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FACEBOOK LIVE

SEPTEMBER

30

UNDERSTANDING WOUND PAIN: THE PHYSIOLOGY OF NOCICEPTORS AND INFLAMMATION

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Objectives

At the end of this presentation, you will be able to:

- Define the pathways and impact of nociceptor fibres throughout tissues
- Identify the physiologic changes associated with the inflammatory signalling cascade that directly impacts nociceptor pain signals
- Review therapeutic options to decrease nociceptor stimulation throughout wounded tissues

Pain has its purposes[1,2]

- Prevents serious injury by eliciting a rapid response to noxious stimulus
- Educates the body on avoidance
- Prevents permanent damage

Nociceptor signalling

- Earliest alert system signalling for[5]:
  - Tissue injury
  - Inflammatory diseases
  - Pathogen exposure
- Initiated by nociceptor transduction of stimuli into neuro-electrical signals[6]

Types of wound pain

- Nociceptive[7]
  - Physiological response to painful stimulus
  - Serves as a biologic function to warn of injury
  - Somatic — sharp, stabbing
  - Onset and duration
    - Acute
    - < 90 days

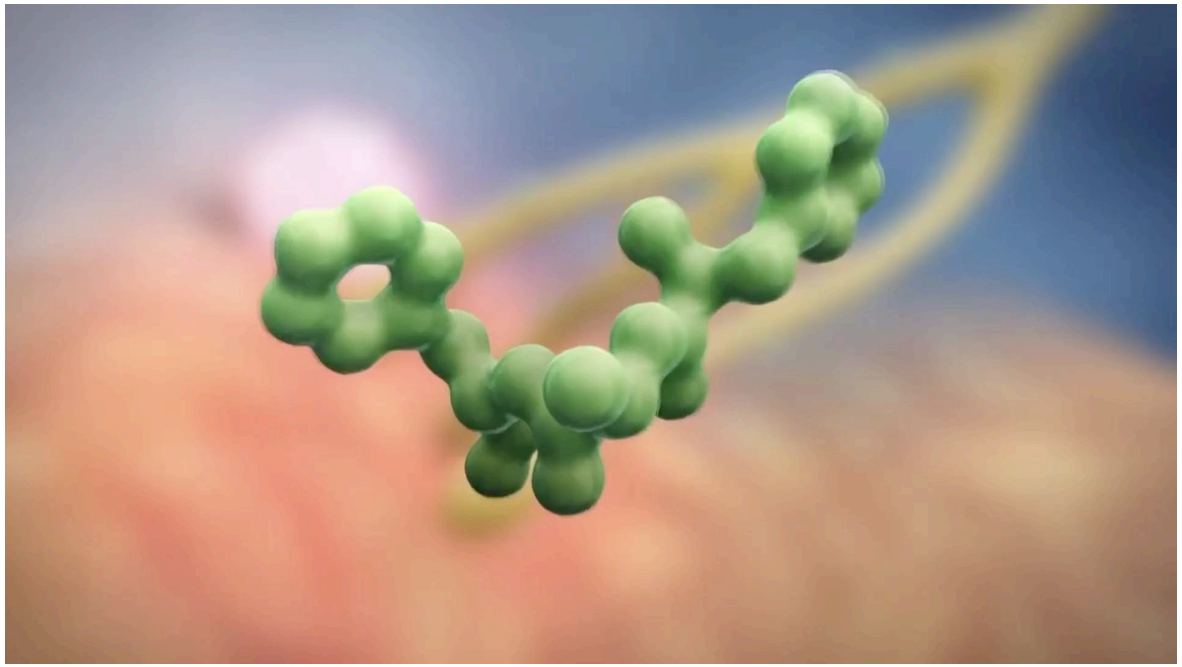
Types of wound pain *continued*

- Neuropathic[8]
  - Caused by dysfunction or damage in the nervous system
  - Sensory abnormalities from loss of sensation to hypersensitivity
  - Results in inappropriate response and damaged nerves cause signals to travel on abnormal pathways

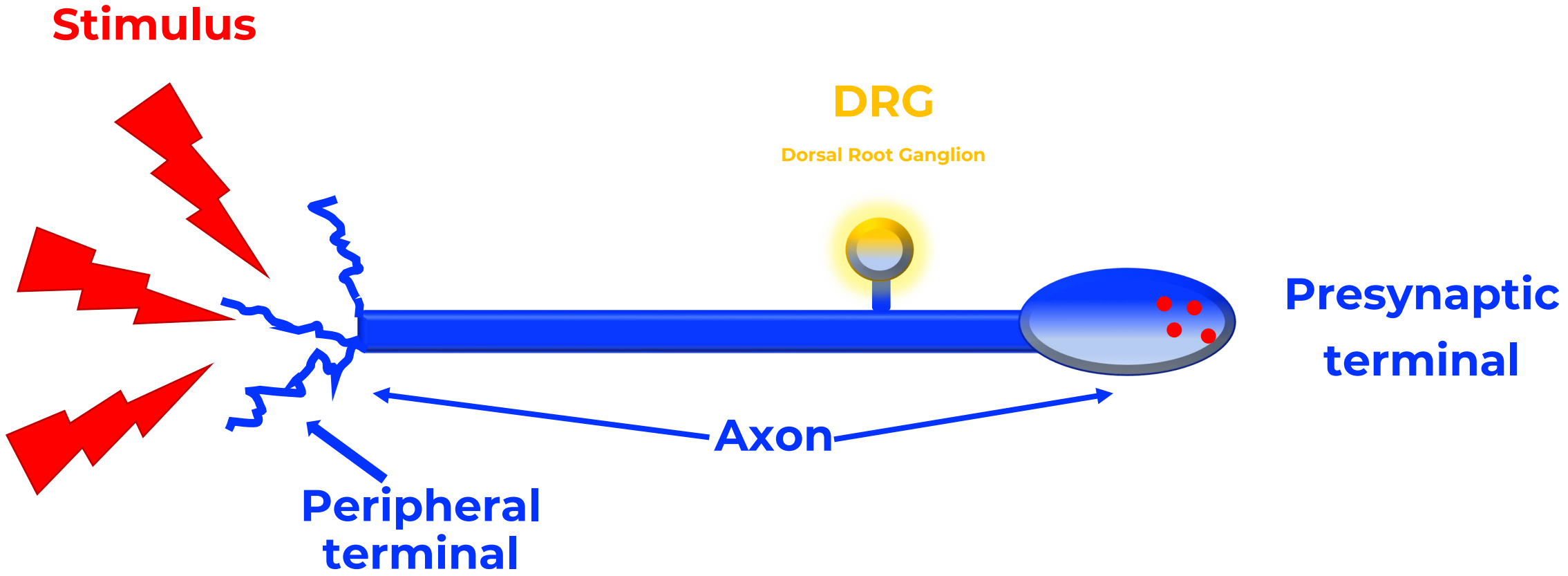
HAS NO PROTECTIVE FUNCTIONS!

What is a nociceptor?

- A free nerve ending that is a receptor for painful stimuli[9]
- Responds to potentially damaging stimuli by sending signals to the spinal cord and brain[10]
- Nociceptor system plays the central role in regulating the entire response to injury[10]
- Primary job everyday: establish and maintain homeostasis of innervated tissues[4]



Structure of nociceptors



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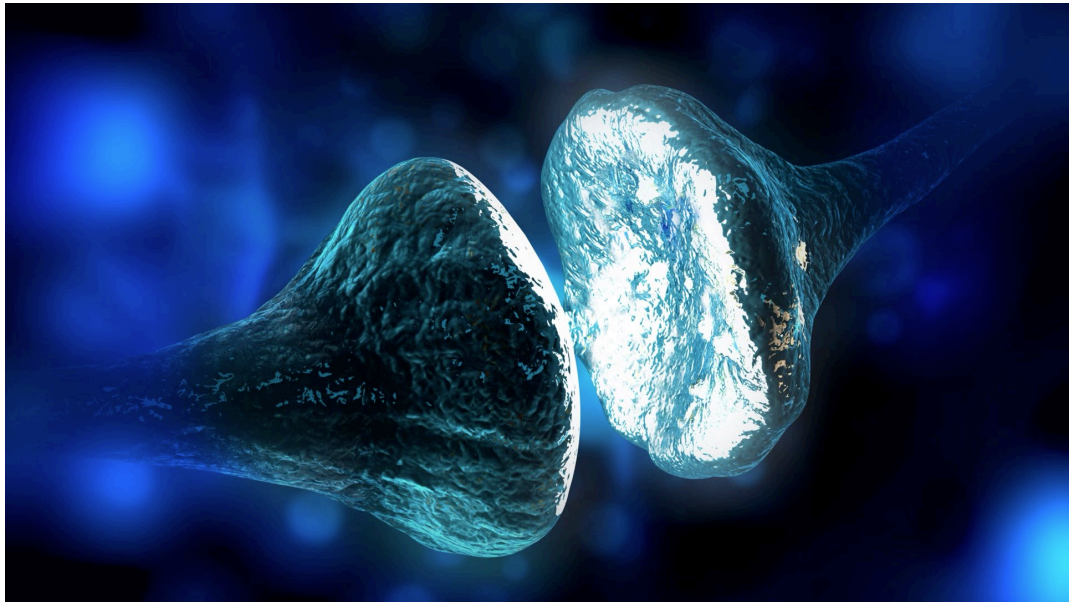
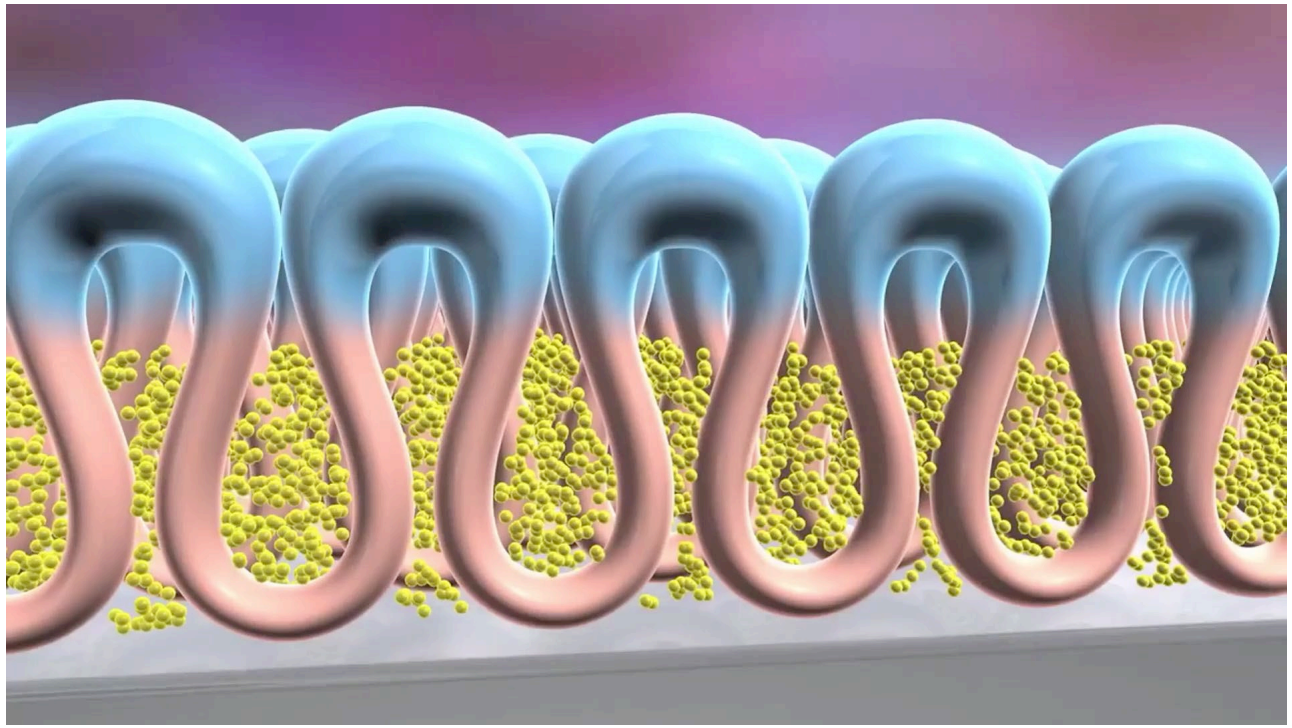
Rates of neuronal signal transmissions

- Thicker the nerve fibre — the faster the signal
- Aα, Aβ and Aδ are insulted with a myelin sheath
  - ↑ conductivity
- C fibers are unmyelinated
  - Slower conductivity
- Aδ and C fibers are primarily responsible for pain signaling



Nociceptor chemical actions and inflammation

- Noxious stimulation creates cellular changes[5]
  - Enzymes released
  - Mediators released
  - Alterations in membrane permeability
  - pH changes
- Stimulation of the inflammatory cascade[6]
  - Histamine and serotonin released
  - ↑ vasodilation
  - ↑ inflammation



5 phases of nociceptive pain[11]

Transduction

Conduction

Perception

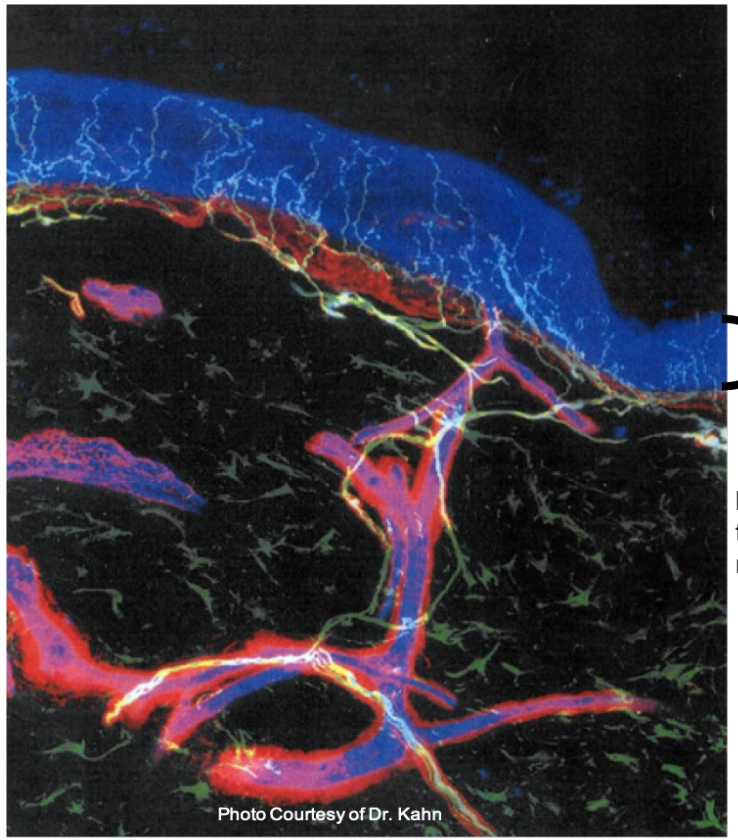
Transmission

Modulation

Phase 1 — transduction

- Nociceptor terminals are densely spread throughout skin
- Nociceptive C and Aδ fibres depolarise due to peripheral noxious mechanical, thermal or chemical stimulation
- Proteins and ion channels convert to an Action Potential

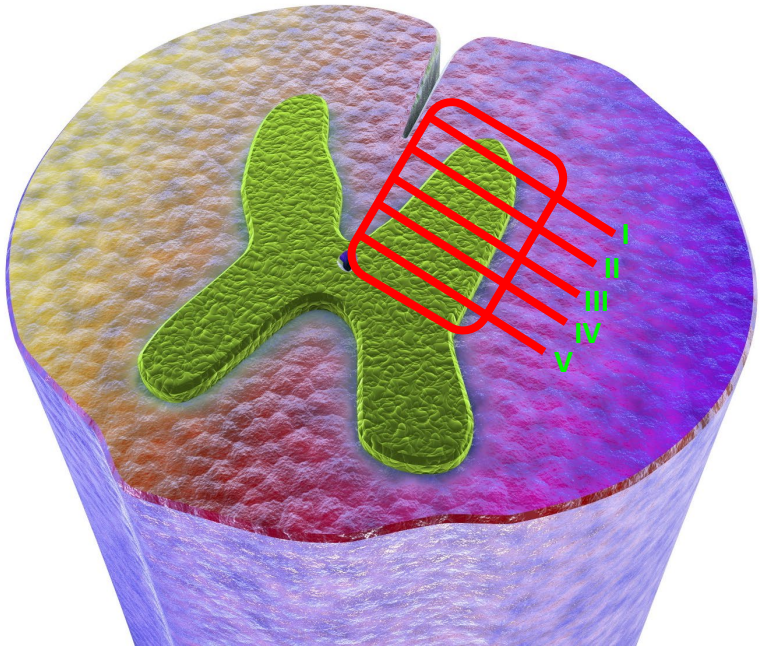
Stained photomicrograph of nociceptors



The lines that look like "lighting bolts" are the inflammatory nerve fibers.

Phase 2 — conduction[11,12]

- Movement of the Action Potential from the peripheral to the central process
- Depolarisation occurs at the presynaptic terminal
- Interneurons transmit or inhibit transmission through the dorsal horn into specific lamina (I–IV)



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Phase 3 — transmission[11,12]

- Aδ and C fibres release pro-nociceptive chemicals to activate post-synaptic receptors
- Results in an influx of ions that depolarise neurons and interneurons
- Creates an Action Potential that is transmitted to the medulla, brain stem and hypothalamus

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Phase 4 — natural modulation[11,12]

- Natural adaptive process with both excitatory and inhibitory mechanisms
- Release of neurotransmitters:
  - Enkephalins
  - Dynorphin
  - Endorphins

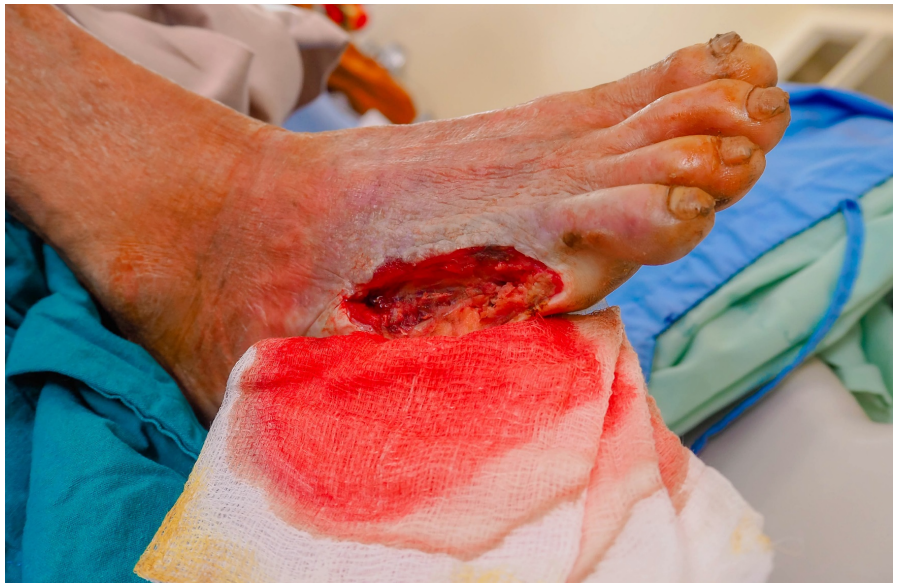
- Inhibit sensitisation of nociceptor terminals via inhibition of cyclooxygenase
- Inhibit depolarisation and repolarisation of the axonal membrane
- Inhibit the inflammatory response

Phase 4 — modulation via medical interventions[11,12]

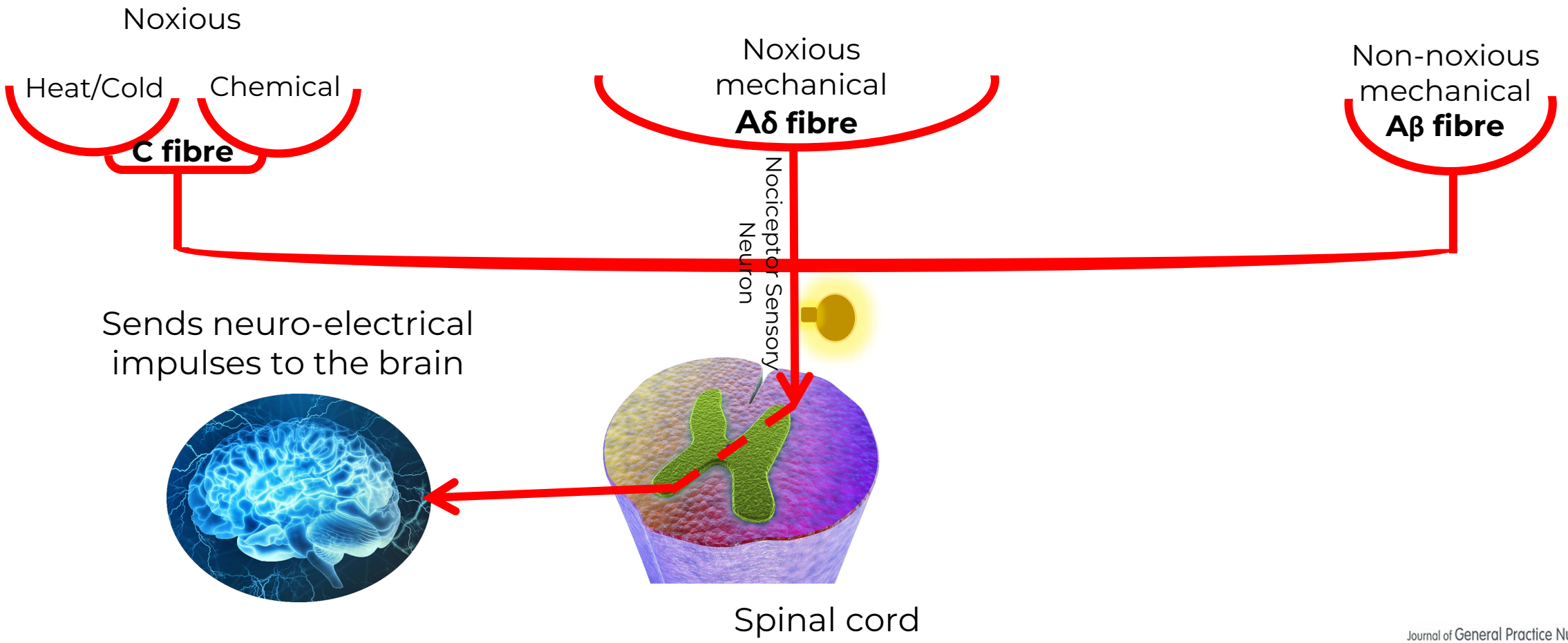
- Adaptive process with both excitatory and inhibitory mechanisms
- Inhibit sensitisation of nociceptor terminals via inhibition of cyclooxygenase
  - Aspirin, ibuprofen, paracetamol
- Inhibit depolarisation and repolarisation of the axonal membrane
  - Local anaesthetics (lidocaine)
- Inhibit the inflammatory response
  - Hydrocortisone
- Stimulate Aβ fibres to induce interneurons to release GABA and glycine
  - TENS

Phase 5 — perception[11,12]

- Dependent upon existing neural processing
- Action Potentials are decoded within the brain and interpreted:
  - Bad, unpleasant sensation
  - Localised to a body region
  - Urgency
  - Intensity
- Complete integration of sensations, emotion and recognition of pain



Nociceptive pathway — autonomic signalling[11,12,13]



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Correlating the nociceptor response in wounds

- Injury biochemical signalling begins
- Inflammatory signalling is stimulated
- ↑ inflammatory mediators
- ↑ interstitial pressures
- ↓ tissue perfusion
- ↑ tissue hypoxia/ischemia
- ↑ nociception cycle

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HOW DO WE TREAT IT?

Most frequently used clinical management options[14,15]

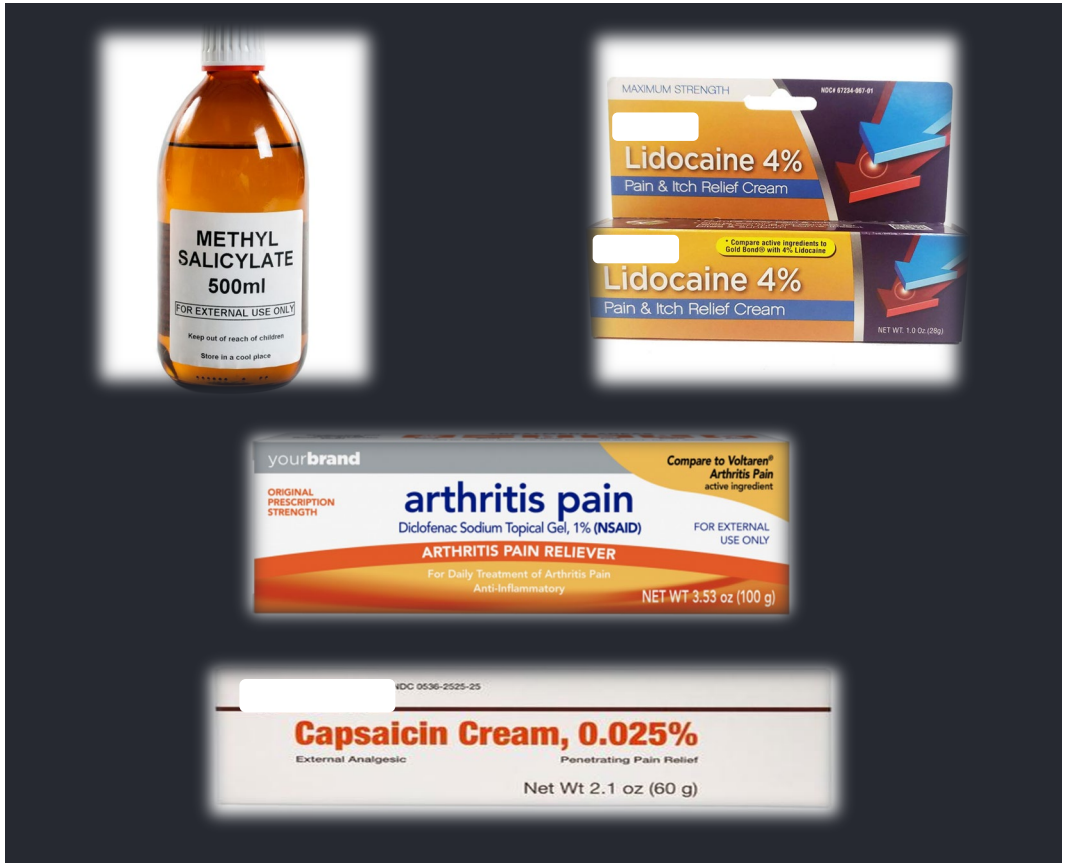
- Pharmacologic (PO/IM/IV)
  - NSAIDs
  - Tricyclic antidepressants
  - SNRIs
  - Anticonvulsants
  - Opioids
    - Short- and long-acting
  - Muscle relaxants

Identified and escalating sequelae[17,18]

- Gastrointestinal side-effects
  - Constipation/NVD
- Liver, kidney dysfunction
- Sedation, dizziness
- Coagulopathies
- Hypotension
- Anaemia
- Electrolyte disturbances
- Dependency/addiction
- Mood changes
- Cardiovascular risk
- Sleep apnea
- Drug tolerance
- Fatal drug interactions
- Non-compliance
- No relief

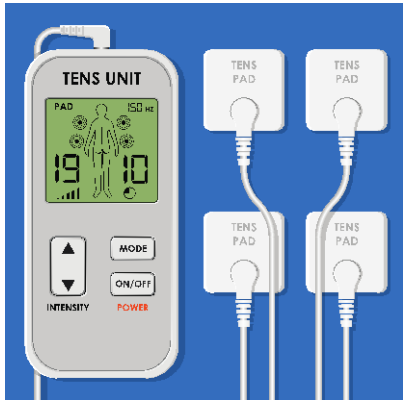
Most frequently used clinical management options — topical analgesia[14,15]

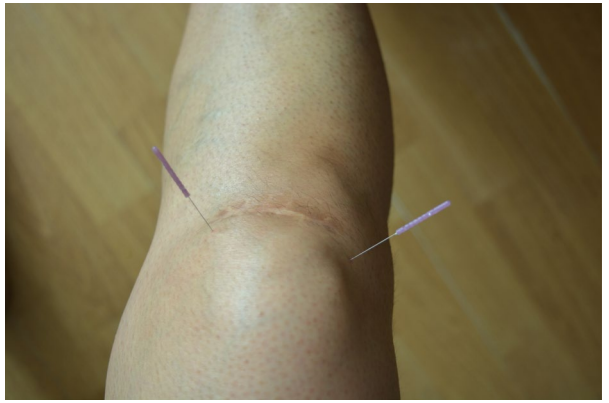
- Pharmacologic and OTC (topical)
  - Capsaicin[16] (C fibres)
  - Diclofenac
  - Lidocaine
  - Menthol/salicylate



Non-pharmacologic alternatives

- Methods
  - TENS
  - Acupuncture/acupressure
  - Psychological intervention
  - Polymeric membrane dressings (PMD)
- Mechanisms
  - Spinal cord modulation
  - Endogenous enkephalins
  - ↓Nociceptor stimulation





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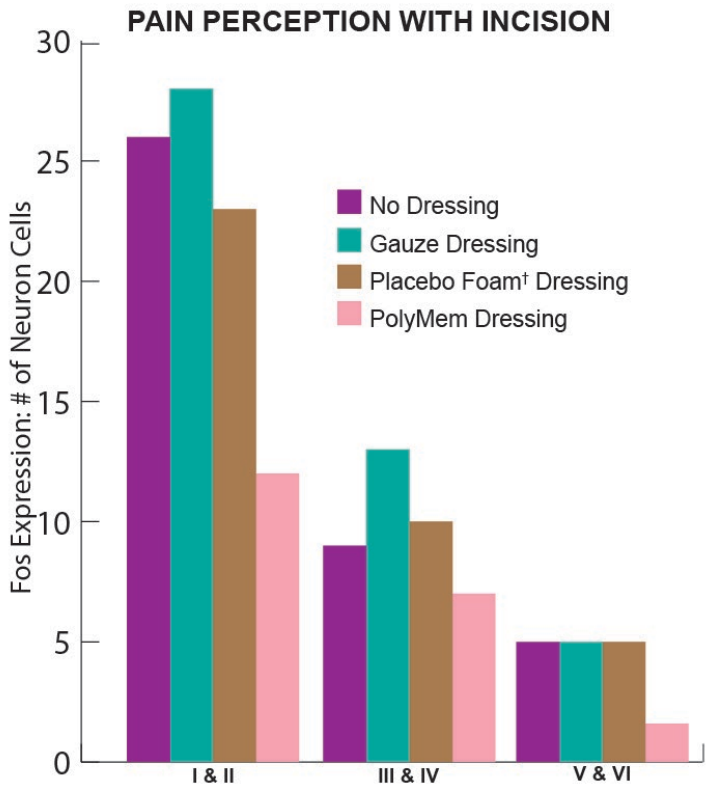
Polymeric membrane dressings elicit antinociceptive properties[19,20,21,22,23]

- Research demonstrated:
  - Reduction of pain caused by surgical incisions
  - Impacts neuropeptide signalling
  - Decrease of nociceptive activity
    - ↓ pain
    - ↓ burning/itching
    - ↓ ecchymosis
    - ↓inflammation



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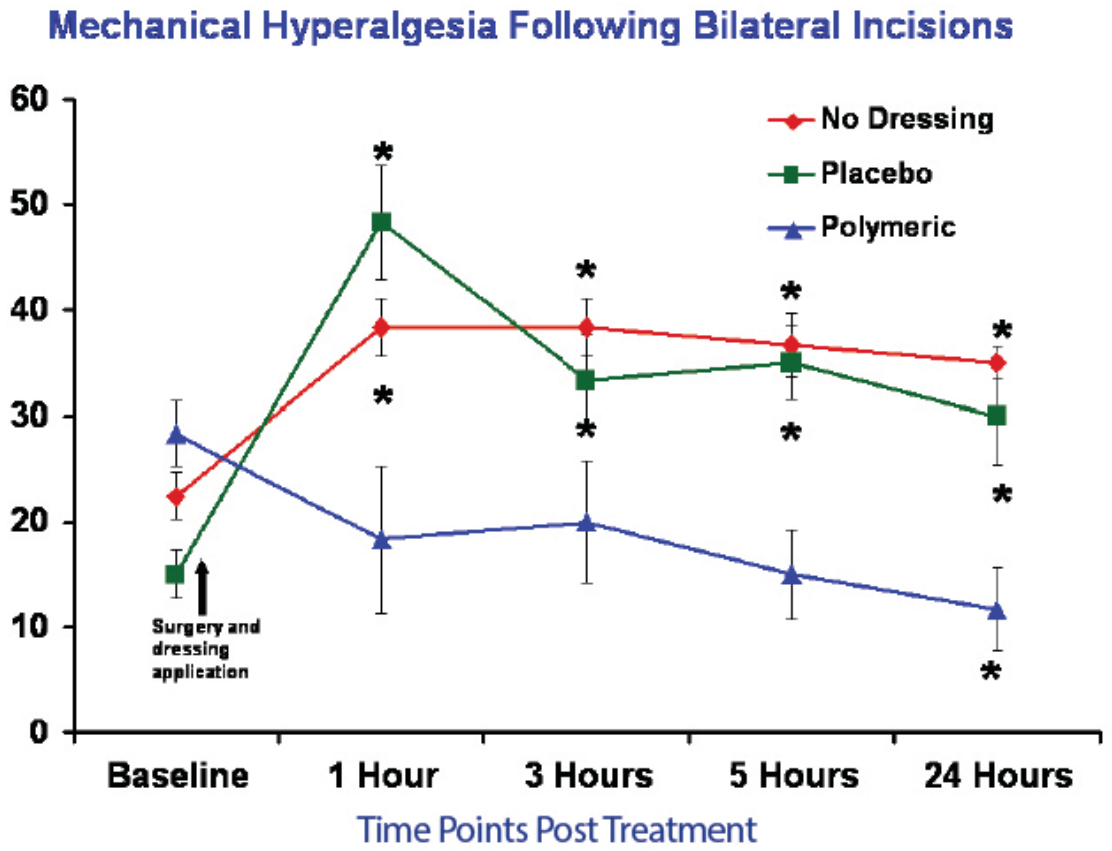

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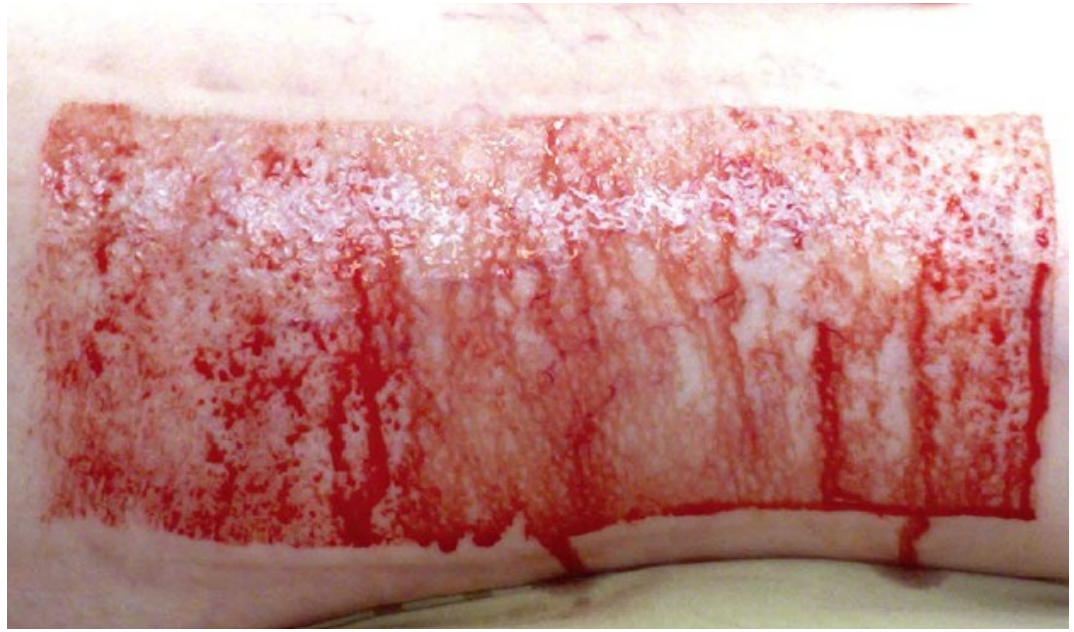
The visual: antinociceptive/inflammatory modulation actions – AND…

- High MVTR protective film
- Continuous cleansing w/surfactant
- Optimises moisture with
  - Superabsorbent and glycerol
- Open cell, hydrophilic PU membrane
- Conforms to irregular-shaped wounds



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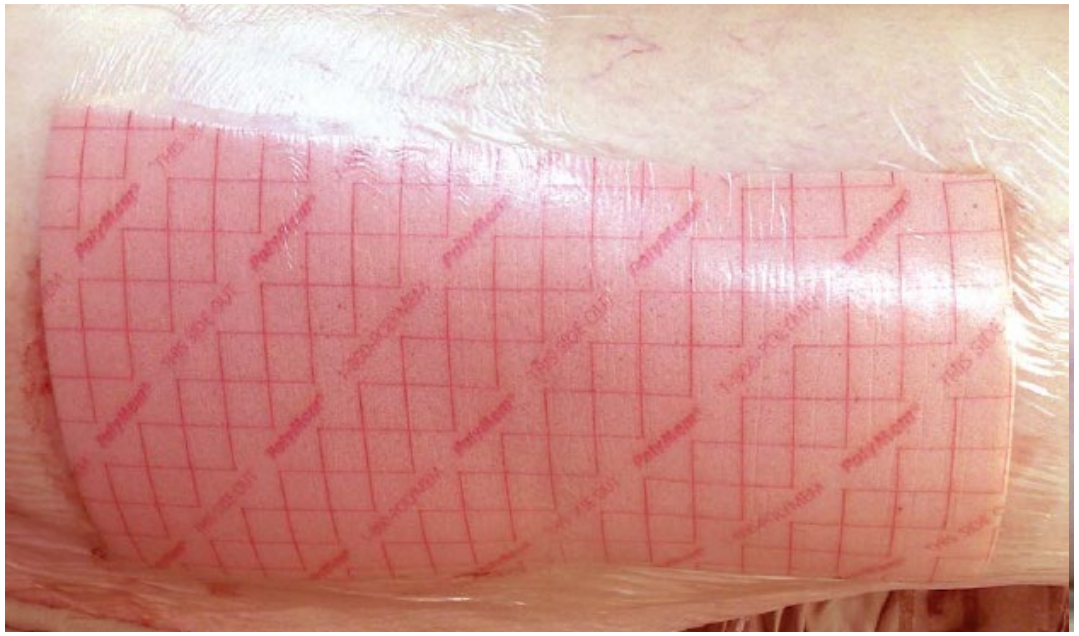

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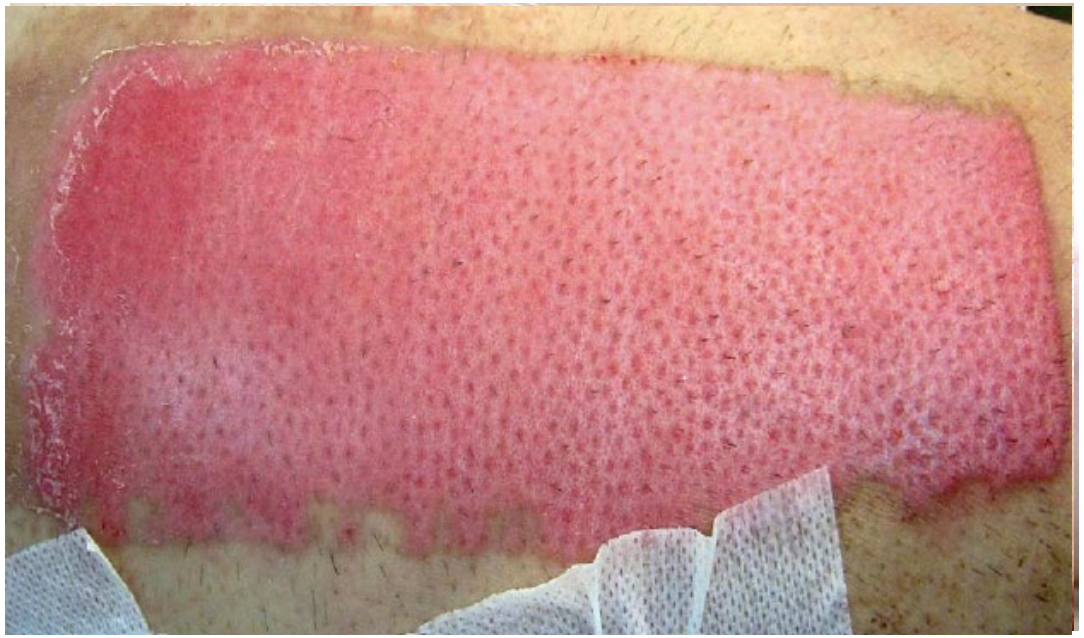
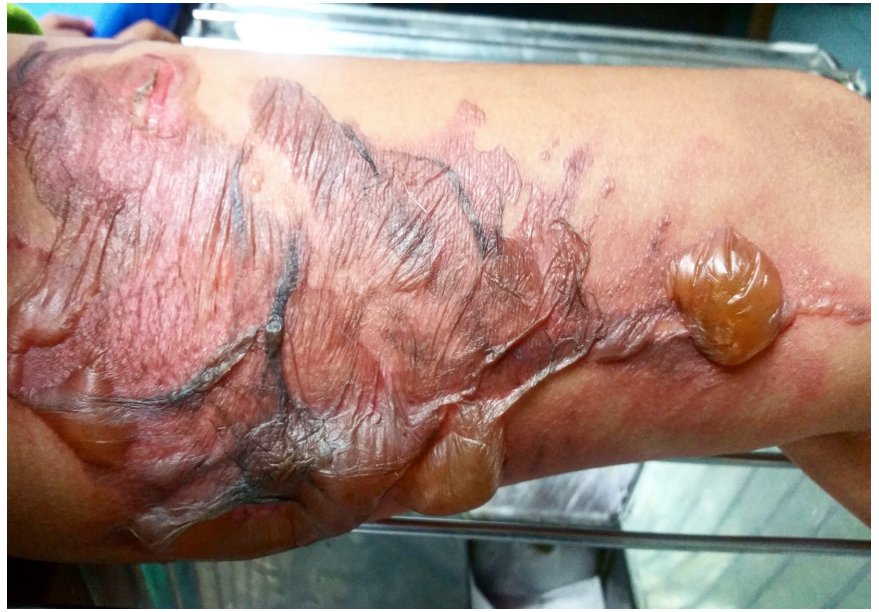


Initial and long-term effects of pain

- Wound pain ↑ psychological and physical stress[3]
- Contributes to patient and caregiver non-compliance with prescribed treatments[4]
- Non-compliance results in[4]:
  - ↑ risk of infection
  - ↑ risk for delayed healing
  - ↑ morbidity and mortality
  - Overall ↑ in total costs to heal the wound



Benefits of non-pharmacologic alternatives

- Eliminates multiple sequelae including:
  - Dependency
  - GI/organ dysfunction
  - Additional painful procedures
  - Most allergic reactions
- Contributes positively to self-care initiatives
- May be successful when pharmacologic options have failed
- Can strategically target nociceptor signaling pathways
  ↑ pain resolution opportunities

Conclusion

- The nociceptive signalling pathways are complex, beneficial and problematic — at the same time
- The physiologic changes associated with the neurochemical signalling cascade directly impact the wound healing environment — especially the early or late onset of pain
- Therapeutic options for wound pain should include a focus on methods known to decrease nociceptor stimulation

PolyMem – polymeric membrane dressing

PolyMem dressings help to:

- Effectively manage and heal wounds
- Absorb fluid and provide a moist healing environment
- Relieve wound pain by inhibiting the action of some pain-sensing nerve fibres (nociceptors)[19]
- Reduce oedema, bruising and the spread of inflammation into surrounding undamaged tissues by altering the action of certain nerve endings[19]

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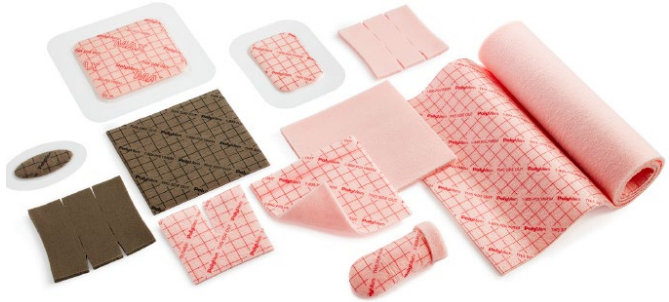

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