Body Pain
Fever

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Objectives

- Describe properties of topical counterirritants including mechanism of how they work and their side effects
- List the components of “RICE” therapy
- Discuss the pathophysiology of fever and its appropriate treatment

Background

- Use of nonprescription systemic and topical analgesics accounts for $2 billion spent annually
- 80% of adults admit to using a pain reliever at least once a week
- Musculoskeletal complains result in significant amount of lost work days, limitations at work, and loss of employment

Muscle Pain

- "Myalgia"
  - Generalized muscle pain
  - Muscle cramp: prolonged muscle spasm causing pain
- Signs
  - Swelling: rare
- Symptoms
  - Dull, ongoing ache
  - Weakness
  - Muscle fatigue
  - Worse with contraction of the muscle affected

Causes of Myalgia

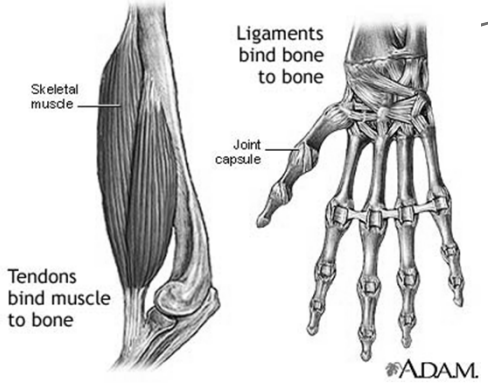
- Diffuse (general)
- Infection
- Rheumatic disease
- Chronic fatigue syndrome
- Metabolic disorders (vit D deficiency)
- Some medications
- Liver disease
- Depression
- Thyroid disease

- Localized
- Unusually strenuous exercise or overuse
- Trauma
- Infection
- Bursitis
- Compartment syndrome

Myalgia

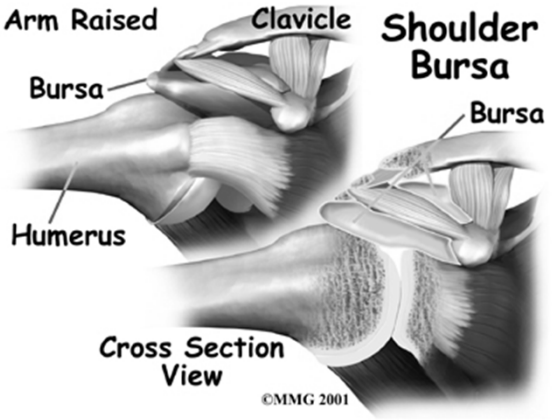
- Onset-depends upon cause
  - Acute/abrupt: trauma, infection
  - Delayed: overexertion (8 hours afterward)
  - Subtle: drug-induced, chronic illness (fibromyalgia, chronic fatigue syndrome), abuse of alcohol (precipitates acute myopathy), vitamin D deficiency

Tendonitis



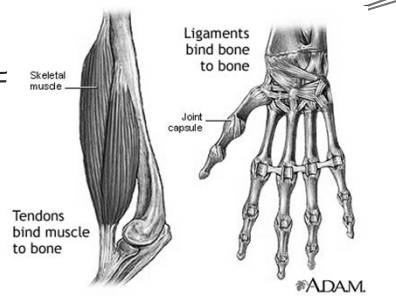
- Inflammation of tendon: acute injury or overuse
  - Example: carpal tunnel syndrome
- Signs: erythema, swelling, warmth near joints (see above)
- Symptoms:
  - Mild to severe pain, usually after use
  - Loss of range of motion
- Causes
  - Trauma such as hyperextension injury
  - Overexertion
  - Drug-induced (fluoroquinolone antibiotics)
  - Inflammatory diseases

Bursitis



- Inflammation of bursae (provides cushion between bones/tendons) in joints (knee, shoulder)
- Signs
  - Warmth
  - Swelling
  - Redness
  - Crepitus (sometimes)
- Symptoms
  - Constant pain that worsens with movement or application of external pressure over the joint
- Causes
  - Acute: trauma, sometimes infection
  - Chronic: excessive use

Sprains



- Sprain
  - Stretching or tearing of ligament
  - Characterized by grade
    - Grade I = excessive stretching
    - Grade II = partial tear
    - Grade III = complete tear of tissue
  - Signs
    - Swelling
      - Max at 48 hours
      - See HCP if >72 hrs
    - Bruising
  - Symptoms
    - Initial severe pain; ongoing pain with joint use
    - Joint instability & loss of function

Strain

- Overextension of muscle or tendon
- Signs
  - Swelling, bruising
- Symptoms
  - Initial severe pain; ongoing pain with joint use & at rest
  - Muscle weakness
  - Some loss of function

Myalgia Prevention

- Stretch prior to physical activity
- Properly hydrate
- Avoid overexertion
- Stretch after physical activity

Stay tuned for self-treatment exclusions!

Goals of Therapy

- Decrease subjective intensity (severity) and duration of pain
- Restoring function of the affected area
- Preventing re-injury and disability
- Preventing acute pain from becoming chronic persistent pain

Exclusions for Self-Treatment

- Pain score more than 6 (scale 0-10)
- Pain longer than
  - 2 weeks (total)
  - 7 days with treatment
- Changes in pain characteristics
- Associated n/v, fever or infection
- Visual deformity, abnormal movement or possible fracture
- OTC intolerances
- Achilles tendonitis
- Third trimester of pregnancy
- < 2 years of age

Nonpharmacologic Treatment

- General care measures
  - Stop etiology
  - Stretching
    - Cautiously
    - No bouncing to avoid muscle strain
  - Massage: helpful for muscle cramps
  - Rest

Ice and Heat

- Ice: as soon as possible following injury, 3-4 times daily x for up to 72 hours
  - Post exercise icing helpful for prevention of inflammation and pain reduction
- Heat: 15-20 minutes, 3-4 times daily (**not within 48 hours of injury** due to potential for exacerbation of vascular leakage and tissue damage from vasodilation)—non-inflammatory conditions only, i.e. acute low back pain, osteoarthritis
  - Avoid use with other topical agents or with broken skin
  - Warm wet compress, heating pad, hot-water bottle, heat generating adhesive wraps (ThermaCare, Prescise, generics)

RICE Therapy

- Rest
  - After injury & until pain decreases (usu. 1-2 days)
- Ice
  - As soon as possible
  - 10-15 minutes, 3-4 times daily (up to 3 days)
- Compression
  - Elastic support/bandage
    - Proper size
    - Unwind 12-18 inches, relax
    - Wrap, overlapping prior layer by ⅓ to ½
    - Begin wrapping distal to injury
    - Decrease tightness as wrap
- Elevate
  - At or above heart 2-3 hours per day

Pharmacologic Treatments

- Systemic analgesics: acetaminophen, NSAIDS
  - Initial: scheduled doses
  - Over 1-3 days: decreasing dose & increasing interval
  - Max 7 days
- Topical counterirritants
  - Apply 3-4 times/day
  - Max 7 days

Acetaminophen

- Central inhibitor of prostaglandin synthesis
- Rapidly absorbed from GI tract and metabolized in the liver
- Onset of action 30 minutes, duration 4 hours (6-8 hours for extended release)
- Max daily dose listed on label changed in 2012 = 3250mg daily instead of 3900mg daily

Acetaminophen Adverse Effects

- Hepatotoxicity with doses > 4 grams/day, especially with chronic use
- Acetaminophen toxicity remains the most common cause of acute liver failure in the United States
  - Most of these cases are intentional overdoses, but a substantial number of patients with significant liver toxicity due to medication misuse

NSAIDS

- Peripheral inhibitors of cycolooxygenase (COX) and subsequent inhibition of prostaglandin synthesis
- Rapidly absorbed from GI tract, metabolized in liver, cleared by kidneys
- Should be taken with food and full glass of water
  - When using aspirin for CVD protection, recommend to take 1 hour before or 8 hours after NSAID

NSAIDS Adverse Effects

- Adverse effects: GI (dyspepsia, heartburn, nausea, anorexia, epigastric pain), dizziness, fatigue
  - GI ulceration: risk factors include age > 60, prior ulcer, concurrent anticoagulant use, higher dose and duration, moderate use of alcohol
  - Use > 3 months associated with rates of gastric ulceration between 15% and 35%, although many of these ulcers may not be clinically significant
- Increased risk for myocardial infarction (ibuprofen), hypertension, edema

FDA NSAID label update

- July 2015: strengthened an existing label warning that NSAIDS increase the chance of a MI or stroke
- Applies to both RX and OTC formulations
- The potentially fatal risk of MI and stroke with NSAIDs, was first summarized in 2005 in the Boxed Warning and Warnings and Precautions sections of the prescription drug labels

FDA NSAID label update: Specifics

- The risk of MI or stroke can occur as early as the first weeks of using an NSAID, and may increase with longer use

- Risk appears to be dose related

- Some NSAIDS are associated with higher risk than others, but not enough information to make specific recommendations

FDA NSAID label update: Specifics

- Risk occurs in patients with or without heart disease or risk factors for heart disease, but appears higher among patients with existing CVD

- Patients taking an NSAID after an MI were more likely to die in the first year compared to patients who were not treated with NSAIDs

- There is also an increased risk of heart failure

Topical Counterirritants

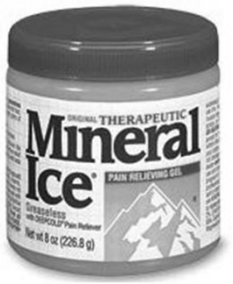
- Relieve pain through nerve stimulation as opposed to depression
- Paradoxical pain relieving effect: producing a less severe pain to counter a more intense pain
- Pain relieving activity tied to psychological effect: pleasant odors, sensation of warmth or coolness they produce on the skin
- Products classified as one of four types depending on mechanism: rubefacient (increase blood flow), cooling, vasodilation, irritant

Topical Counterirritants

- Methyl salicylate *(wintergreen oil, sweet birch oil)*
  - Mechanism of action: Rubefacient
    - mild, local inflammation, providing relief

    another site
    - Vasodilation of cutaneous blood vessels
    - "hot"
    - Central and peripheral inhibition of prostaglandin synthesis

Methyl Salicylate



Camphor

Menthol

Methyl Salicylate Side Effects

- Allergy (esp. if allergic to aspirin)
- Blistering, erythema
- Prevention
  - Avoid occlusive dressings
  - Avoid concomitant heating pad use (increases systemic absorption)
  - Avoid in children, asthma, nasal polyps
  - Do not use on open wounds
  - Lower concentrations
  - Combination products ok but avoid dual products

Topical counterirritants

- Camphor *(camphor tree)*
  - Mechanism of action: cooling sensation
  - Camphor: concentrations >3%
    - Stimulates skin nerve endings to mask deeper pain
- Menthol *(extracted from peppermint)*
  - concentrations >1.25%
    - Activates transient receptor potential (TRP) M8 sensory neurons; cool sensation distracts from pain sensation

Camphor & Menthol Side Effects

- Camphor:
  - High doses: nausea, vomiting → convulsions, death
  - Infant nostrils: respiratory collapse
  - In children – 5ml of 20% camphor liniment is potentially lethal

- Menthol
  - Can sensitize some people
  - Stop using if rash, irritation, swelling, etc.

Histamine Hydrochloride

- Vasodilation mediated by prostaglandin biosynthesis
- Other effects
  - Reduces reactive oxygen species
  - Suppresses pro-inflammatory cytokines
  - Increases blood flow, which facilitates healing
- Usually in combination with other counterirritants

Capsaicin

- Indirect vasodilation via stimulation of TRPV1 receptor, causes feeling of warmth
- Isolated from hot peppers
- Depletes substance P (implicated in pain transmission)
- Must be used regularly to take effect
- Used twice daily to 4 times daily
  - Pain relief within 14 days, but can take up to 4-6 weeks
- Avoid getting gel/cream in eyes or mouth, wash hands after use
- Available as cream, gel, lotion (0.025-0.075% concentrations)

Capsaicin Side Effects

- Capsaicin
  - Redness, burning, stinging 40-70% (decreases with continued use), some patients experience coughing with application
  - Avoid if allergic; stop using if ulcers visible

Counterirritant Interactions

- NSAIDS (prostaglandin inhibitors) & histamine dihydrochloride
- Avoid combinations of drugs with same mechanism of action
  - E.g. ammonia water & methyl salicylate
  - E.g. capsicum & capsaicin
- Avoid combination with local anesthetic (LA)
  - LA depress cutaneous nerve sensation
- Avoid combination with skin protectants (oppose counterirritants)
  - E.g. zinc oxide, cocoa butter, lanolin, white petrolatum

Indications

Tendonitis: Onset, general care

- Onset-usually gradual, worsened by joint movement
- Non-drug/general care measures
  - Stop etiology
  - Stretching
    - Cautiously
    - No bouncing
  - Rest
  - Ice
    - As soon as possible!
    - Up to 15 minutes, 3-4 times a day until swelling improves
      - Usually 12-24 hours
  - Heat:
    - not within 48 hours of injury
    - 15-20 minutes, 3-4 times daily

Tendonitis OTC Therapies

- Systemic analgesics: acetaminophen, NSAIDS
  - Which preferred? Why?

- Topical analgesics/counterirritants
  - Lower concentrations of counterirritants may also produce analgesia!

Bursitis:
Onset, general care, treatment

- Onset-usually acute, worsened by joint movement
- Non-drug/general care measures
  - Rest
  - Immobilization
- Nonprescription treatments
  - See Tendonitis OTC Therapies slide

Sprains & Strains: Onset, Care

- Onset: acute at time of injury
- General care:
  - RICE
  - Stretching
  - Protection (tape, brace, cane)
- OTC therapies
  - Systemic analgesics
  - Topical counterirritants

Shin Splints

- What?
  - Pain from knee to ankle
    - Worsens with activity
- Who?
  - Runners, walkers
- Why?
  - Overuse on hard surfaces
  - Improper stretching
  - Improper footwear
- Treatment
  - RICE therapy
  - Systemic analgesics
  - Shoe orthotic
  - Medical referral if pain becomes cramping or burning tightness

Patient Counseling

- Expected benefit
- Dose and drug administration schedule
- Application directions
  - I.e. rub a thin layer of product until it's not visible, avoid thick layering, wash hands after application
- Potential adverse reactions
- Drug-drug or drug-disease interactions
- Self-monitoring to assess response to treatment
- When to contact health care provider

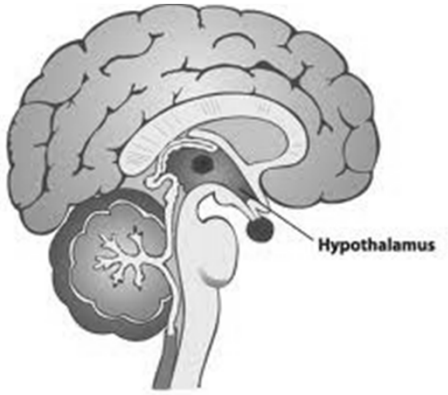
Fever

Fever - Background

- Most common reason for visits to pediatrician's offices
- Leading cause of ED visits in children under age 15
- Fever versus hyperthermia
  - Fever is regulated rise in body temperature maintained by the hypothalamus in response to a pyrogen (fever-producing substance)
  - Hyperthermia is malfunction of normal thermoregulatory process in the hypothalamus

Normal Temperature Variations

- Temperature controlled by thermoregulatory center located in the anterior hypothalamus
- Older adults have lower body temperatures, elevations in temperature with illness less pronounced
- Normal variation up to 1ºF
  - After meals
  - Evening
  - During and after ovulation
  - Pregnancy



Fever

- Elevation in core body temperature above the daily range for an individual
- Characteristic of most infections but can also stem from non-infectious origin such as auto-immune or inflammatory disease, malignancy, dehydration, heat stroke, hyperthyroidism
- In general, morning temperature >98.9ºF or afternoon temps > 99.9ºF considered a fever

Detection of Fever

- Temperature varies with location of measurement: rectal ~ 1°F higher than oral (due to mouth breathing)
- Fever is considered:
  - Rectal: > 100.4 F
  - Oral: > 99.7 F
  - Axillary: > 99.3 F
  - Tympanic: > 100 F

Detection of Fever

- Rectal: preferred in infants age < 6 months
- Oral
  - Avoid when pt is hyperventilating or not fully alert
  - Not for children < 3 years old, can't form tight seal
  - Avoid vigorous activity, hot or cold drinks, smoking or coffee for at least 20 minutes before measurement
- Tympanic
  - Accuracy depends on proper placement
  - Variations due to cerumen impaction, inflammation in ear canal, age of patient (avoid in infants < 6 months old)
- Axillary
  - Not as reliable if performed with digital thermometer
  - Variations due to inappropriate placement, arm movement

Febrile Seizures

- Seizure with fever in infants/children without intracranial infection, metabolic disturbance, or a defined cause
- Occur in 2-5% of children age 6 months to 5 years
  - Peak occurrence 18-24 months
- Simple febrile seizure most common type
- Antipyretics do not reduce the risk of recurrent seizure
- Prophylaxis with antiepileptics NOT recommended

Pathophysiology of fever

- Regulated in the hypothalamus
- Thermoregulatory center "thermostat" shifts upward during a fever
- Caused by "pyrogens" (fever inducing substances)
  - Exogenous pyrogens – infectious
  - Endogenous pyrogens - cytokines
  - Trigger elevation of PGE2 levels

Elevated PGE2

- Leads to vasoconstriction (narrowing of blood vessles) – produces cold sensation in hands/feet
- PGE2 in periphery (hands/feet) – myalgia
- Blood shunted away from periphery to internal organs, decreasing heat loss from skin
- Thermogenesis in fat or muscle
  - Through uncoupling proteins, releases ATP and heat
- Behavior instincts: seeking warm rooms, adding extra clothing, reducing activity

To treat or not to treat?

- Elevated core temperature increases oxygen demand
- Every increase in 1ºC above 37ºC = 13% increase in oxygen consumption
- Fever can aggravate pre-existing heart or lung disease
- Fever can induce mental changes in patients with organic brain disease (Alzheimer's Disease)
- Except in rare circumstances, no benefit to allow fever to persist

Exclusions for Self Treatment

- Patients > 6 months with rectal temp ≥ 104 F or equivalent
- Infants < 6 months with rectal temp ≥ 101 F
- Severe symptoms of infection that are not self limiting
- Risk for hyperthermia
- Impaired oxygen utilization (COPD, respiratory distress, heart failure)
- Impaired immune function (HIV, cancer)
- CNS damage (head trauma, stroke)
- Children with history of febrile seizures
- Fevers that persist beyond 3 days with or without tx
- In children: if rash, refusing to drink fluids, extreme lethargy, vomiting and can't keep down fluids

Nonpharmacologic therapy

- Adequate fluid intake
  - Children: increase by at least 1-2oz per hour
  - Adults: increase by at least 2-4oz per hour
- Sponging or baths have limited utility
  - Uncomfortable and induces shivering, which can raise body temperature
  - Avoid isopropyl or ethyl alcohol for body sponging due to increased risk for alcohol toxicity, esp in children
- Avoid ice water baths
- Lightweight clothing, remove blankets, maintain comfortable room temperature (68 F)

Treatment of fever

- Inhibition of synthesis of PGE2 (blockade of COX enzyme in CNS)
- Acetaminophen: poor cyclooxygenase inhibitor in periphery (no anti-inflammatory features)
  - Oxidized in the brain by P450 enzyme system, the oxidized form inhibits cyclooxygenase
- NSAIDS
- Aspirin versus acetaminophen?
- Corticosteroids
- Which is preferred and why?

Acetaminphen

- Reaches maximum temperature reduction 2 hours post-dose
- Usual recommended dose 10-15 mg/kg every 4-6 hours, max 5 doses per day (weight based dosing, not age based)
- Loading dose?
- Available as rectal suppository
  - For children who can't take oral medications, are vomiting, or in setting of febrile seizure
  - Erratic absorption
- Should not be used for longer than 3 days
- Liquid pediatric formulations are all 160mg/5ml for children younger than 12 years old

Ibuprofen

- Most common NSAID used for fever
- Reaches maximum temperature reduction at 2 hours; dose = 5-10mg/kg every 6-8 hours, max 4 doses daily (weight based dosing in children, not age based)
- NOT for use in infants < 6 months old
- Should not be used for longer than 3 days

Liquid Non-prescription Products

- High rate of errors: inappropriate dosing, inaccurate measurement, duplication of therapy
- FDA guidelines in 2011
  - Liquid preparations dispensed with dropper, cup, syringe, or spoon
  - Dosing device should be calibrated to recommended dose
  - Markings remain visible even when liquid is in the device

Reversal of fever

- Hypothalamic set-point reset downwards
- Heat loss accelerated through vasodilation and sweating, continue until temperature of blood supplying hypothalamus matches the lower setting
- Behavior changes: removal of insulating clothing or bedding

Patient Education

- Proper monitoring
  - Address “fever phobia”
- Exclusions for self care
- Nonpharmacologic (fluid, things to avoid)
- Pharmacologic
  - Dosing
  - Avoid alternating acetaminophen and ibuprofen due to complexity of regimen and increased risk for error
  - Use measuring device
  - Do not treat fever for longer than 3 days without seeking advice from HCP