconceptions about fever & pain.

2. Differentiate between pediatric patients presenting with fever and/or pain who may appropriately be considered for treatment with nonprescription products and patients requiring referral.

3. Select appropriate therapies (pharmacologic & nonpharmacologic) for fever & acute pain management in the pediatric population.

FEVER

(Pyrexia)

Thought Starters (T/F)

1. Fevers over 41°C require immediate referral to an emergency department.
2. The severity of fever does not always correspond with the severity of illness.
3. You should recommend alternating ibuprofen and acetaminophen to “break” a fever and/or for acute pain management.
4. Acetaminophen and Ibuprofen have similar safety profiles when taken at recommended OTC doses.
5. Sponge-baths are a recommended nonpharmacologic method to for low-grade fevers.

Thermoregulation

- *Hypothalamus* maintains core body T at a "set point" (~**37°C** / 98.6°F)
  - Negative feedback system between thermoregulatory center in hypothalamus & thermosensitive neurons in the skin & CNS
  - Compensatory physiologic mechanisms & behavioral adaptations help return the T to normal if above or below set point
  - Infants < 3 mo.: immature thermoregulatory system & incompletely vaccinated

Fever is of higher clinical importance!

Image taken from: https://www.medicalnewstoday.com/articles/312628.php

Normal Body T

- Follows a **circadian rhythm**[1]
  - *Lowest point* in early morning (~6am): 37.2°C
  - *Highest point* in late afternoon (~4-6pm): 37.7°C
  - May vary daily by as much as 0.5°C[1,2]

- Varies depending on site of measurement[2]

Site of Measurement	Normal T Range
Rectal	36.6°C to 38°C (97.9°F-100.4°F)
Tympanic	35.8°C to 38°C (96.4°F-100.4°F)
Oral	35.5°C to 37.5°C (95.9°F-99.5°F)
Axillary	36.5°C to 37.5°C (97.8°F-99.5°F)

[1]Shevchuk YM. Fever. In: Jovaisas B, ed. *Compendium of Therapeutics for Minor Ailments* 2nd ed. Ottawa, ON: Canadian Pharmacists Association; 2018:79-95.
[2]Leduc D, Woods S, Community Paediatrics Committee C. Temperature measurement in paediatrics. [Position Statement]. 2017; https://www.cps.ca/en/documents/position/temperature-measurement. Accessed November 18, 2018.

Definition[1,2] & Prevalence[2]

- A regulated elevation in body T above the normal core T range
  - **FEVER = T > 38°C (rectal or rectal equivalent)**

Site of Measurement	Fever
Rectal	>38°C (>100.4°F)
Tympanic	>37.8°C (>37.8°F)
Oral	>37.5°C (>99.5°F)
Axillary	>37.5°C (>99.5°F)

  - **HIGH FEVER > 40.5°C (104.9°F)**
  - **HYPERPYREXIA > 41.1°C (106°F)**

- 30% of children presenting to their MD's have fever as a complaint
  - Leading cause of ER visits for children <15 y/o

[1]Shevchuk YM. Fever. In: Jovaisas B, ed. *Compendium of Therapeutics for Minor Ailments* 2nd ed. Ottawa, ON: Canadian Pharmacists Association; 2018:79-95.
[2]Lemay V, Feret BM. Fever. In: Krinsky DL, ed. *Handbook of Nonprescription Drugs: An Interactive Approach to Self-Care.* 19th ed. Washington, DC: American Pharmacists Association; 2018:97-110.

While most fevers are self-limited and nonthreatening, they can cause a great deal of discomfort and may indicate a serious underlying pathologic condition.

Clinical Presentation

- Headache
- Backache
- Myalgia
- Arthralgia
- Somnolence
- Chills
- Rigors
- Irritability/ crying
- Diaphoresis
- Clammy skin
- Flushing
- Malaise
- Fatigue
- Anorexia
- Tachycardia
- Tachypnea

[1]Shevchuk YM. Fever. In: Jovaisas B, ed. *Compendium of Therapeutics for Minor Ailments* 2nd ed. Ottawa, ON: Canadian Pharmacists Association; 2018:79-95.
[2]Lemay V, Feret BM. Fever. In: Krinsky DL, ed. *Handbook of Nonprescription Drugs: An Interactive Approach to Self-Care.* 19th ed. Washington, DC: American Pharmacists Association; 2018:97-110.

"Most children will tolerate a fever well, so if they continue to be alert, play normally, and stay hydrated, the fever is not of great concern."

Lemay V, Feret BM. Fever. In: Krinsky DL, ed. *Handbook of Nonprescription Drugs: An Interactive Approach to Self-Care.* 19th ed. Washington, DC: American Pharmacists Association; 2018:97-110.

Fever Phobia

- Exaggerated, unrealistic fear of fever
  - May prompt overly aggressive patient monitoring
  - May lead to inappropriate treatment of fever
- Pharmacists should undertake educational interventions to ensure appropriate management of fever & rational use of antipyretics
- Provide parents with appropriate monitoring schedules

TO TREAT OR NOT TO TREAT… THAT IS THE QUESTION

- Fever is usually benign & self-limited
- Fever is an important defense mechanism that enhances the immune system
- The possible elimination of a valuable diagnostic or prognostic sign
- Possible AE's of antipyretic medications

- Enhanced QOL: relieve symptoms associated with fever that may cause substantial discomfort
- Treatment of fever does little harm and has not been shown to clinically alter the course of common bacterial and viral infections

The decision to treat fever is based on a patient-specific risk-benefit ratio.

Goals of Therapy

1. **Alleviate patient discomfort**
2. Reduce or relieve parental anxiety
3. Balance the benefit of symptomatic treatment with possible adverse effects & cost of medication

UK Stance

"The data suggests [ibuprofen and acetaminophen] have **similar safety profiles** in [the treatment of fever **in distressed** children] and in the absence of underlying health issues, **ibuprofen seems to be more effective** than acetaminophen in reducing 'distress'."

Kanabar D. A practical approach to the treatment of low-risk childhood fever. *Drugs R D*. 2014;14(2):45-55. http://subjectguides.uwaterloo.ca/c.php?g=695555&p=4933484. Published June 2014. Accessed November 26, 2018

RED FLAGS[1,2]

Immediately REFER to the **EMERGENCY DEPARTMENT:**

- Age < 3 months
- Presence of stiff neck, seizure, localized pain, redness, swelling or heat
- New wheeze/cough
- Recent cancer therapy
- Child appearing very ill, excessively fussy, irritable, crying inconsolably or other symptom(s) worrying the parents/caregivers

[1]Shevchuk YM. Fever. In: Jovaisas B, ed. *Compendium of Therapeutics for Minor Ailments* 2nd ed. Ottawa, ON: Canadian Pharmacists Association; 2018:79-95.
[2]Lemay V, Feret BM. Fever. In: Krinsky DL, ed. *Handbook of Nonprescription Drugs: An Interactive Approach to Self-Care.* 19th ed. Washington, DC: American Pharmacists Association; 2018:97-110.

RED FLAGS[1,2]

REFER to URGENT CARE OR PRIMARY CARE PHYSICIAN:

- Age 3-6 months
- High fever
- Persistent wheeze/cough
- New onset rash and fever
- Difficult to rouse, confused or delirious
- Presence of serious underlying illness
- Recent surgery or dental procedure
- Recent travel
- Recent consumption of raw or undercooked meat or fish
- Recent initiation of new medication
- Fever has not resolved after 72 h

[1]Shevchuk YM. Fever. In: Jovaisas B, ed. *Compendium of Therapeutics for Minor Ailments* 2nd ed. Ottawa, ON: Canadian Pharmacists Association; 2018:79-95.
[2]Lemay V, Feret BM. Fever. In: Krinsky DL, ed. *Handbook of Nonprescription Drugs: An Interactive Approach to Self-Care.* 19th ed. Washington, DC: American Pharmacists Association; 2018:97-110.

Patient Assessment

- Step 1: Obtain an objective, accurate T measurement
  - patient's age
  - time of day
  - level of physical & emotional stress
  - anatomic site of T measurement
- Step 2: If fever is present, assess:
  - its history
  - its severity
  - potential fever inducers
  - other associated symptoms
  - the seriousness of the underlying cause

Age	Recommended technique
Birth to 2 years	1. Rectal (definitive) 2. Axillary (screening low risk children)
Over 2 years to 5 years	1. Rectal (definitive) 2. Axillary, Tympanic (or Temporal Artery if in hospital) (screening)
Older than 5 years	1. Oral (definitive) 2. Axillary, Tympanic (or Temporal Artery if in hospital) (screening)

Leduc D, Woods S, Community Paediatrics Committee C. Temperature measurement in paediatrics. [Position Statement]. 2017; https://www.cps.ca/en/documents/position/temperature-measurement. Accessed November 18, 2018.

PAIN

Thought Starters (T/F)

1. Infants do not feel pain as their nervous system is not developed.
2. Children do not remember pain, so acute painful events won't have a lasting impression.
3. The FLACC scale is the preferred tool to assess pain severity in a verbal 5 y/o.
4. Naproxen is a safe and effective OTC treatment option for acute pain in children under 12 y/o.
5. Ibuprofen 200mg ≅ Aspirin 650mg ≅ Acetaminophen 650mg

Acute Pediatric Pain

- One of the most common symptoms experienced by patients
- Temporary (may last for minutes or up to several weeks)
- Evaluation includes:
  1. Recognizing the patient is in pain
  2. Determining the underlying type, source/location, and severity of pain
  3. Tailoring treatment to the level and type of pain
- Presenting patients should be assessed efficiently, calmly and with empathy

Bailey B. Acute Pain. In: *Compendium of Therapeutic Choices*. Ottawa, ON: Canadian Pharmacists Association; 2018. www.rxtx.ca. Accessed November 20, 2018.
Hauer J, Jones BL. Evaluation and management of pain in children. In: Armsby C, ed.: Wolters Kluwer; 2018: www.uptodate.com. Accessed November 20, 2018.

Self-report of pain remains the recommended method to **assess pain severity** in children. Self-reporting relies upon the cognitive ability of the child to classify and communicate pain severity. However, young children often do not have the cognitive or verbal skills necessary to report and describe pain. Reliable **use of a tool or scale** can facilitate information gathering & help inform therapy.

Crellin DJ, Harrison D, Hutchinson A, Schuster T, Santamaria N, Babl FE. Procedural Pain Scale Evaluation (PROPoSE) study: protocol for an evaluation of the psychometric properties of behavioural pain scales for the assessment of procedural pain in infants and children aged 6-42 months. *BMJ Open*. 2017;7(9):e016225.

Pain Assessment

Nonverbal children (or ≤3 y/o)

- Behavioural indices
- **F**ace, **L**egs, **A**ctivity, **C**ry, **C**onsolability (FLACC) Scale[1]
  - r-FLACC[2] (if cognitively impaired)

The FLACC scale

Face		
0 - No particular expression or smile	1 - Occasional grimace or frown, withdrawn, disinterested	2 - Frequent to constant frown, clenched jaw, quivering chin
Legs		
0 - Normal position or relaxed	1 - Uneasy, restless, tense	2 - Kicking or legs drawn up
Activity		
0 - Lying quietly, normal position, moves easily	1 - Squirming, shifting back/forth, tense	2 - Arched, rigid, or jerking
Cry		
0 - No cry, awake or asleep	1 - Moans or whimpers, occasional complaint	2 - Crying steadily, screams or sobs, frequent complaints
Consolability		
0 - Content, relaxed	1 - Reassured by occasional touching, hugging, or "talking to," distractible	2 - Difficult to console or comfort

Interpreting the score

0 =	Relaxed and comfortable
1-3 =	Mild discomfort
4-6 =	Moderate pain
7-10 =	Severe pain or discomfort or both

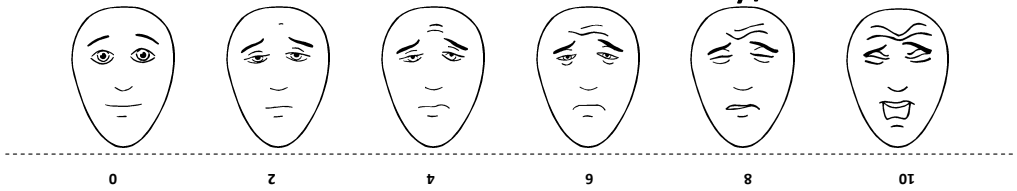
[1]Willis MH, Merkel SI, Voepel-Lewis T, Malviya S. FLACC Behavioral Pain Assessment Scale: a comparison with the child's self-report. *Pediatric nursing.* 2003;29(3):195-198.
[2]SickKids staff. Tools for measuring pain. 2009; https://www.aboutkidshealth.ca/Article?contentid=2994&language=English. Accessed November 10, 2018.

Pain Assessment

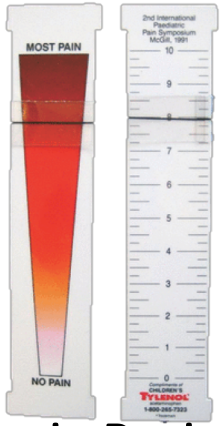
Younger children (3-8 y/o)

- Faces Scales
  - Wong Baker FACES Pain Rating Scale[1]: 3-6+ y/o

  - Faces Pain Scale – Revised[3,4]: 4+ y/o



- Visual Analog Scales (VAS)
  - Color Analogue Scale (CAS)[2]: 4-5+ y/o



- Verbal Numeric Rating Scale (vNRS)[5]: now validated in ≥6 y/o

NEW (2018) Research

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[1]Wong-Baker FACES Foundation. Wong-Baker FACES Pain Rating Scale. *Faces of Pain Care* http://wongbakerfaces.org. Accessed November 10, 2018.
[2]Bulloch B, Garcia-Filion P, Notricia D, Bryson M, McConahay T. Reliability of the color analog scale: repeatability of scores in traumatic and nontraumatic injuries. *Acad Emerg Med.* 2009;16(5):465-469.
[3]Hicks CL, von Baeyer CL, Spafford PA, van Korlaar I, Goodenough B. The Faces Pain Scale-Revised: toward a common metric in pediatric pain measurement. *Pain.* 2001;93(2):173-183.
[4]Bieri D, Reeve RA, Champion GD, et al. The Faces Pain Scale for the self-assessment of the severity of pain experienced by children: development, initial validation, and preliminary investigation for ratio scale properties. *Pain.* 1990;41(2):139-150.
[5]Tsze DS, von Baeyer CL, Pahalyants V, Dayan PS. Validity and Reliability of the Verbal Numerical Rating Scale for Children Aged 4 to 17 Years With Acute Pain. *Ann Emerg Med.* 2018;71(6):691-702 e693

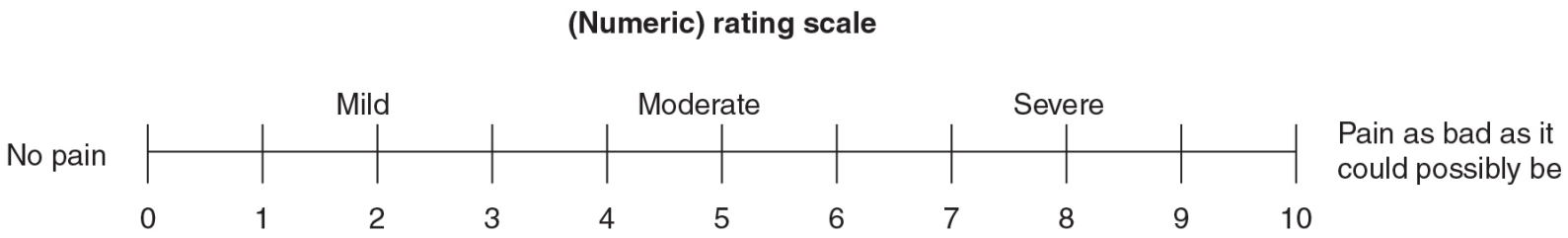
Pain Assessment

Older children (8-11 y/o)

- Visual analog tools that rate pain intensity on a horizontal or numeric scale

Adolescents

- Numeric rating scale without accessory pain assessment tool



Tips for Using Self-Report Pain Scales

- Ensure age-appropriateness

- If possible, introduce the scale to the child when they are **not** in pain
  - Offer the child a chance to practice with the scale by rating hypothetical situations that would produce low and high levels of pain

- When possible, obtain successive pain ratings over time to track events known to cause pain as well as the efficacy of interventions

McGrath PA, Seifert CE, Speechley KN, Booth JC, Stitt L, Gibson MC. A new analogue scale for assessing children's pain: an initial validation study. *Pain.* 1996;64(3):435-443.

RED FLAGS[1,2]

- Age <2 years
- NRS ≥ 7
- Pain due to trauma
- Pelvic or abdominal pain *(exception: primary dysmenorrhea)*
- Pain that does not improve or worsens with treatment
- Concurrent signs/symptoms indicative of systemic infection
- Other indicators warranting referral based on nature of pain

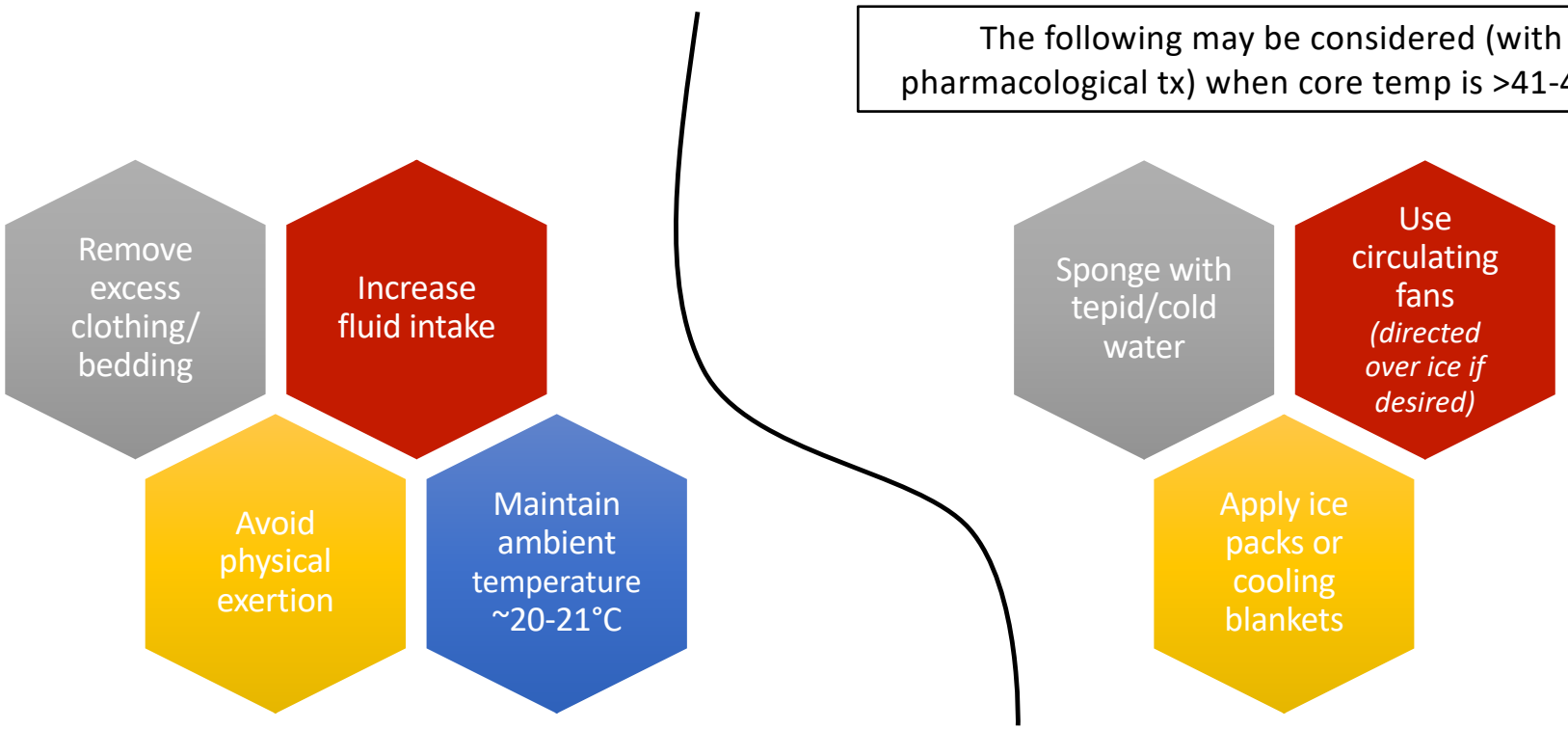
[1]O'Donnell FT, Rosen KR. Pediatric pain management: a review. *Mo Med.* 2014;111(3):231-237.
[2]medSask. Musculoskeletal strains and sprains – guidelines for prescribing NSAIDs. University of Saskatchewan. http://medsask.usask.ca/professional/guidelines/musculoskeletal-strains-and-sprains.php. Published May 2010. Updated August 2017. Accessed November 26, 2018.

Goals of Therapy

1. Relieve the pain until the cause is managed
2. Identify and treat the cause of pain
3. If possible, prevent the pain

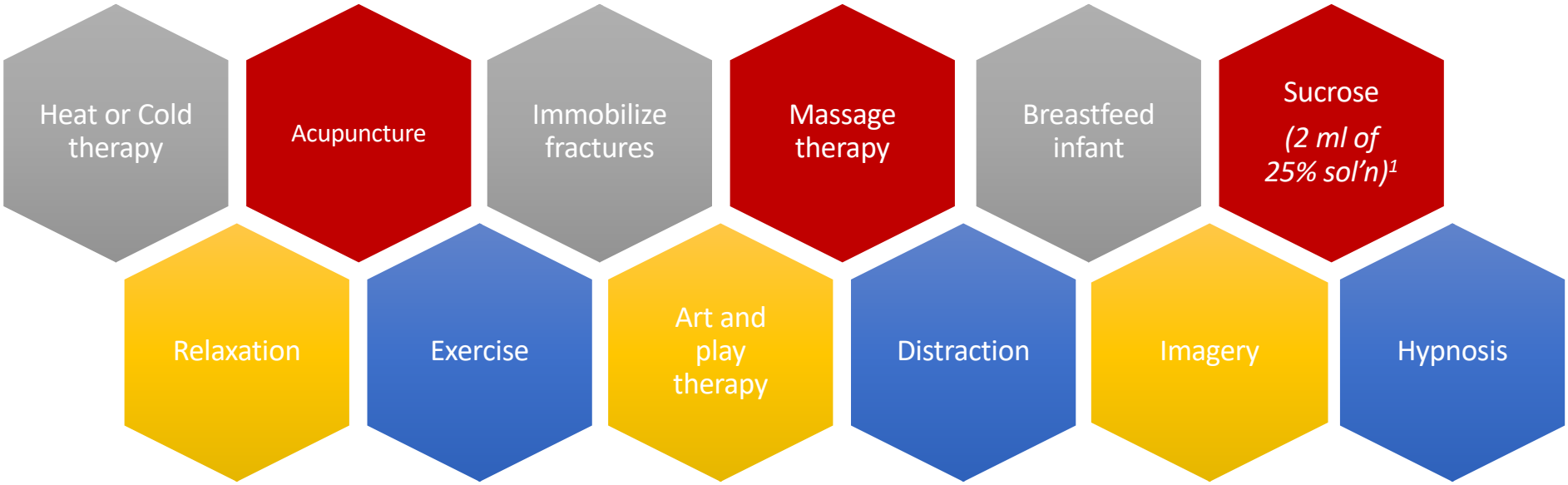
THERAPY

Nonpharmacologic Strategies for Fever



[1]Shevchuk YM. Fever. In: Jovaisas B, ed. *Compendium of Therapeutics for Minor Ailments* 2nd ed. Ottawa, ON: Canadian Pharmacists Association; 2018:79-95

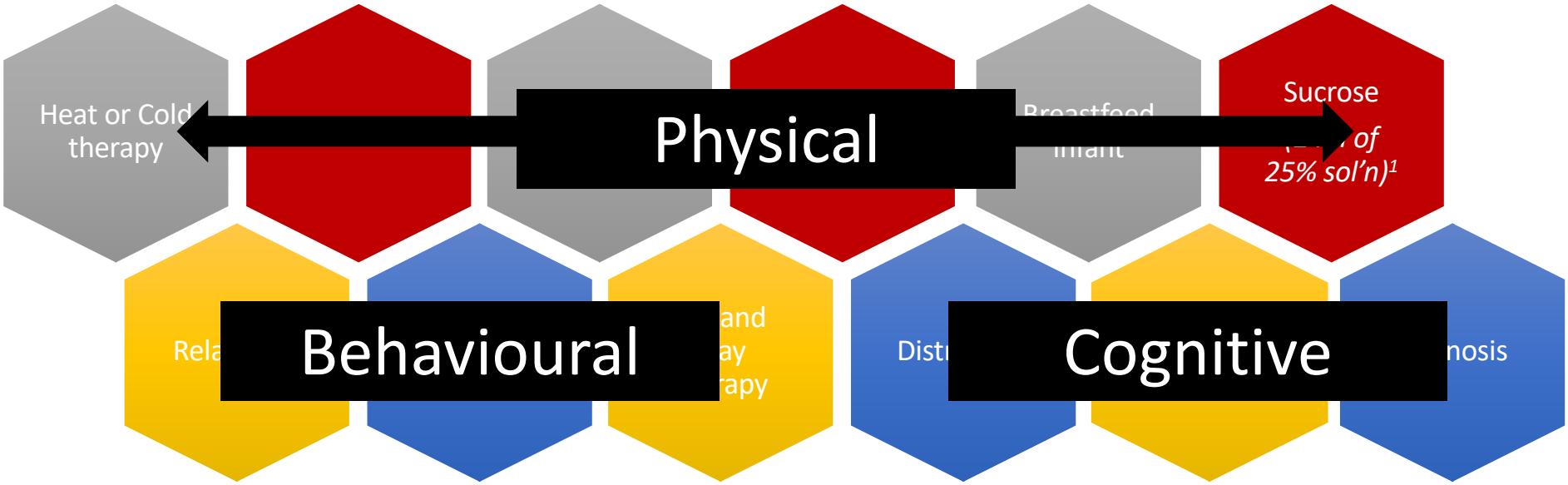
Nonpharmacologic Strategies for Pain*



***Note:** list is not exhaustive

[1]Regier L, Jensen B, Kessler B. Pediatric pain: treatment considerations, Q&As. RxFiles. RxFiles.ca Published March 2017. Accessed November 26, 2018.
Shevchuk YM. Chapter 7: Fever. Compendium of Therapeutics for Minor Ailments. 2nd ed. Ottawa, ON: Canadian Pharmacists Association; 2016:84-97.
Hauer J, Jones BL. Evaluation and management of pain in children. In: Post T, ed. *UpToDate*. Waltham, MA: UpToDate; 2018. www.uptodate.com. Accessed November 26, 2018.

Nonpharmacologic Strategies for Pain*



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[1]Regier L, Jensen B, Kessler B. Pediatric pain: treatment considerations, Q&As. RxFiles. RxFiles.ca Published March 2017. Accessed November 26, 2018.
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Hauer J, Jones BL. Evaluation and management of pain in children. In: Post T, ed. *UpToDate*. Waltham, MA: UpToDate; 2018. www.uptodate.com. Accessed November 26, 2018.

Pharmacologic OTC Options for Fever AND Pain

Variable	Acetaminophen	Ibuprofen
Dose	**PO:** 10–15 mg/kg q4-6h PRN **PR:** 15-20 mg/kg/dose	**PO:** 5–10 mg/kg q6-8h PRN
Maximum daily dose	**Neonates:** 60 mg/kg **Older infants & children:** 75mg/kg	40mg/kg
Onset (hr)	<1	<1
Time to peak effect (hr)	2–4	2 – 4
Duration of effect (hr)	**Pain & fever:** 4–6	**Pain:** 4–6; **Fever:** 6–8
Adverse effects (AEs)	Uncommon with infrequent use & recommended OTC dose	
Other Info/Concerns	Hepatotoxicity in acute overdose setting	GI: dyspepsia, abdominal pain Nephrotoxicity in children with: pre-existing renal disease, dehydration, nephrotoxic agents, CVD

Benoit B. Acute pain. In Compendium of Therapeutic Choices. Ottawa, ON: Canadian Pharmacists Association. [Updated May 2018; Accessed November 26, 2018]. https://myrxtx.ca.
Shevchuk YM. Chapter 7: Fever. Compendium of Therapeutics for Minor Ailments. 2nd ed. Ottawa, ON: Canadian Pharmacists Association; 2016:84-97.
Feret BM. Fever. In: *Handbook of Nonprescription Drugs*. 18th ed. Washington, DC: American Pharmacists Association; 2015. p. 83-96.
Sullivan, Janice E., and Henry C. Farrar. "Fever and Antipyretic Use in Children." *Pediatrics* 127, no. 3 (March 1, 2011): 580–87.
Ibuprofen. In: Lexi-Drugs. Hudson, OH: Lexi-Comp, Inc. [Updated November 27, 2018; Accessed November 27, 2018]. http://online.lexi.com/lco/action/doc/retrieve/docid/patch_f/7066.

A variety of dosage forms and flavours are available

Shared decision-making ensures product selection is evidence-based and acceptable to the patient.

Alternating Acetaminophen and Ibuprofen

- The safety & effectiveness of this practice in improving overall comfort has not been determined

- AAP & CPS **do not recommend** it
  - Risk of overdose
  - Risk of medication dosing errors
  - Risk of increased adverse effects (e.g., renal)

- Monotherapy sufficient & preferred for vast majority
  - If response is inadequate, it is reasonable to initiate treatment with acetaminophen or ibuprofen, then switch to the alternate medication if the patient's fever does not respond *well* to the initial agent

Mistry N, Hudak A. Combined and alternating acetaminophen and ibuprofen therapy for febrile children. *Paediatrics & Child Health.* 2014;19(10):531-532.
Chung AM. An evaluation of community pharmacy recommendations regarding alternating antipyretics in children. *J Am Pharm Assoc (2003).* 2018;S1544-3191(18):30320.
Fever and Antipyretic Use in Children. Janice E. Sullivan, Henry C. Farrar, the Section on Clinical Pharmacology and Therapeutics and Committee on Drugs *Pediatrics* 2011;127;580.
Hoover L. AAP Reports on the Use of Antipyretics for Fever in Children. Available at: http://pediatrics.aappublications.org/content/127/3/580.full
Mayoral CE, Marino rv, Rosenfeld W, et al. Alternating antipyretics: is this an alternative? Pediatrics. 2000;105:1009–12.

Alternative Options for Fever AND Pain

Variable	Naproxen Sodium	Prescription Analgesic (e.g., NSAIDs, opioids)
Dose	*Children ≥12 years* → **PO:** 220 mg q8-12h	*May be used when OTC therapy has failed or is inappropriate.* *Consult appropriate drug resources for more detail.*
Maximum daily dose	440 mg (self-care)	
Onset (hr)	<1	
Duration of effect (hr)	7-12	
Adverse effects (AEs)	Dyspepsia, NV, abdominal pain, dizziness, headache	
Other Info/Concerns	Nephrotoxicity in children with: pre-existing renal disease, dehydration, nephrotoxic agents, CVD	

Naproxen. In: Lexi-Drugs. Hudson, OH: Lexi-Comp, Inc. [Updated November 26, 2018; Accessed November 26, 2018]. http://online.lexi.com/lco/action/search?q=aleve&t=name&va=.

Alternative Options for Pain

Topical Agents

Topical anaesthetics (e.g., EMLA, Ametop, Maxilene)

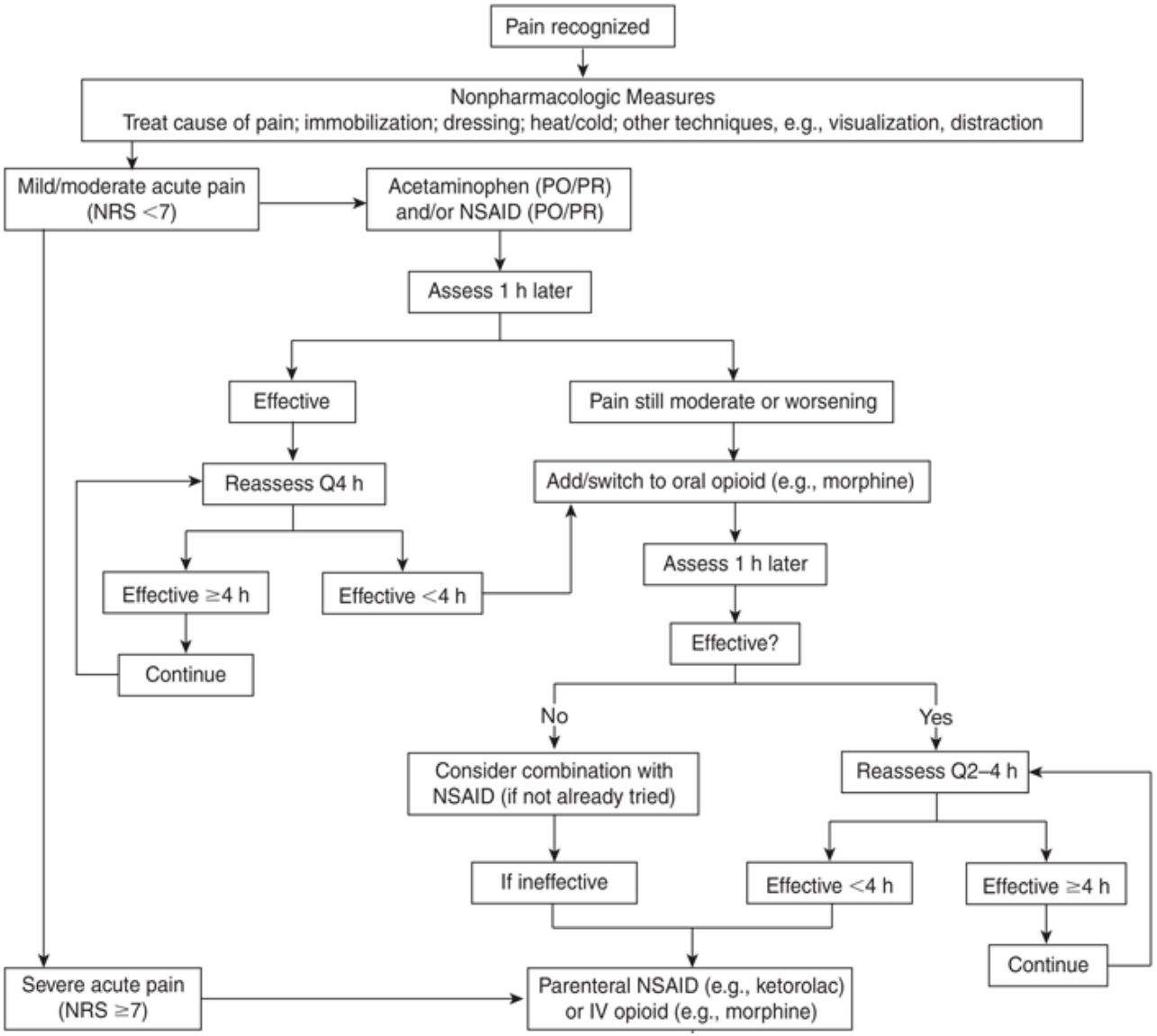
- Can be used to reduce pain associated with minor procedures
- EMLA and Ametop are indicated for use in infants *(>1 month of age for Ametop)*

Topical analgesics (e.g., Voltaren Emulgel, Rub A535)

- Can be used for treatment of acute musculoskeletal pain
- More localized pain relief and fewer systemic effects than oral therapies
- Voltaren Emulgel 1.16% is indicated for use in adolescents ≥16 years of age

Other non-prescription topical agents may be appropriate for pediatric use.
Consult appropriate drug resources for age restrictions and instructions for use.

Benoit B. Acute pain. In Compendium of Therapeutic Choices. Ottawa, ON: Canadian Pharmacists Association. [Updated May 2018; Accessed November 26, 2018]. https://myrxtx.ca.
Regier L, Jensen B, Kessler B. Pediatric pain: treatment considerations, Q&As. RxFiles. RxFiles.ca Published March 2017. Accessed November 26, 2018.
Diclofenac. In: Lexi-Drugs. Hudson, OH: Lexi-Comp, Inc. [Updated November 24, 2018; Accessed November 26, 2018]. http://online.lexi.com/lco/action/search?q=voltaren&t=name&va=.



Bailey B. Acute Pain. In: *Compendium of Therapeutic Choices*. Ottawa, ON: Canadian Pharmacists Association; 2018: www.rxtx.ca. Accessed November 20, 2018.

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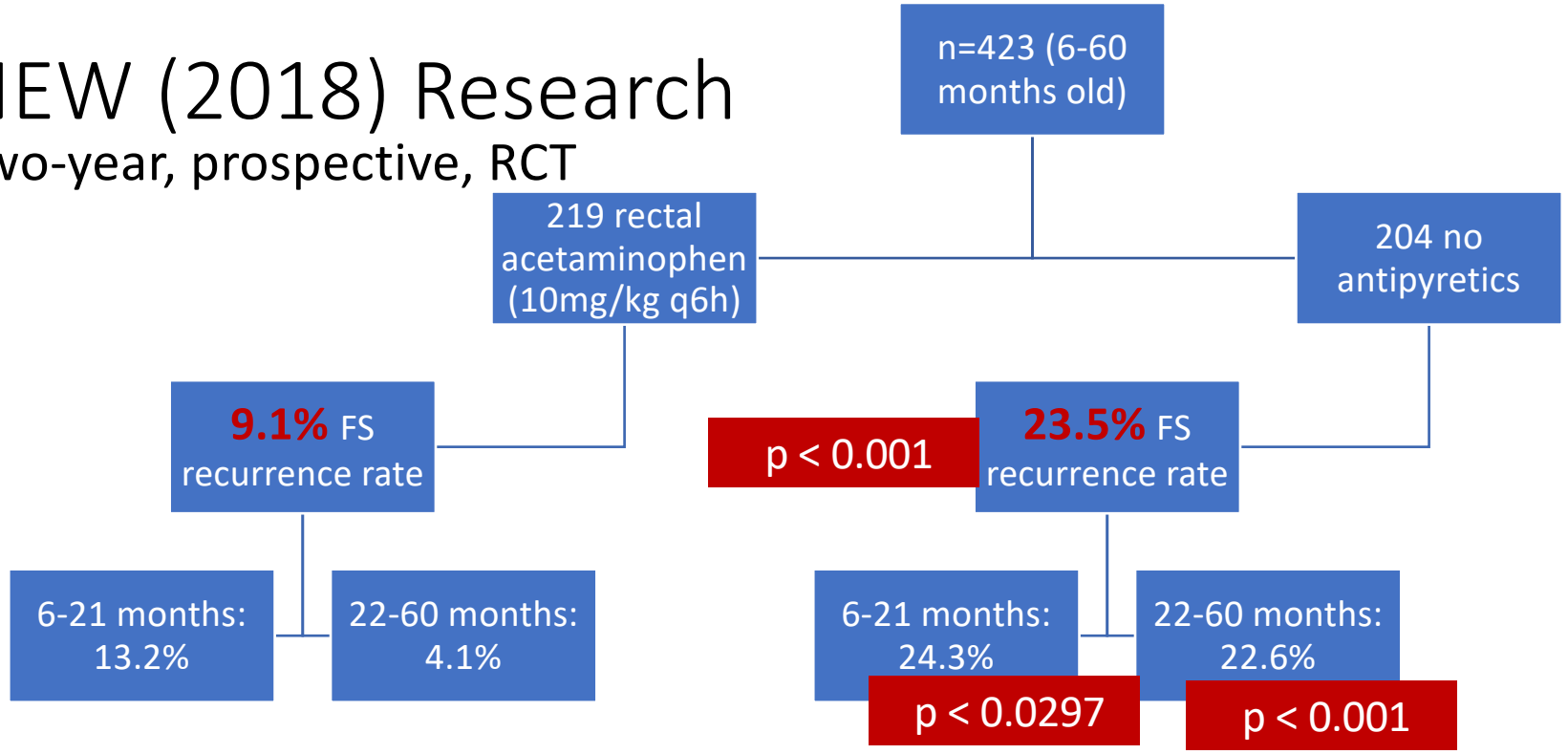
NOT Recommended

- Alcohol
  - Can be absorbed through the skin, inhaled or ingested if used for sponging
  - Has been linked to hypoglycemia, intoxication and coma
- Aspirin
  - Not recommended in patients ≤18 years of age due to risk of Reye's syndrome
- Codeine, tramadol
  - Not recommended in children ≤12 years of age due to variation in metabolism *(CYP2D6 metabolism)*
  - Should be used cautiously in children >12 years of age
  - Not recommended for children of any age following tonsillectomy and/or adenoidectomy

Shevchuk YM. Chapter 7: Fever. Compendium of Therapeutics for Minor Ailments. 2nd ed. Ottawa, ON: Canadian Pharmacists Association; 2016:84-97.
Hauer J, Jones BL. Evaluation and management of pain in children. In: Post T, ed. *UpToDate*. Waltham, MA: UpToDate; 2018. www.uptodate.com. Accessed November 26, 2018.

NEW (2018) Research

Two-year, prospective, RCT



Rectal acetaminophen is safe & effective for FS prevention during same fever episode

Murata S, Okasora K, Tanabe T, et al. Acetaminophen and Febrile Seizure Recurrences During the Same Fever Episode. *Pediatrics.* 2018;142(5).

1998 CPS Position Statement[1]:

Acetaminophen and Ibuprofen in the management of fever and mild to moderate pain in children

Acetaminophen & Ibuprofen have reasonable efficacy & safety for over-the-counter use

- No reports of hepatotoxicity for acetaminophen
- No reports of gastrointestinal bleeding & renal toxicity for ibuprofen[2]
  - Reports suggested association between severe soft tissue superinfections & the use of NSAIDs – more studies required to rule out possibility of rare serious events

However, due to overwhelming safety data in favour of Acetaminophen, it remain the drug of first choice...

- Ibuprofen should be reserved for more problematic cases until a greater volume of safety data is collected

[1]Canadian Paediatric Society. Acetaminophen and ibuprofen in the management of fever and mild to moderate pain in children. *Paediatrics & child health*. 1998;3(4):273-277.

[2]*JAMA*. 1995 Mar 22-29;273(12):929-33.

Updates since the 1998 CPS Position Statement

STUDY	POPULATION	MAIN FINDINGS

Boston University Fever Study[1] (2003)	• 84,192 febrile children (6 months-12 yrs)
	• Received q4-6h PRN (up to 5X/day):
	  • Ibuprofen 5 mg/kg or
	  • Ibuprofen 10 mg/kg or
	  • Acetaminophen 12 mg/kg
		• **Hospitalization** for GI bleeding, renal failure and anaphylaxis were **comparable** between medications
		• **No increased risk** for GI bleeding, renal failure, anaphylaxis or Reye's syndrome for ibuprofen vs. acetaminophen

Children's Analgesic Medicine Project (CAMP) Study[2] (1999)	• 41,810 children (1 month-18 yrs) • Ibuprofen suspension vs. acetaminophen suspension for fever and/or pain	• **No cases** of GI bleeding, renal failure, necrotizing fasciitis, Stevens Johnson syndrome, or anaphylaxis in either group • More adverse events were reported with ibuprofen than acetaminophen but overall differences were small and not clinically important

[1]Lesko SM. The safety of ibuprofen suspension in children. *Int J Clin Pract Suppl*. 2003;135:50-53.
[2]Ashraf E, Ford L, Geetha R, Cooper S. Safety profile of ibuprofen suspension in young children. *Inflammopharmacology*. 1999;7(3):219-225.

Updates since the 1998 CPS Position Statement

STUDY	DETAILS	MAIN FINDINGS

Pierce and Voss (2010)	• Meta-analysis of:
	  • 31 studies on safety
	  • 18 studies on pain
	  • 30 studies on fever
		• 30/31 studies found **no statistical difference in pediatric AEs** for ibuprofen and acetaminophen
		• 11/18 studies showed **no significant difference in efficacy** for ibuprofen and acetaminophen in the treatment of **pain**
		  • 6/18 studies showed **ibuprofen was superior**
		• 15/30 studies showed **no significant difference in efficacy** for ibuprofen and acetaminophen in the treatment of **fever**
		  • 15/30 studies concluded that **ibuprofen was superior**

Southey et al. (2009)	• Comparison of:
	  • 24 RCTs
	  • 12 other studies
		• **No significant difference in AEs** for ibuprofen and acetaminophen
		• Ibuprofen, acetaminophen and placebo have **similar safety profiles** in terms of GI symptoms, asthma and renal effects

[1]Pierce CA, Voss B. Efficacy and safety of ibuprofen and acetaminophen in children and adults: a meta-analysis and qualitative review. *Ann Pharmacother*. 2010;44(3):489-506.
[2]Southey ER, Soares-Weiser K, Kleijnen J. Systematic review and meta-analysis of the clinical safety and tolerability of ibuprofen compared with paracetamol in paediatric pain and fever. *Curr Med Res Opin*. 2009;25(9):2207-2222.

Updates Since the 1998 CPS Position Statement

STUDY	DETAILS	MAIN FINDINGS

Lesko et al. (2001)	• Children <19 years of age
	  • 52 cases GAS infections
	  • 172 cases of uncomplicated varicella infections
		• **No association between ibuprofen and necrotizing soft tissue infections**
		• **Association was found** between **ibuprofen PLUS acetaminophen with invasive GAS infections**

Rainsford (2009)	• Review of recent studies on ibuprofen in adults and children	• Ibuprofen has a **low possibility of causing serious** GI, renal or CV **events** when used at **OTC doses** • There is **no risk of liver injury** associated with OTC ibuprofen

Conclusions:

- Ibuprofen and acetaminophen have similar safety profiles when used at recommended OTC doses
- Ibuprofen may be more effective in treating fever than acetaminophen
  - Evidence suggests ibuprofen lowers temperature faster and for a longer duration

Lesko SM, O'Brien KL, Schwartz B, et al. Invasive group A streptococcal infection and nonsteroidal antiinflammatory drug use among children with primary varicella. *Pediatrics*. 2001;107:1108-1115.
Rainsford KD. Ibuprofen: pharmacology, efficacy and safety. *Inflammopharmacology*. 2009;17(6):275:342.

Therapeutic Tips for Fever Management

- The degree of illness and **not** the T should ultimately guide therapy & referral
  - Reiterate fever is rarely harmful and treatment is only necessary if child is distressed
- Dosing should be based weight-based
  - Assist caregivers in calculating
- Ensure an appropriate measuring device is provided and that caregivers understand how to use correctly
  - Gold standard = oral syringe
- Remind caregivers to check concentrations of liquid acetaminophen and ibuprofen, as it varies according to product
- Inquire about other medication use to ensure MDDs are not being exceeded

Shevchuk YM. Fever. In: Jovaisas B, ed. *Compendium of Therapeutics for Minor Ailments* 2nd ed. Ottawa, ON: Canadian Pharmacists Association; 2018:79-95.

Therapeutic Tips for Pain Management[1]

- From the newborn period onwards, children are capable of experiencing pain
- Choose the medication and route of administration according to severity of pain and desired onset and duration of action
- Oral analgesics should be used when possible to avoid painful routes of administration.
- Choose the most appropriate analgesic, considering hepatic and renal function and concurrent medication
- Allow an adequate amount of time before performing a painful procedure or assessing whether an analgesic is effective
- Consult specialized acute pain services as needed

Benoit B. Acute pain. In Compendium of Therapeutic Choices. Ottawa, ON: Canadian Pharmacists Association. [Updated May 2018; Accessed November 26, 2018]. https://myrxtx.ca.

Monitoring & Follow-Up for Fever

Monitoring Parameters	Desired Outcome	Time Frame for degree of change	Patient to Monitor	RPh to Monitor & Follow-Up
FEVER REDUCTION	Reduction in temperature	1 - 2 hours	≤2-3 times daily*	2-3 days
DISCOMFORT	50%	2 - 3 hours	Daily	2-3 days
SIDE EFFECTS**	None	Throughout course of therapy	Daily	2-3 days

*Temperature monitoring may contribute to fever phobia, so more frequent monitoring is not recommended
**Only If patient is given an antipyretic

Note: Timeliness of patient follow-up is vital in determining the presence of a non-self-limiting underlying cause, however, a response to therapy does **NOT** exclude the possibility of a serious underlying illness

Fever and Antipyretic Use in Children. Janice E. Sullivan, Henry C. Farrar, the Section on Clinical Pharmacology and Therapeutics and Committee on Drugs *Pediatrics* 2011;127;580.
Ann Pharmacother 2011 Jun;45(6):797-804.

Monitoring & Follow-Up for Pain

Monitoring Parameters	Desired Outcome	Time Frame for degree of change	Patient to Monitor	RPh to Monitor & Follow-Up
PAIN RELIEF	Reduction in pain	Within 60 mins of taking PO analgesic	Regular intervals (q4h)	2-3 days
SIDE EFFECTS	None	Throughout course of therapy	Daily	2-3 days

Note: *monitoring & follow-up should be individualized based on type of pain being treated*

Summary

- The primary goal of treating fever in children should be to improve overall comfort rather than focus on the normalization of body temperature.
- The fever severity does not always correspond with the illness severity.
- Pediatric pain evaluation includes determining the underlying type, source, location and severity of pain.
- Pediatric pain assessment and management requires the use of assessment tools based on cognitive ability.
- Pharmacists should promote the selection and appropriate use of analgesics/antipyretics by helping inform the patient's/caregiver's self-care decisions, advocating for simplified formulations, and by providing appropriate dosing devices and clear counselling on instructions for dosing and storage.

Answers- Fever

1. Fevers over 41°C require immediate referral to an emergency department → **False**
2. The severity of fever does not always correspond with the severity of illness → **True**
3. You should recommend alternating ibuprofen and acetaminophen to "break" a fever and/or for acute pain management → **False**
4. Acetaminophen and Ibuprofen have similar safety profiles when taken at recommended OTC doses → **True**
5. Sponge-baths are a recommended nonpharmacologic method to for low-grade fevers → **False**

Answers- Pain

1. Infants do not feel pain as their nervous system is not developed → **False**[1]
2. Children do not remember pain, so acute painful events won't have a lasting impression → **False**
3. The FLACC scale is the preferred tool to assess pain severity in a verbal 5 y/o → **False**
4. Naproxen is a safe and effective OTC treatment option for acute pain in children under 12 y/o → **False**
5. Ibuprofen 200mg ≅ Aspirin 650mg ≅ Acetaminophen 650mg → **True**[2]

[1]Lederhaas G. Pediatric pain management. *J Fla Med Assoc.* 1997;84(1):37-40.
[2]Bailey B. Acute Pain. In: *Compendium of Therapeutic Choices.* Ottawa, ON: Canadian Pharmacists Association; 2018: www.rxtx.ca. Accessed November 20, 2018.

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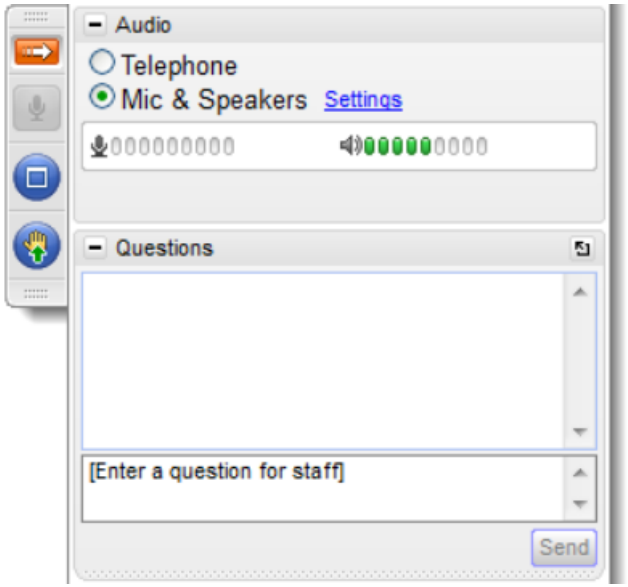

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