



## **The 411 on Nonprescription Analgesics: When to Hold 'Em, When to Fold 'Em**

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### **Disclosure**

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The  
Nothing  
Club



## Learning Objectives

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- At the conclusion of this presentation the participant will be able to:
  - Describe the mechanism of action of common nonprescription analgesics.
  - List and explain contraindications to self-treatment for tension headache and musculoskeletal pain.
  - Given a simulated patient with a complaint of pain, select a nonprescription analgesic and provide dosing and use instruction.



## OTC Analgesic Facts

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- OTC analgesics are the most frequently used of all OTCs
- About 20% of the population uses OTC analgesics weekly
- 87% of women vs. 80% men used OTC analgesics in past year
- Most commonly used OTC in children were analgesics/antipyretics
- About 50% of patients who use OTC analgesics do not read the labels of these products



Terrie YC. Pharmacy Times, 2013. <http://www.pharmacytimes.com/print.php?url=/publications/otc/2013/otcguide-2013/pain-control-using-nonprescription-analgesics>

## OTC Analgesic Facts

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- > 43% of those surveyed were not aware of potential adverse effects of taking OTCs with Rx medications
- > 40% did not know about potential drug interactions or GI side effects
- > 60% did not know the precautions for these drugs for those with hepatic or renal disease
- > 80% did not know about potential for adverse effects when aspirin is used in asthmatics



Terrie YC. Pharmacy Times, 2013. <http://www.pharmacytimes.com/print.php?url=/publications/otc/2013/otcguide-2013/pain-control-using-nonprescription-analgesics>

## Jerome

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- Jerome is a 26 year old man who presents in the pharmacy asking for advice to treat this “relentless” headache he’s had for the past several days
- Jerome has graduated from law school, and he is studying furiously for the law bar exam
- He denies having chronic headaches, but notices a pattern of headache when he is stressed and anxious (like now)



## Jerome

- He describes the pain as bilateral, extending over the top of his head and the base of his skull
- Jerome describes the pain as constricting, like his hat is too tight
- He states the pain evolved gradually over 4-6 hours, and has been present for two days
- He denies any throbbing sensation, pressure behind his eyes or face, and the pain is not worsened by light or sound

**Pain**WEEK



PAIN LOCATOR



Sounds like a  
**TENSION**  
**HEADACHE**

## Acetaminophen – Mechanism of Action

- Increases pain threshold
- Reduces nitric oxide pathway
- Selectively inhibits COX-2
- Interacts with the endocannabinoid system
- Reduces PG in the CNS, inhibiting endogenous pyrogens

Analgesic  
Antipyretic



Mallick-Searle T. J for Nurse Prac 2016;12(3)174-180.

## Acetaminophen – Adverse Effects

- Hepatotoxicity
  - Nausea, vomiting
  - Abdominal pain, jaundice
  - Fatigue
  - Skin rashes and/or itching of skin
  - Fluid retention



## Acetaminophen

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- Analgesic/antipyretic
- Preferred analgesic for the elderly
- Preferred analgesic in patients taking warfarin
- Do not exceed 4 grams a day; consider all drugs
  - Found in over 600 OTC and prescription products
- Caution/avoid with liver disease
- Caution/avoid with alcohol use

**PainWeek.**

## NSAID Mechanism of Action

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- Ibuprofen, Naproxen
  - Inhibits cyclooxygenase (COX), reducing prostaglandin & thromboxane synthesis
  - Interacts with the endocannabinoid system
- Aspirin
  - Nonselective and irreversibly inhibits COX reducing PG and thromboxane A2 synthesis producing analgesic, anti-inflammatory, and antipyretic effects and reducing platelet aggregation

Analgesic, Antipyretic Anti-inflammatory, Antiplatelet
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**PainWeek.**

## NSAID – Adverse Effects

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- Gastrointestinal toxicity, bleeding
  - Diarrhea, epigastric/abdominal pain, nausea/vomiting,
- Platelet inhibition
- Cardiovascular toxicity – hypertension, MI
- Renal toxicity
  
- Respiratory (aspirin)

**PainWeek.**

## NSAIDs

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- Analgesic, anti-inflammatory, antipyretic, antiplatelet
- Avoid with CVD (hyperlipidemia, diabetes, hypertension, other macrovascular disease)
  - PRECISION trial showed celecoxib non-inferior to ibuprofen and naproxen for CV adverse outcomes
- Caution/avoid in GI disorders/bleeding
- Caution with renal impairment

**PainWeek.**

## OTC Analgesics for Adults and Children > 12

Agent	Dosage Forms	Usual Adult Dose (maximum daily dose)
Acetaminophen	<div>Immediate-release tablets</div> <div>Extended-release tablets</div> <div>Effervescent tablets</div> <div>Disintegrating tablets</div> <div>Rapid-release tablets</div> <div>Chewable tablets</div> <div>Capsules</div> <div>Liquid drops</div> <div>Elixir</div> <div>Suspension</div> <div>Suppositories</div>	325-1000 mg every 4-6 hours (suggested 3250 mg; FDA max )
Ibuprofen	Immediate release and chewable tablets Suspension; liquid drops	200-400 mg every 4-6 hours (1200 mg)
Naproxen sodium	Tablets	220 mg every 8-12 hours (660 mg) Over age 65: 220 mg every 12 hours (440 mg)
Aspirin	Immediate-release, buffered, enteric-coated, film-coated, effervescent and chewable tablets Suppositories	650-1000 mg every 4-6 hours (4000 mg)
Magnesium salicylate	Tablets	650 mg every 4 hours or 1000 mg every 6 hours (4000 mg)



Krinsky D, et al. Handbook of Nonprescription Drugs, 18<sup>th</sup> ed. APhA, 2014.

## FDA Approved Doses for OTC Analgesics in Children < 12 years

Age (years)	Weight (lb)	Ibuprofen (mg) Dose by body weight (mg/kg): 5-10 mg/kg	Acetaminophen (mg) 10-15 mg/kg	Aspirin (mg) 10-15 mg/kg
< 2	< 24	Ask prescriber	Ask prescriber	Ask prescriber
2-3	24-35	100	160	160
4-5	36-47	150	240	240
6-8	48-59	200	320	320
9-10	60-71	250	400	400
11	72-95	300	480	480



Krinsky D, et al. Handbook of Nonprescription Drugs, 18<sup>th</sup> ed. APhA, 2014.



## Clinically Important Drug-Drug Interactions

Analgesic/ Antipyretic	Drug	Potential Interaction	Management/Preventive Measure
Acetaminophen	Alcohol	Increased risk of hepatotoxicity	Avoid concurrent use if possible; minimize alcohol intake when using acetaminophen
Acetaminophen	Warfarin	Increased risk of bleeding (↑ INR)	Limit acetaminophen to occasional use; monitor INR for several weeks when acetaminophen 2-4 grams daily is added or discontinued in patients on warfarin
Aspirin	Valproic acid	Displacement from protein-binding sites and inhibition of valproic acid metabolism	Avoid concurrent use; use naproxen instead of aspirin (no interaction)
Aspirin	NSAIDs, including COX-2 inhibitors	Increased risk of gastroduodenal ulcers and bleeding	Avoid concurrent use if possible; consider use of gastroprotective agents (e.g., PPIs)



Krinsky D, et al. Handbook of Nonprescription Drugs, 18<sup>th</sup> ed. APhA, 2014.

## Clinically Important Drug-Drug Interactions

Analgesic/ Antipyretic	Drug	Potential Interaction	Management/Preventive Measure
Ibuprofen	Aspirin	Decreased antiplatelet effect of aspirin	Aspirin should be taken at least 30 minutes before or 8 hours after ibuprofen. Use acetaminophen (or other analgesic) instead of ibuprofen
Ibuprofen	Phenytoin	Displacement from protein-binding sites	Monitor free phenytoin levels; adjust dose as indicated
NSAIDs (several)	Bisphosphonates	Increased risk of GI or esophageal ulceration	Use caution with concomitant use
NSAIDs (several)	Digoxin	Renal clearance of digoxin inhibited	Monitor digoxin levels; adjust dose as indicated
Salicylates and NSAIDs (several)	Antihypertensive agents; beta-blockers, ACE inhibitors, vasodilators, diuretics	Antihypertensive effect inhibited; possible hyperkalemia with potassium-sparing diuretics and ACE inhibitors	Monitor BP, cardiac function, and potassium levels



Krinsky D, et al. Handbook of Nonprescription Drugs, 18<sup>th</sup> ed. APhA, 2014.

## Clinically Important Drug-Drug Interactions

Analgesic/ Antipyretic	Drug	Potential Interaction	Management/Preventive Measure
Salicylates and NSAIDs	Anticoagulants	Increased risk of bleeding, especially GI	Avoid concurrent use, if possible; risk is lowest with salsalate and choline magnesium trisalicylate
Salicylates and NSAIDs	Alcohol	Increased risk of GI bleeding	Avoid concurrent use, if possible; minimize alcohol intake when using salicylates and NSAIDs
Salicylates and NSAIDs (several)	Methotrexate	Decreased methotrexate clearance	Avoid salicylates and NSAIDs with high-dose methotrexate therapy; monitor levels with concurrent treatment
Salicylates (moderate-high doses)	Sulfonylureas	Increased risk of hypoglycemia	Avoid concurrent use, if possible; monitor blood glucose levels when changing salicylate dose



Krinsky D, et al. Handbook of Nonprescription Drugs, 18<sup>th</sup> ed. APhA, 2014.

## Does Jerome have exclusions for self-tx?

- Severe head pain
- Headaches that persist for 10 days with or without treatment
- Last trimester of pregnancy
- $\leq 8$  years of age
- High fever or signs of serious infection
- History of liver disease or consumption of  $\geq 3$  alcoholic drinks per day
- Headache associated with underlying pathology (secondary headache), except for minor sinus headache
- Symptoms consistent with migraine but no formal diagnosis



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## Pick a drug...any drug?

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- Asthma & nasal polyps, chronic/recurrent GI ulcers, gout, coagulation disorder or anticoagulant therapy, hypertension, CHF, kidney disease, h/o allergy
  - Avoid salicylates and NSAIDs
- < 12 years of age – avoid naproxen
- ≤ 15 years of age – avoid salicylates if symptoms of viral illness are present
- Recommend acetaminophen or NSAID; non-pcol tx

**Pain**week.

## Topical Analgesics

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**Pain**week.

## Sally

- Sally is a 68 year old woman who presents to the pharmacy on Monday with complaints of an aching back. She is inquiring as to what she can take to “make the pain go away!”
- She states that since the weather was so gorgeous on Saturday, she spent all day outside gardening. Then on Sunday, she babysat her toddler grandson and was constantly chasing him and picking him up.
- She denies other signs/symptoms, including weakness.
- She has a past medical history of hypertension (uncontrolled), dyslipidemia and osteoarthritis.

**PainWeek.**

## Sally



- She describes her pain as “achy” and “sore,” and states it’s mostly located in her mid to lower back.
- She rates her pain as a 5/10.
- She tried the ThermaCare® HeatWrap but has not experienced any significant relief.

**What are our options?**

**PainWeek.**

## Counterirritants – Mechanism of Action

- Paradoxical pain-relieving effect – produce a less severe pain to counter a more intense one
- Relieve pain indirectly by stimulating cutaneous receptors to induce sensations of cold, warmth, or even itching and distracting from deep-seated pain in muscles, tendons, joints, etc.
- Psychological component

**PainWeek.**

## Counterirritants

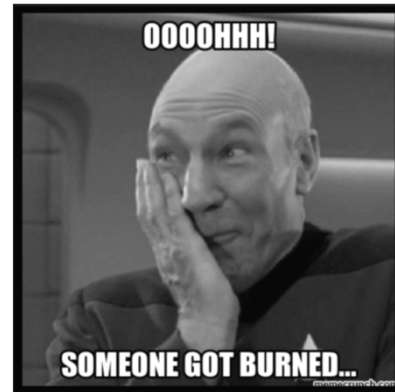
Group	Ingredients	Concentration (%)	Mechanism of Action	Frequency and Duration of Use
A	Allyl isothiocyanate	0.5-5	Rubefacients (increase blood flow)	Apply no more than 3-4 times daily for up to 7 days
	Ammonia water	1-2.5		
	Methyl salicylate	10-60		
	Turpentine oil	6-50		
B	Camphor	3-11	Produce cooling sensation	Same as group A
	Menthol	1.25-16		
C	Histamine dihydrochloride	0.025-0.1	Cause vasodilation	Same as group A
	Methyl nicotinate	0.25-1		
D	Capsicum	0.025-0.25	Incite irritation without rubefaction; are as potent as group A ingredients	Acute pain: Same as group A Chronic pain: Apply 3-4 times daily for duration of pain
	Capsicum oleoresin	0.025-0.25		
	Capsaicin	0.025-0.25		

**PainWeek.**

## Counterirritants – Adverse Effects

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- Skin irritation and/or rash
- Erythema
- Blistering
- Thermal hyperalgesia
- Systemic reactions
  - Salicylate toxicity



**Pain**WEEK.

## Counterirritants - Application

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- If pain, swelling, or blistering of the skin occurs after application of a topical analgesic, patients should immediately discontinue use of the product and seek medical attention.
- Do not bandage the area tightly where the product has been applied.
- Do not use any heat where the product has been applied.
- Do not apply to wounded, damaged, broken, or irritated skin.
- Do not allow these medications to come in contact with the eyes, or inside the nose, mouth, or genitals.

**Pain**WEEK.

## Counterirritants

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### ▪ Methyl salicylate

- Occurs naturally as wintergreen oil or sweet birch oil
- Usually combined with other ingredients (e.g., menthol and/or camphor)
- Responsible for the “hot” action in many topical counterirritant products
- Mechanism of action:
  - Vasodilation of cutaneous vasculature → reactive hyperemia + increase in localized skin temperature = counterirritant effect
  - Inhibition of central and peripheral prostaglandin synthesis
- Contraindications/Precautions:
  - Avoid heat exposure and exercise after application
  - Avoid use in children and patients with aspirin sensitivities, severe asthma or nasal polyps due to possible percutaneous absorption

**PainWeek.**

## Counterirritants

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### ▪ Camphor

- Obtained naturally from camphor tree, but majority is synthetic
- Mechanism of action – Dose-dependent effect
  - **Camphor 0.1-3%:** Depresses cutaneous receptors and acts as a topical analgesic, anesthetic, and antipruritic
  - **Camphor > 3%:** Stimulates nerve endings in the skin and induces relief of pain and discomfort by masking moderate-severe deeper visceral pain, with a milder pain arising from the skin at the level of innervation
- Precautions:
  - Camphor toxicity – tonic-clonic seizures, nausea, vomiting, colic, headache, dizziness, delirium, coma, and death

**PainWeek.**




## Counterirritants

### ▪ Menthol

- Extracted from peppermint oil or prepared synthetically
- Also used as a flavoring agent and permeability enhancer
- Responsible for the “cold” action in many topical counterirritant products
- Mechanism of action – Dose-dependent effect
  - **Menthol <1%:** Depresses cutaneous receptor response (anesthetic)
  - **Menthol >1.25%:** Stimulates cutaneous receptor response (counterirritant)
  - Activates TRPM8 menthol receptor, triggering the sensation of cold.
- Contraindications/Precautions:
  - C/I in patients with hypersensitivity or sensitization to the agent (e.g., urticaria, erythema, and other cutaneous lesions)

**Pain**WEEK.




## Counterirritants: Examples

Product	Ingredients	Packaging
Bengay Ultra Strength Pain Relieving Cream	Methyl salicylate 30% Menthol 10% Camphor 4%	
Icy Hot Cream Extra Strength/Precise Pain Relieving Cream	Methyl salicylate 30% Menthol 10%	
Salonpas Pain Relief Patch	Methyl salicylate 10% Menthol 3%	

**Pain**WEEK.



## Counterirritants: Examples

Product	Ingredients	Packaging
Tiger Balm Arthritis Rub Cream	Camphor 11% Menthol 11%	
Aspercreme Heat Pain Relieving Gel	Menthol 10%	
Mineral Ice	Menthol 2%	

**PainWeek**

## Counterirritants

### ▪ Capsaicin

- Major ingredient in hot chili peppers
- Available OTC in a roll-on applicator or patch formulation
- Available Rx as Qutenza® (capsaicin 8% patch)
- Mechanism of action:
  - Depletion of substance P from sensory neurons
  - When substance P is released, burning pain occurs but diminishes with repeated application

**PainWeek**

## Counterirritants




### ▪ Capsaicin

#### – Patient counseling points:

- Instruct patients to wear gloves during application and wash hands following use; if the hands are the site of application, the patient should wait 30 minutes after application and then wash their hands.
- Do not allow capsaicin to come into contact with eyes or mucous membranes.
- Pain relief is usually noted within 14 days but can take up to 6 weeks.
- Adherence is important – once capsaicin has begun to relieve pain, its use must be continued regularly 3-4 times daily.



## Counterirritants: Examples

Product	Ingredients	Packaging
Capzasin Arthritis Pain Relief No-Mess Applicator	Capsaicin 0.15%	
Capzasin-HP Arthritis Pain Relief Cream	Capsaicin 0.1%	
Zostrix Arthritis Pain Relief Cream	Capsaicin 0.025%	



## Heat/Thermal Wraps

- Non-pharmacologic option
- May help reduce pain by increasing blood flow
- Has been studied in the treatment of acute low back pain (< 4 weeks duration) with favorable effects.
- Osteoarthritis guidelines recommend heat as adjunct non-pharmacologic treatment for pain and stiffness.
- Apply for 15-20 minutes 3-4 times daily (regular heat); ThermaCare® products can be worn for up to 8-12 hours.
- Should not be applied to recently injured (< 48 hours) or inflamed areas; should not be used with other topical agents or over broken skin.



## Transcutaneous Electrical Nerve Stimulation (TENS)



- Class II Medical Device FDA-approved for the relief of pain associated with sore, aching muscles, joint pain, or chronic intractable pain.
- Mechanism of action:
  - Alteration of pain transmission
  - Increase in production of natural endorphins
- Typically used for 15-30 minutes up to 3 times daily.
- Should not be used in patients with internal or attached medical devices (e.g., pacemakers, defibrillators), pregnant patients or in the pediatric population.



## Does Sally have any exclusions for self tx?

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- Moderate-to-severe pain (pain score > 6)
- Pain that lasts > 10 days
- Pain that continues > 7 days after tx w/ a topical analgesic
- Increased intensity or change in character of pain
- Pelvic or abdominal pain (other than dysmenorrhea)
- Accompanying nausea, vomiting, fever or other signs of systemic infection or disorder
- Visually deformed joint, abnormal movement, weakness in any limb, or suspected fracture
- Third trimester of pregnancy
- < 2 years of age

**PainWeek.**

## Sally

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- She does not have any exclusions to self-treatment
- But she has a history of uncontrolled hypertension
  - Avoid NSAIDs, can recommend acetaminophen instead
- Recommend a topical analgesic
  - Apply SalonPas original patch (methyl salicylate 6.3%, menthol 5.7%, and camphor 1.2%) to back 3-4 times a day.
    - This is just one example. Any available OTC patch would work!
  - Can use for up to 7 days.
  - Do not use heat when you are using this medication.

**PainWeek.**



## **The 411 on Nonprescription Analgesics: When to Hold 'Em, When to Fold 'Em**

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