



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

Alexandra L. McPherson, PharmD, MPH

Disclosure

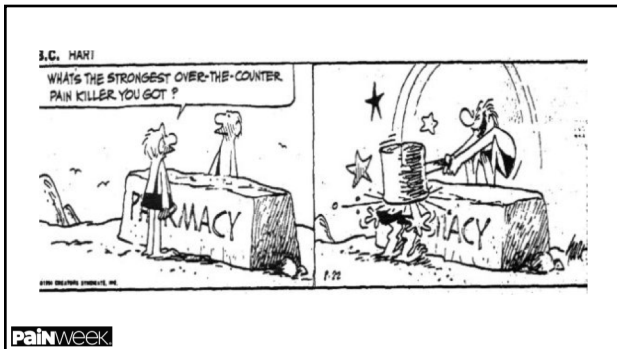
Alexandra L. McPherson, PharmD, MPH
Palliative Care
Clinical Pharmacy Specialist
MedStar Washington Hospital Center
Washington, DC




Learning Objectives

- 1) Describe the mechanism of action of common nonprescription analgesics
- 2) List and explain contraindications to self-treatment for tension headache and musculoskeletal pain
- 3) Given a simulated patient with a complaint of pain, select a nonprescription analgesic and provide dosing and use instruction





This should only hurt a little!



- Pain encountered in community pharmacies are typically mild-to-moderate and self-limiting
- Typical conditions include toothaches, headaches, dysmenorrhea, arthritis, and musculoskeletal injuries

PainWeek

OTC Analgesics

Oral	Topical	Other
<ul style="list-style-type: none"> • Acetaminophen • NSAIDs 	<ul style="list-style-type: none"> • Counterirritants • CBD oil • Blue emu 	<ul style="list-style-type: none"> • Heat/thermal wraps • TENS

PainWeek

OTC Analgesic Facts

- Analgesics = most frequently used of all OTC products
- 20% of the population uses OTC analgesics weekly
- 87% of women and 80% men used OTC analgesics in past year
- Most commonly used OTC products in children were analgesics/antipyretics



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

Half of all patients don't read the label!



So what?

Drug-Disease Interactions

- 58% do not consider their pre-existing medical conditions when selecting an OTC analgesic
- >80% did not know about the potential for adverse effects when aspirin is used in asthmatics
- >60% did not know the precautions for these drugs in those with hepatic or renal disease

Drug-Drug Interactions

- 65% do not consider other OTC medicines they're taking when selecting an OTC analgesic
- 88% are not aware that ibuprofen may interfere with the cardioprotective benefits of aspirin

Dosing

- 33% admit that they have taken more than the recommended amount of an OTC medication





Jerome

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

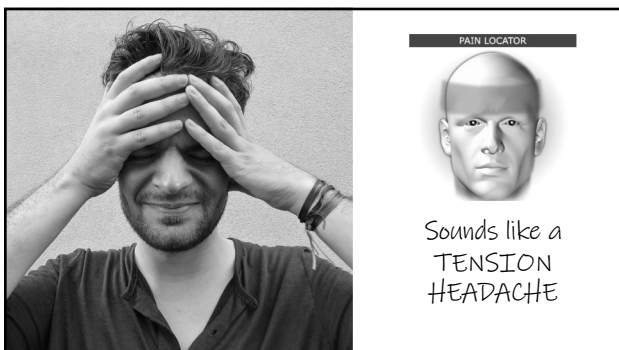
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Jerome (cont’d)

- 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, feels like his hat is too tight
- He states the pain evolved gradually over 4-6 hours, and has been present for 2 days
- He denies any throbbing sensation, pressure behind his eyes or face, and the pain is not worsened by light or sound

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OTC Analgesics

Oral	Topical	Other
<ul style="list-style-type: none">• Acetaminophen• NSAIDs	<ul style="list-style-type: none">• Counterirritants• CBD oil• Blue emu	<ul style="list-style-type: none">• Heat/thermal wraps• TENS

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Acetaminophen – Mechanism of Action

- Mechanism is poorly understood
- Weak COX-2 inhibitor
- Reduces PG in the CNS, inhibiting endogenous pyrogens
- Interacts with the endocannabinoid system
- Reduces nitric oxide pathway
- Activates descending serotonergic pain pathways

Analgesic
Antipyretic

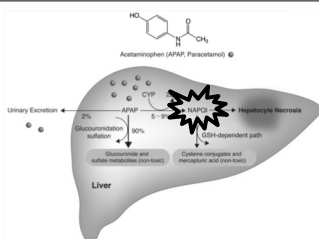
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Mallick-Searle T. J for Nurse Prac 2016;12(3)174-180.

Acetaminophen – Adverse Effects

- Hepatotoxicity
 - Early symptoms:
 - Abdominal pain
 - Nausea/vomiting
 - Diarrhea
 - Fatigue
 - ↑ LFTs
 - Jaundice
 - Encephalopathy
 - Coma



Acetaminophen

- Preferred in the following patient populations:
 - Elderly
 - History of peptic ulcer disease, GI bleed
 - Patients taking warfarin
 - Recommend limiting acetaminophen dose to ≤ 2 g weekly
- Labeled acetaminophen dosing varies by formulation
 - Do not exceed 4 grams daily; consider all drugs
- Use caution/avoid with liver disease, chronic alcohol use



NSAIDs – Mechanism of Action

- Ibuprofen, naproxen, aspirin
 - Nonselective inhibition of COX-1 and 2, reducing prostaglandin and thromboxane synthesis
 - Interact with endocannabinoid system
- Aspirin
 - Binds irreversibly to COX-1
 - Anti-inflammatory effect is seen at higher doses

*Analgesic
Antipyretic
Anti-inflammatory
Antiplatelet*

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NSAIDs – Adverse Effects

- | | |
|---|---|
| <ul style="list-style-type: none"> ▪ Gastrointestinal <ul style="list-style-type: none"> – Epigastric pain, dyspepsia, nausea/vomiting (most common) – Gastric ulceration with/without bleeding, peptic ulcer disease, or GI perforation ▪ Cardiovascular <ul style="list-style-type: none"> – Myocardial infarction, stroke – Increase systolic blood pressure by ~ 4 mmHg | <ul style="list-style-type: none"> ▪ Renal <ul style="list-style-type: none"> – Decreased synthesis of PGs involved in maintaining renal blood flow can result in sodium and water retention ▪ Respiratory <ul style="list-style-type: none"> – Bronchospasm, deterioration of symptoms in asthmatics |
|---|---|

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NSAIDs

- Use at the **lowest possible dose** for the **shortest possible duration**
- Labeled NSAID dosing varies by formulation
- Use caution/avoid in the following patient populations:
 - GI disorders/bleeding
 - Cardiovascular disease, heart failure, or a history of stroke
 - Renal impairment
 - Asthma

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OTC Analgesics for Adults and Children > 12

Agent	Dosage Forms	Usual Adult Dose (maximum daily dose)
Acetaminophen	Immediate-release tablets Extended-release tablets Effervescent tablets Disintegrating tablets Rapid-release tablets Chewable tablets	Capsules Liquid drops Elixir Suspension Suppositories
Ibuprofen	Immediate release tablets Chewable tablets Suspension, Liquid drops	225-1000 mg every 4-6 hours (FDA recommended max 4 g daily)
Naproxen sodium	Tablets	200-400 mg every 4-6 hours (1200 mg)
Aspirin	Immediate-release, buffered, enteric-coated, film-coated, effervescent and chewable tablets Suppositories	220 mg every 8-12 hours (660 mg) Over age 65: 220 mg every 12 hours (440 mg)
Magnesium salicylate	Tablets	650-1000 mg every 4-6 hours (4000 mg)

PainWeek Kirsnsky D, et al. Handbook of Nonprescription Drugs, 18th 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

PainWeek Kirsnsky D, et al. Handbook of Nonprescription Drugs, 18th 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 (eg, PPIs)

PainWeek Kirsnsky D, et al. Handbook of Nonprescription Drugs, 18th ed. APHA, 2014.




Sally

- Sally is a 68-year-old woman who presents to the pharmacy with complaints of an aching back. She wants to know what she can take to "make the pain go away!"
- *"Since the weather was so gorgeous yesterday, I spent all day outside gardening and playing with my toddler grandson. I was constantly chasing him around and picking him up."*
- She denies other signs/symptoms, including weakness.
- Her past medical history includes hypertension (uncontrolled), dyslipidemia & osteoarthritis

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Sally (cont'd)




- 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?

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OTC Analgesics



Topical	Other
<ul style="list-style-type: none"> • Counterirritants • CBD oil • Blue emu 	<ul style="list-style-type: none"> • Heat/thermal wraps • TENS

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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 itching and distracting from deep-seated pain in muscles, tendons, joints, etc
- Psychological component

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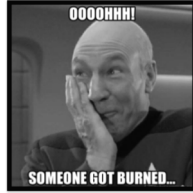
Counterirritants

Group	Ingredients	Concentration	Mechanism of Action	Frequency and Duration of Use
A	Allyl isothiocyanate Ammonia water Methyl salicylate Turpentine oil	0.5 – 5 % 1 – 2.5 % 10 – 60 % 6 – 50 %	Rubefacients (increase blood flow)	Apply no more than 3-4 times daily for up to 7 days
B	Camphor Menthol	3 – 11 % 1.25 – 16 %	Produce cooling sensation	Same as group A
C	Histamine dihydrochloride Methyl nicotinate	0.025 – 0.1 % 0.25 – 1 %	Cause vasodilation	Same as group A
D	Capiscum Capsicum oleoresin Capsaicin	0.025 0.25 % 0.025 – 0.25 % 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

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Counterirritants – Adverse Effects

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



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Counterirritants – Application

- 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

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Counterirritants

- **Methyl salicylate**
 - Occurs naturally as wintergreen oil or sweet birch oil
 - Usually combined with other ingredients (eg, 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

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Counterirritants (cont'd)

▪ **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






Counterirritants (cont'd)

▪ **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 (eg, urticaria, erythema, and other cutaneous lesions)






Counterirritants – Product 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%	



Counterirritants – Product Examples (cont'd)

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

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Counterirritants

▪ **Capsaicin**

- Major ingredient in hot chili peppers
- Available OTC in many different formulations
- 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

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Counterirritants (cont'd)

▪ **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

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Counterirritants – Product 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%	



Cannabidiol (CBD) Oil



- Most comes from industrial hemp; extracted then added to a carrier oil
- Commonly used for arthritis pain
- Concentrations found to vary significantly from product labeling



Blue Emu

- Originates from Australian Aborigines
- Comes from emu fat
- Anti-inflammatory properties
- Shown to be effective in mice



Heat/Thermal Wraps

- 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 nonpharmacologic 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 (eg, pacemakers, defibrillators), pregnant patients, or in the pediatric population



Does Sally have any exclusions for self-tx?

- 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



Sally

- 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





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