Pain Slows Healing:

Part 1(I – III): Understanding the Inflammatory Response to Soft Tissue Injury
Part 2 (IV – V): How to Assess and Address Patients' Pain and Inflammation

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Overview

Definition (from the International Association for the Study of Pain, or IASP):

"Pain is a sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage"[1]

The goal of pain management is to restore function to an acceptable (to whom?) level.[2]

Addressing pain is standard of care: pain is the 5th vital sign. It is important because of reimbursement (both Medicare's Shared Savings Program and CMS measure patient satisfaction and return to former function, which usually involves controlling pain). Patient satisfaction also influences your reputation in the community, and thus the bottom line. And most of us want to address pain out of a sense of altruism – we want to do the right thing. However, pain is not only a quality of life issue: it also directly influences *wound healing outcomes*.[1,3]

Pain is what the patient feels. Period. Don't try to distinguish between physical and psychological pain – it can't be done, and the attempt is not helpful![4]

Prevalence and incidence:

- Fully 92% of all out-patients at one wound clinic reported pain[5]
- In another study, 88% of the patients said their wound pain interfered with activity
- Internationally, 36% of chronic wound patients have pain most or all of the time
- 63% of patients complained of dressing change pain, and an additional 30% experienced pain during routine wound cleansing[5]
- Over 40% say painful dressing changes are the worst part of living with a wound.
- 18% described dressing changes as "horrible" or "excruciating"[3]
- In one study, 84% of pressure ulcer patients had persistent wound pain[6]
- Up to 80% of venous leg ulcer patients have significant wound pain. Pain disturbs the sleep of one third of all venous leg ulcer patients. What effect would this have on healing?
- 7% of the general population experiences pain due to nerve damage neuropathy[7]

Only 6% of the pressure ulcer patients who reported pain or discomfort received analgesics[3] – if you assess it, help the patient manage it![3]

"Pain is God's greatest gift to mankind"

– Paul Brandt, worked with leprosy patients in India, then DFU patients in the USA

I. The Benefits and Disadvantages of Pain

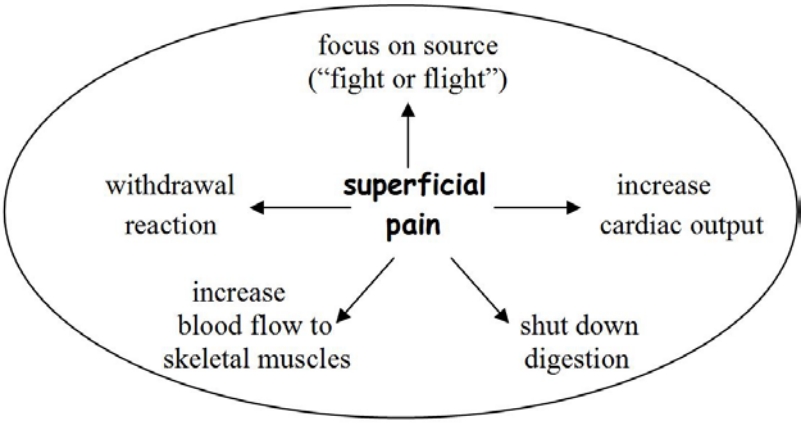
A. Positive aspects of pain - benefits

1. Pain helps us avoid injury
2. Pain is often the first sign of injury
3. The character & intensity of pain can be diagnostic (somatic vs. visceral pain)[8]
4. Helps prevent reinjury

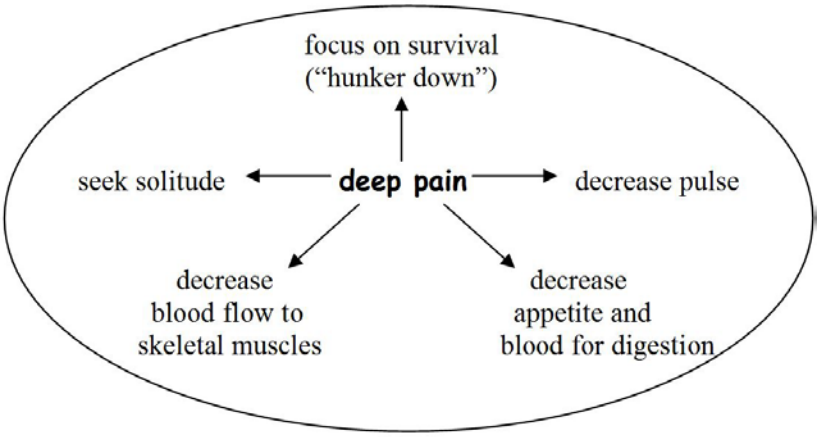
5. Increased pain is often the first sign of infection (due to the inflammation)[9]
6. Persistent pain may signal that a problem persists

B. Disadvantages of Pain (ways in which pain inhibits healing)[10(pp425-453)]

1. Response alters chemicals throughout the body
   a. When? When pain exceeds a threshold (or anticipatory, chronic)
   b. Why? Protecting from death
   c. What? Catabolic state to produce energy, adrenalin, prevent sepsis… (catabolism = breaking down tissue, the inflammation stage)
   d. Problem because we want anabolic state (building tissue: proliferation)



Resources are shifted from growth to the skeletal muscles



Resources are shifted from growth to the immune system

2. Either superficial or deep pain can become chronic. Disadvantages are:[11]
   a. The body stays in a catabolic state
   b. Resources are shifted away from growth
   c. Digestion is impaired (poor nutrition)
   d. Patient withdraws from healthy activities
   e. Leads to a long-term inflammatory state

II. Why Injury Leads To So Much Inflammation and Pain[10(pp425-453)]

A. How Injury Causes Inflammation

Excitatory (Increase Pain and Inflammation Overall)			
Chemicals	**Released by**	**Acts on**	**To Cause**
Cell-derived Inflammatory Mediators: **Histamine** **Prostaglandin** **Bradykinin**	➢ Mast cells (histamine only) ➢ Macrophages (triggered by bacteria, H+ & K+ from injured cells) ➢ Tissues at injury area ➢ Platelets ➢ Brain via nociceptors (Prostaglan, bradykinin)	Capillaries & Arterioles Peripheral Terminals of the Nociceptors	Vessels leak & get wider, (edema, heat, redness, bruising) Recruit MMPs & Growth Factors Smooth muscles contract (prevents hemorrhage) Nociceptors release P & CGRP (increase inflammation) Brain feels pain and/or itch
Pro-Inflammatory Cytokines: **Substance P** **CGRP**	Nociceptors (vesicles signaled by histamine at the injury site)	Mast cells (Substance P → release histamine) Capillaries & Arterioles	Brain feels pain Vessels leak & get wider Inflammation increases
Inhibitory (Decrease Pain Overall)			
Modulators: **Endorphins** **Seratonin**	Nociceptors, when signaled by brain	Inhibit Prostaglandin and Bradykinin	Endorphins: Decreased pain and inflammation Seratonin: Decreased pain, but can prolong inflammation

1. Injured cells release hydrogen, potassium → cytokine release
2. Mast cells, bacteria → histamine → stimulates nociceptors
3. Nociceptors release neuropeptides (Substance P, CGRP…) which spreads inflammation to undamaged tissue
4. Neuropeptides cause increased capillary permeability
5. Neuropeptides cause smooth muscle contraction
6. Neuropeptides cause mast cells to release histamine
7. Inflammation spreads like dominoes going in all directions

B. What does this release of inflammatory mediators do?

1. Increased blood vessel permeability

   WBCs enter tissue to kill bacteria (needed)

   Enzymes arrive to clean up area (needed)

   Albumin escapes → Edema (can decrease circulation)

   Red Blood cells escape → Bruising, pain (also not good)

2. Vasodilation

   Repair cells (MMPS, growth factors) arrive (needed)

   → Warmth and redness

3. Smooth muscle contraction → Cramps (to stop bleeding)

III. The Role of the Nociceptors in Healing

A. The action of the nociceptors in soft tissue injury[12]

1. Specific to sources of cell damage, like cutting, chemicals, cold, heat

2. Vesicles in nociceptors release neuropeptides to amplify reaction
3. Leads to walling off infection via massive inflammation
4. Inflammation beyond damaged tissues: neurogenic inflammation
5. When threat is gone, brain should send chemicals to calm the reaction
6. Classic signs of inflammation
    a. Redness – from increased circulation
    b. Swelling – from capillary leakage
    c. Heat – from increased circulation
    d. Pain – from nerves being stimulated and the muscle cramping
    e. Immobility – from all of the above

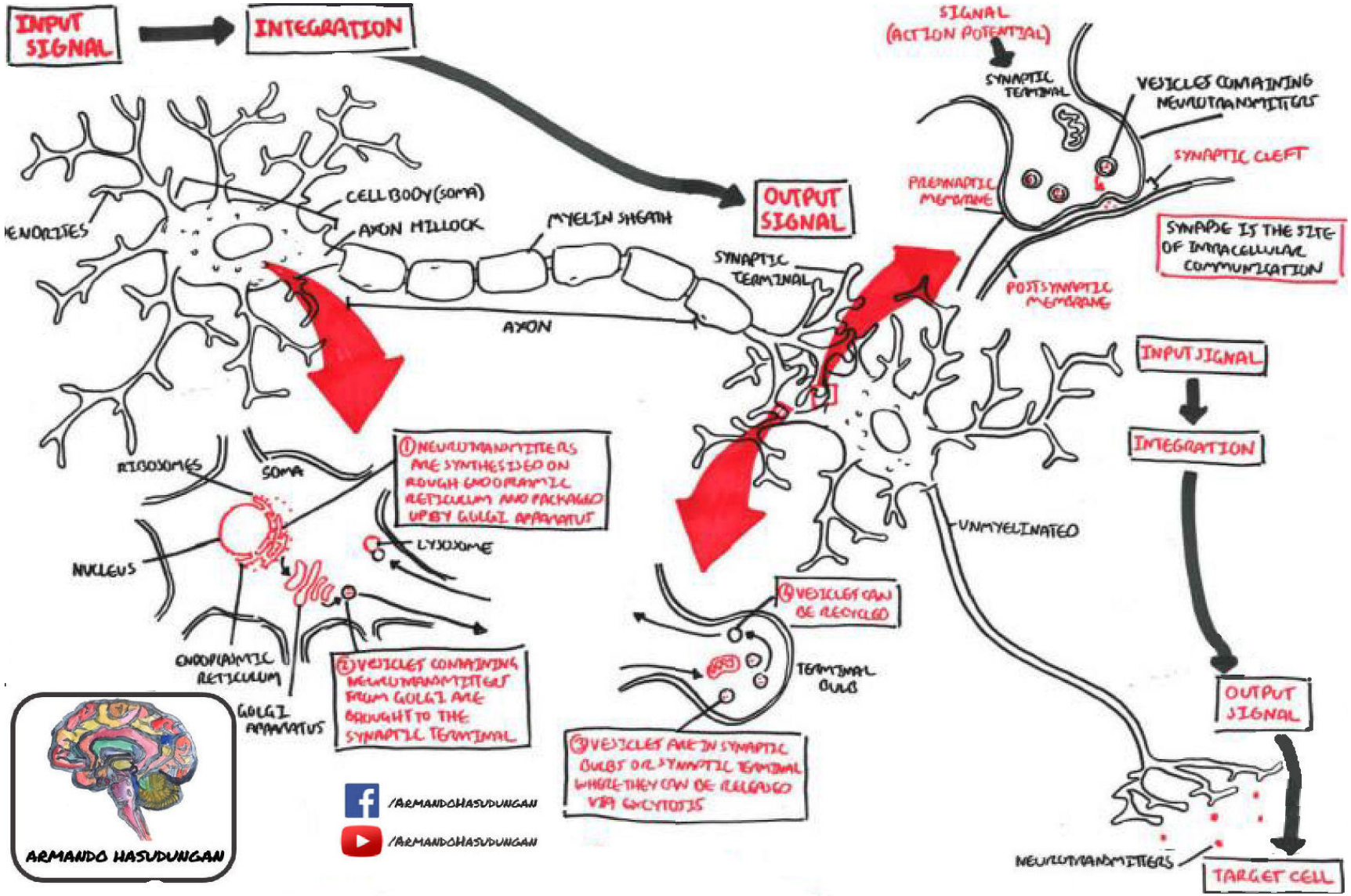
. B. How Pain and Inflammation Can Slow Healing (Especially Chronic Pain)

1. Results of excessive nociceptor activity in WOUNDS
    a. Increases pain (decreased mobility is the GOAL – the body is trying to get the patient to take the wound seriously (death)
    b. Causes secondary ischemic injury (from the edema)
    c. Delays healing by keeping the wound area in a catabolic state
        i. increased enzymes to break down dead and damaged tissue
        ii. Doesn't bring in the builders – less angiogenesis
    d. Keeps the patient sedentary
        i. Decreases quality of life (not able to perform usual roles)
        ii. Glycemic control is dramatically influenced by activity
        iii. Depression from pain is exacerbated by lack of exercise
    e. Increases scarring (such as keloid formation) due to prolonged inflammatory mediators from the mast cells[13]
2. Chronic pain and inflammation leads to nerve damage
    a Hyperalgesia – the nociceptors are extra sensitive[3]
    b. Allodynia – normally non-painful stimuli are painful[3]
    c. Neuropathic pain – nerve damage after the injury is gone[3]
3. Uncontrolled inflammation leads to chronic wounds

Pressure Ulcers, Venous (Stasis) Leg Ulcers, Diabetic Foot Ulcers

Diseases underlie each of these wound types, but inflammation helps determine which at-risk patients will develop open wounds

Nociceptors Regulate the Pain and Inflammation Response: see https://www.youtube.com/watch?v=fUKlpuz2VTs https://www.youtube.com/watch?v=cdCh4_Ckor0 and https://www.youtube.com/watch?v=aD6UD1ETMCg



IV Pain assessment

A. Type of pain – assess and address all three:

1. Procedural – anticipate need for pre-op medications[3]

Patient handling (gentle turning, getting out of bed, ambulating)

Blood draws, IVs, catheters: explain procedures to decrease anxiety

Cough & deep breathing: teach splinting with a pillow before eliciting

Wound management: dressing changes, debridement, even cleansing

a. Mechanical debridement is painful and traumatic. Scrubbing wounds with a soft saline-soaked sponge led to infection in 100% of the cases.[14]

Conservative sharp debridement is more selective, trauma still a problem

Autolytic debridement is least painful and most selective; skin protectant or vertically wicking moisture balancing dressing to prevent maceration

Polymeric membrane dressings augment autolytic with surfactant to break bonds adhering slough, glycerol to recruit fluid, and a super-absorbent[15]

Honey augments autolytic with several complex sugars to recruit fluid

Maggot debridement is often painful,[16] does not speed healing vs. autolytic,[17] is *usually* selective,[18] and removes some (not all) bacteria[17,19]

Enzymatic debridement is selective, but expensive and not more effective than true (sufficiently moist) autolytic debridement[20,21]

b. Nonadherent dressings are essential!!! (no drying onto wound)[3]

Ingrowth of tissue is a problem with some foams and meshes[22]

Negative pressure wound therapy has a REAL problem with tissue ingrowth and destroys granulation tissue too[23,24]

Adhesives (skin stripping) very individualized ideal for one patient may not keep the dressing in place for another)[3]

i. Remove dressings parallel to skin, adhesive remover

ii. Use stretch netting, or protect skin with adhesive film[3]

iii. Silicone adhesive (tape) if it will stick well enough[1]

c. Minimize disruptive wound cleansing when possible[25]

The hyperalgesia and allodynia resulting from unaddressed wound pain are real!

2. Activity pain: dependent vs. elevated, walking, standing in line, sitting

a. How far someone can tolerate walking is a measure of disability

b. Compression decreases pain from venous ulcers, lack of support

d. Arterial insufficiency tends to cause more pain with elevation

c. Sometimes exercise can decrease pain with activity; difficult to break the cycle; diabetic foot ulcers must be offloaded

e. Neuropathy influences activity pain unpredictably

3. Continuous, persistent, background pain – noticed more at rest[22]

a. Eliminate (or minimize) desiccation, pressure, inflammation[22]

b. Address infection[22]

c. Avoid pain caused by treatment when possible

NPWT leads to the release of large amounts of substance P and CGRP, which cause pain and inflammation. Studies show gauze is less painful under NPWT than foam[26]

Pain due to the cycling of NPWT machines[24]

Larval debridement and honey can be very painful[27]

B. Objective quantitative assessment measures (stress is a surrogate for pain)[1]

1. Salivary cortisol levels[9]

(challenges: expensive, fluctuates naturally throughout the day)

2. Salivary Alpha Amylase (sAA)[28]

a. Another surrogate for CNS activity, also responds to stress

b. Stable, immediately responsive

c. Inexpensive test

d. Less well studied (don't replace salivary cortisol yet!)[28]

C. Subjective Quantitative Assessment

1. Cannot compare one patient's pain scores with another's, but can look for responses to treatments (change in a patient's scores over time)

2. Use a validated scale when possible

a. VAS – most validated, very consistent results, but often used incorrectly. Be careful, or at least be consistent.[29,30]

0 – 10 not 1 – 10; what is a 10? "Worst pain *imaginable*"

A slider decreases recall of previous score (see next p)[1]

b. Original Wong-Baker FACES scale – good start, but problematic

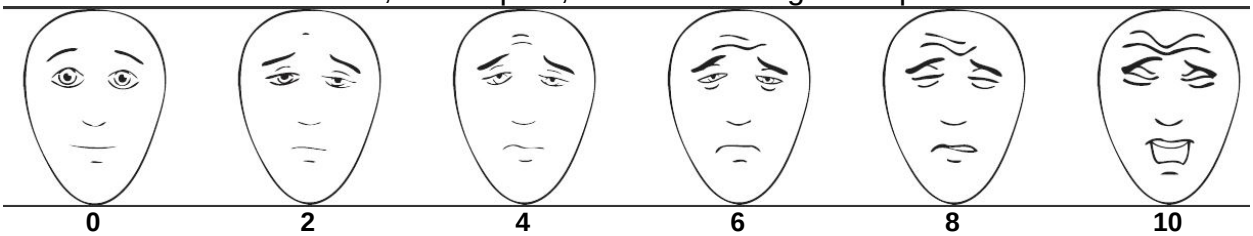
i. copyrighted – expensive to use in some settings

ii. smile at 0 and tears at 10 – emotions; not specific to pain

c. Oucher scale for kids – same problem with emotions, endpoint is inappropriate for kids with chronic health problems

d. IASP developed new Faces pain scale – revised (FPS – R)

0 – 10, 0 = no pain, 10 = worst imaginable pain



Faces Pain Scale – Revised (FPS-R) from IASP.org

e. Pain AD for cognitively impaired, nonverbal patients (see next p)

f. FLACC for infants and cognitively impaired children (see next p)

The Visual Analogue Scale is appropriate for most patients. Use the FPS-R scale for children. Use the FLACC Pain Scale for infants or cognitively impaired children. The PAINAD scale is designed for adults with advanced dementia.

FLACC Scale	Score
Face 0 - No particular expression or smile 1 - Occasional grimace or frown, withdrawn, disinterested 2 - Frequent to constant quivering chin, clenched jaw	
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 and forth, tense 2 - Arched, rigid or jerking	
Cry 0 - No cry (awake or asleep) 1 - Moans or whimpers, ocassional complaint 2 - Crying steadily, screams or sobs, frequent complaints	
Consolability 0 - Content, relaxed 1 - Reassured by occasional touching, hugging or being talked to, distractible 2 - Difficult to console or comfort	
Total Score	

Pain Assessment IN Advanced Dementia- PAINAD (Warden, Hurley, Volicer, 2003)

ITEMS	0	1	2	SCORE
Breathing Independent of vocalization	Normal	Occasional labored breathing. Short period of hyperventilation	Noisy labored breathing. Long period of hyperventilation. Cheyne-stokes respirations.	
Negative vocalization	None	Occasional moan or groan. Low- level of speech with a negative or disapproving quality	Repeated troubled calling out. Loud moaning or groaning. Crying	
Facial expression	Smiling or inexpressive	Sad, frightened, frown	Facial grimacing	
Body language	Relaxed	Tense. Distressed pacing. Fidgeting	Rigid. Fists clenched. Knees pulled up. Pulling or pushing away. Striking out	
Consolability	No need to console	Distracted or reassured by voice or touch	Unable to console, distract or reassure	
			TOTAL*	

D. MUST add: Location and quality or character of pain (headache)

1. Location: document each pain location individually on the chart
2. Quality, or character, of pain: provide examples, ask for free response.

   Sharp, dull, aching, burning, shooting, fiery, cramping, splitting, pounding, pressure, stabbing… 64 descriptors have been identified!
3. Chronology – when did it begin, when is it worst? Is it intermittent?
4. Precipitating and alleviating factors: Did the medicine help?[31]
5. Explore cultural/experiential aspects of this patients' pain (Das in India: 50% reduction in VAS scores was considered "effective in providing relief of pain"[32])

E. Referred pain – follows the dermatome map

1. Most signals go up the nerve fibers to the dorsal root ganglia
2. However, some go back down the nerve branches (tree)
3. Nociceptors release neuropeptides in undamaged tissue.

V. Interventions to address wound pain safely and effectively

A. Goals and Fundamentals

1. Begin with patient-centered goals. Patients may feel frustrated, angry, helpless, hopeless, and "old than my age."[5]

2. Research on wound pain is lacking – most of it addresses only procedural pain. This is a big issue (it can take up to two hours for the increased pain from dressing changes to subside),[27] but it is by no means the only pain issue in wound

3. Nurses without prescriptive authority may fail to address wound pain because they feel powerless.

4. Pain is made worse by fear, anxiety, sleep deprivation, depression. **Trust** decreases fear and anxiety, and **exercise** helps with sleep and depression. Clearly everyone on the team can help decrease wound pain! 5. Learn motivational interviewing:

   http://www.healthteamworks.org/guidelines/motivational-interviewing.html

6. Gate-control theory: when sensory (non-nociceptive) nerve fibers are activated, their signals can interfere with signals from pain nerve fibers.[9]
7. Address (decrease) the cause of the pain first, when possible
   a. Inflammation – Cold packs, compression, PMDs, systemic medications
   b. Hypoxia - Heat (careful!), keep dependent, exercise, medications (? statins, niacin[24]), arterial insufficiency surgery, compression

      NPWT increases hypoxia. It is dangerous on hypoxic wounds![24]
   c. Infection – cleanse, debride, antimicrobial dressings, dressings that continuously cleanse wounds, topical or systemic antibiotics (only when needed!)
   d. Maceration – chronic wound fluid can "burn" the periwound[27]

e. Neuropathic pain (check vitamins D & B_{12}, fenofibrate, exercise, etc.)

f. Procedural pain – use nonadherent dressings that minimize trauma and manipulation of the wound bed: atraumatic debridement (autolytic, or continuously cleansing dressings), avoid even rinsing if possible

8. Systemic medications are undesirable due to side effects.

a. Opioids act at the level of the brain and the spinal cord → neurological side effects.

b. Antidepressants & anticonvulsants block the nociceptor response at the spinal cord.

c. Non-opioid analgesics work on the nociceptor response locally and at the spinal cord.

d. Topical analgesics: if they were not absorbed, they would not have systemic effects at all. But they are absorbed, especially from open wounds, so they need to be used with caution.

B. Topical Medications – Many are contraindicated in open wounds due to toxicity[2,29,33] which includes increased prothrombin times and hepatotoxicity

1. Mostly for procedural & activity pain (few have long-term effectiveness)
   a. Lidocaine, EMLA, etc. are only partially effective. Toxicity and delayed healing are issues as well.[34,35]
   b. NSAIDs delayed healing and/or were toxic[36]
   c. Morphine seems to slow healing; often had no effect on pain[37]
   d. Capsaicin – need high concentration for effectiveness, seems to damage nerve endings[38–40]
   e. Aloe vera cream, Turmeric, etc. are promising[29,41]
   f. Menthol, etc. gate theory (lowers cold sensor threshold)[10(p441)]
   g. Nitroglycerin ointment: increases oxygen and nitric oxide – win![42]
   h. Laser acupuncture (red, infrared) – decreased pain and inflammation, stimulated healing. Unsure of dosage[43]
2. Dressings – like most of the benefits of most creams, due to occlusion – they soothe the raw nerve endings by preventing dehydration and keep the wound bed undisturbed[3]
   a. Occlusive dressings: hydrocolloids, hydrogels, some silicone and foams, NOT gauze![22]
   b. Polymeric membrane dressings are uniquely pain-relieving and anti-inflammatory dressings; subdue the nociceptor response.[44,45] http://www.wcei.net/code/webinar/webinardetail.asp?id=293
   c. Use dressings that are non-adherent & no tissue ingrowth[22]
   d. Edema? Compression is also provided by some dressings
   e. Infection? Use nontoxic antimicrobial dressings when indicated[22]

C. Non-Topical Pain Relievers: Medications and Other Alternatives

1. Systemic Medications

a. Narcotics – not for neuropathy (don't help much),[3] lots of side-effects, give stool softeners from the outset of narcotic therapy

b. Prescription anti inflammatories act on nociceptors; side effects!!

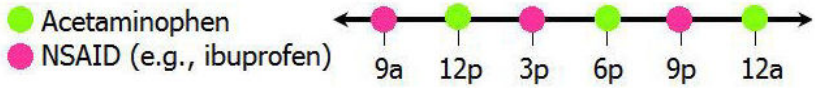
c. Over the counter – caution! kidney and liver concerns (http://www.medscape.com/viewarticle/822725)

i. NSAIDs (non-steroidal anti inflammatories – OTC doses!)

ii. Paracetamol (acetaminophen) was as effective as morphine by 8 hours post op (**not initially**)[46]

iii. Paracetamol (acetaminophen) potentiates effects of NSAIDs, allowing lower doses to be effective[46]

(Alternate OTC dose of paracetamol & ibuprofen every 6 hours, giving *something* for pain every 3 hrs).



d. Neuropathy often responds to neuro-active medications[22] (anti-depressants like amitriptyline, and anti-epileptics, particularly calcium channel blockers like gabapentin)

2. Gate theory methods of pain control (may break pain-stress cycle[27]):

a. Distraction capitalizes upon complex relationship between pain and emotions: music, TV, imagery, video games, sweets[47]

verbal contract with the patient – don't breach trust

b. Acupuncture, stroking or pinching elsewhere in the region[3]

c. Electrical stimulation (TENS) helps with neuropathic pain[39]

3. Increasing patient control (children studied[28]): low-stress environment. Advise patient to call "time outs," perform dressing changes, etc.[3]

4. Exercises – conditioning exercises for the lower leg (CALF) if unable to walk[48]

Avoid Trade-offs. The lesser of two evils is still evil, so try to find a third choice. Look for win-win solutions.

In closing, I would like you to think of ONE patient with pain issues. What can you offer that patient from this presentation to help address their pain?

Remember, you offer your knowledge and skills as a gift, but the patient makes the final decision.

Never* lose sight of the fact that the patient is the HEAD of the wound management team and their goals differ from yours – *it is their body, their choice

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