

# Preventing and Managing Wound Infections



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# Faculty Disclosures

**I have the following relevant financial relationship with a commercial interest:**

**I am employed as the Clinical Research, Education, and Charity Liaison  
for Ferris Mfg. Corp. (makers of PolyMem® dressings)**

**I am also an Independent Researcher improving health in developing countries**

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# Educational Objectives:

Upon completion of this learning activity, participants should be able to:

1. Distinguish between high bioburden, inflammation, and infection.
2. Identify at least one wound management protocol that recent research shows actually increases the risk of infection
3. Summarize current best practices for wound management protocols





# Acute Wounds Are Problems Everywhere





# Wounds Due to Chronic Illnesses



[101, 102]

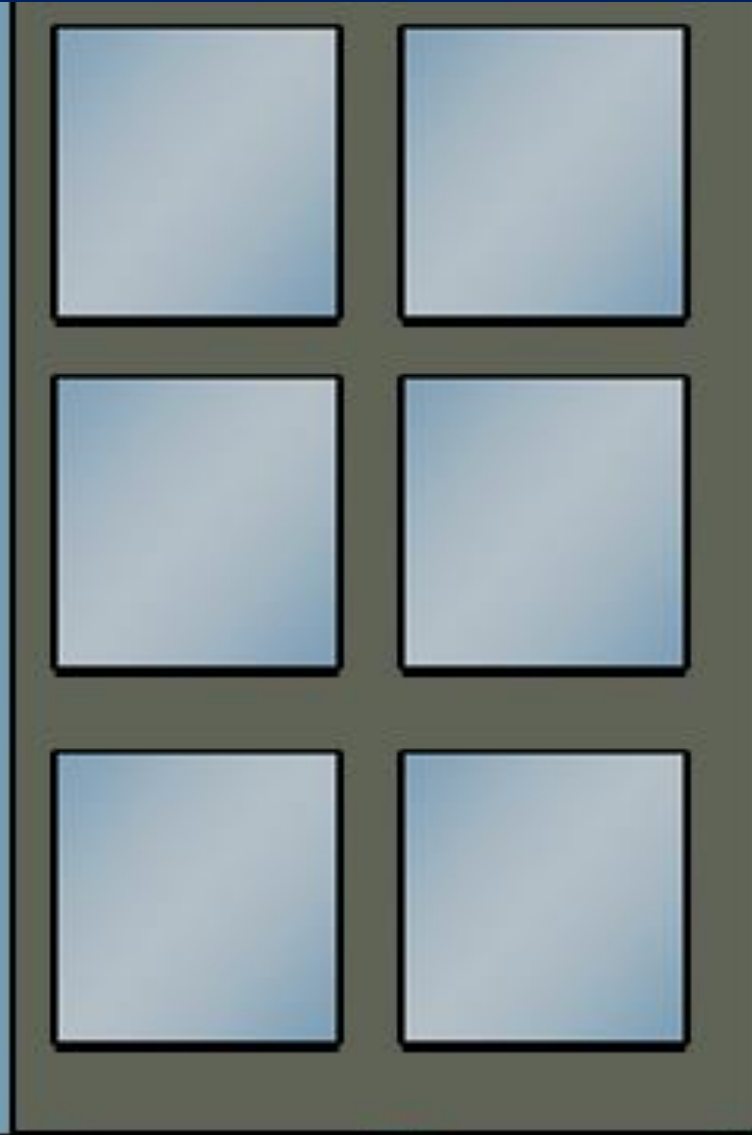
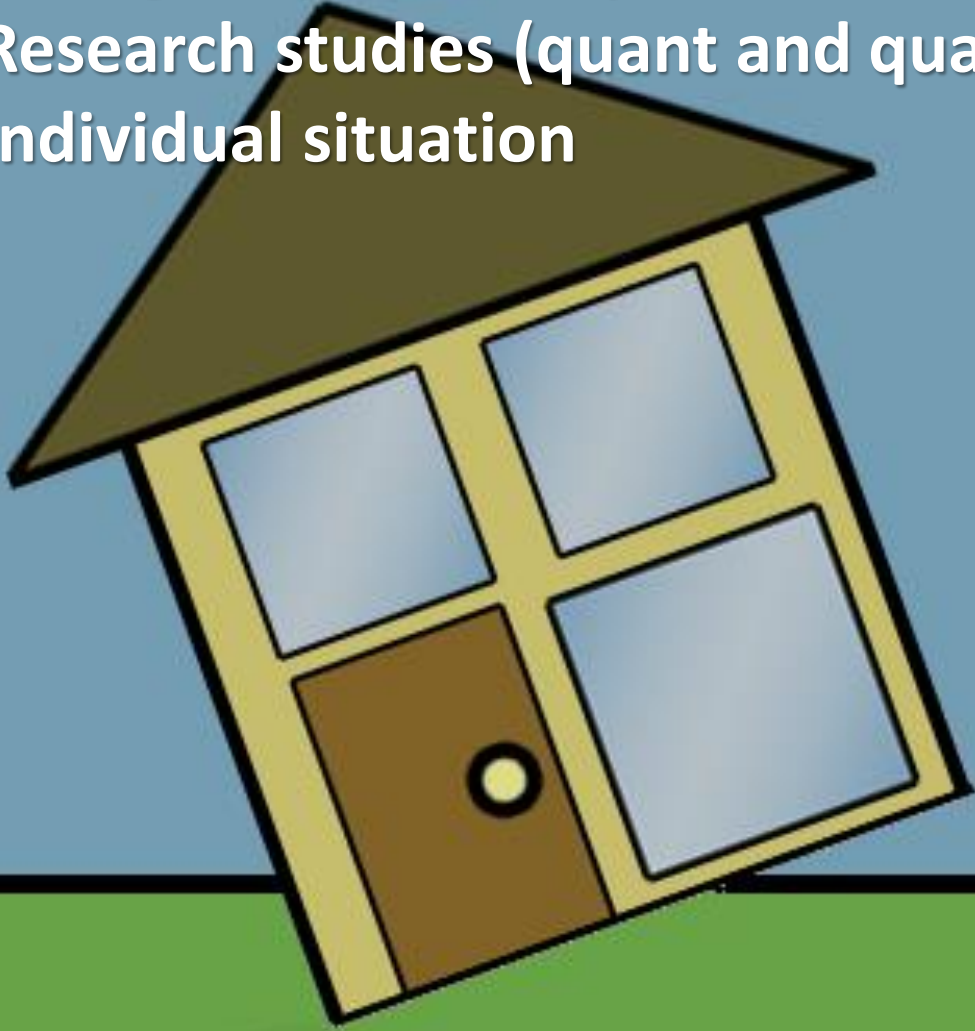


# Aftermath of GSWs and Fights



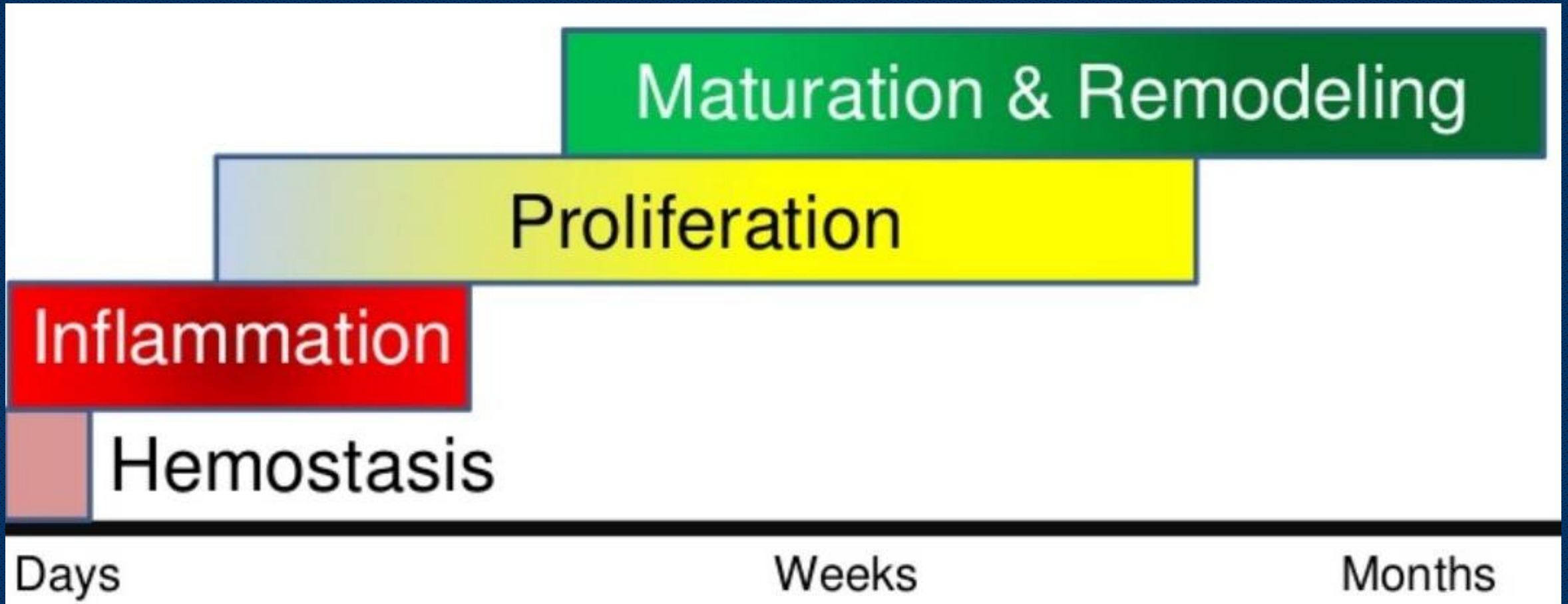
## Evidence:

- ◆ Biological plausibility
- ◆ Research studies (quant and qual)
- ◆ Individual situation





# Stages of Wound Healing



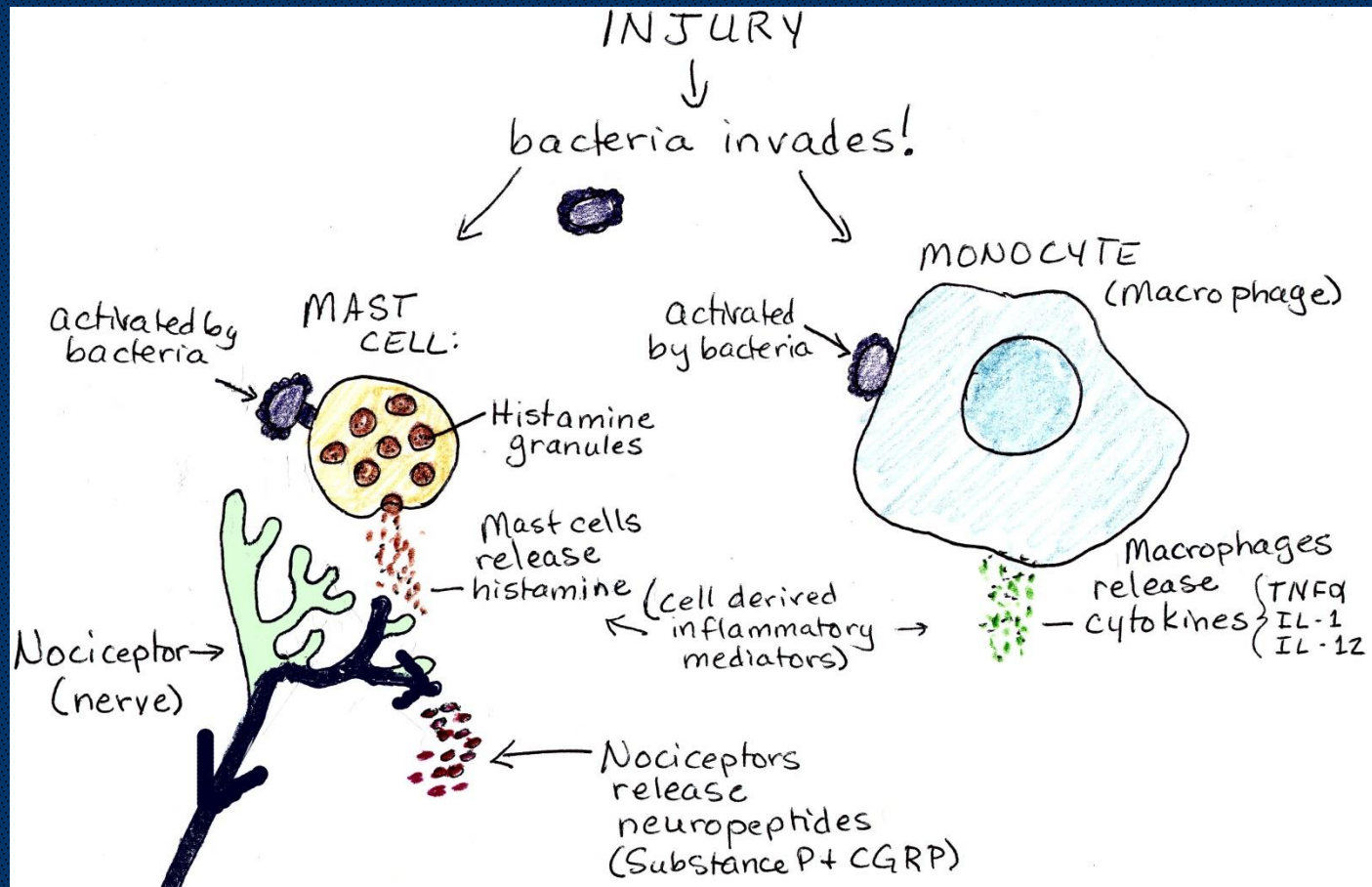
# Stages of Wound Healing: Hemostasis

- ◆ Stop bleeding!
- ◆ Communication cells (cytokines) recruit
- ◆ Preparation for cleanup





# Stages of Wound Healing: Inflammation



Goal: Prevent sepsis by:

- ♦ walling off area

- ♦ cleaning wound

Damaged cells release chemicals → inflammation

Central nervous system enhances inflammation

# Stages of Wound Healing: Inflammation

Pain, heat, redness, swelling, increased exudate, immobility  
*(even without infection!)*

White blood cells:

- ◆ Recycle debris
- ◆ Search and destroy bacteria
- ◆ Recruit growth factors
- ◆ Recruit cytokines

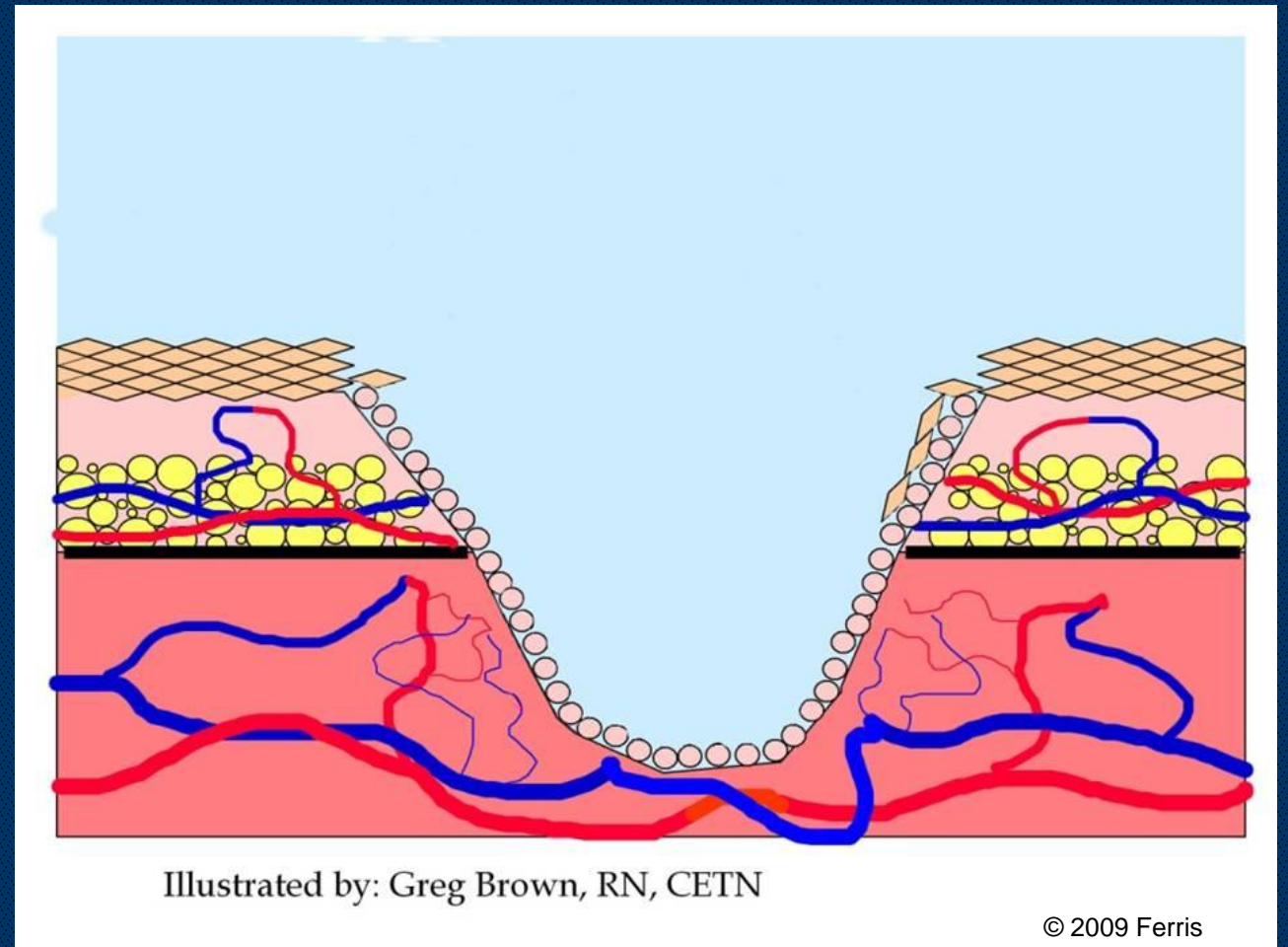




# Stages of Wound Healing: Proliferation

- ◆ Fibroblasts migrate
- ◆ Angiogenesis
- ◆ Contraction
- ◆ Granulation
- ◆ Epithelialization

[youtube.com/watch?v=Z8Zj6n\\_iH3Q](https://youtube.com/watch?v=Z8Zj6n_iH3Q)



# Moist Wound Healing

- ◆ Autolytic debridement cleans wounds
- ◆ Neutrophils migrate best with ideal moisture (no dead space)
- ◆ The complement system functions best under occlusion
- ◆ Semi-occlusive dressings promote angiogenesis (hypoxia at the surface)
- ◆ Moist dressings promote the release of growth factors (doubles healing rates)
- ◆ Occlusion decreases pain (pain increases infection risk)

[6a&b, 8, 17, 41-45, 69]





# Stages of Wound Healing: Proliferation

## Requirements:

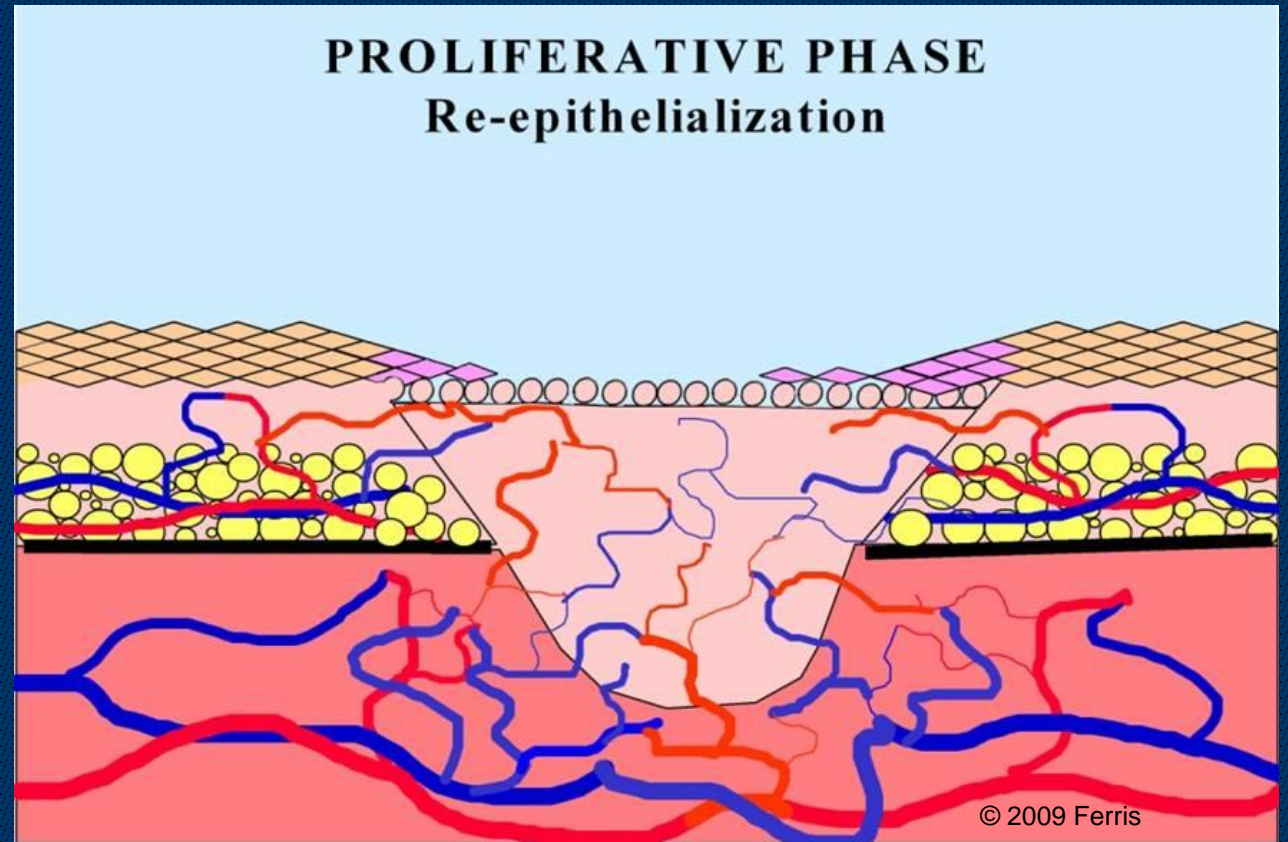
- ◆ Appropriate moisture
- ◆ Nourishment
- ◆ Enzymes & growth factors
- ◆ Adequate warmth
- ◆ Open Edges



# Keeping the wound in the Proliferation Stage

Need to not have:

- ◆ Dirt or debris
- ◆ Infection
- ◆ Desiccation (drying)
- ◆ Pressure/Repeat injury
- ◆ Poor perfusion/nutrition
- ◆ Maceration
- ◆ Cooling





# Stages of Wound Healing: Maturation (Remodeling)

“Closed”

- ◆ Enzymes
- ◆ Collagen → strength
- ◆ Smoother, flatter
- ◆ Final scar



# Uncontrolled Inflammation → Chronic Wounds

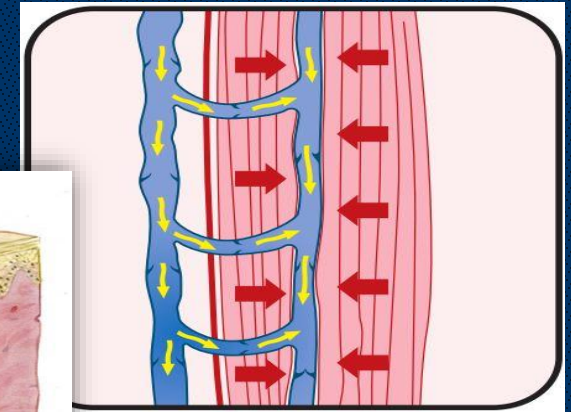
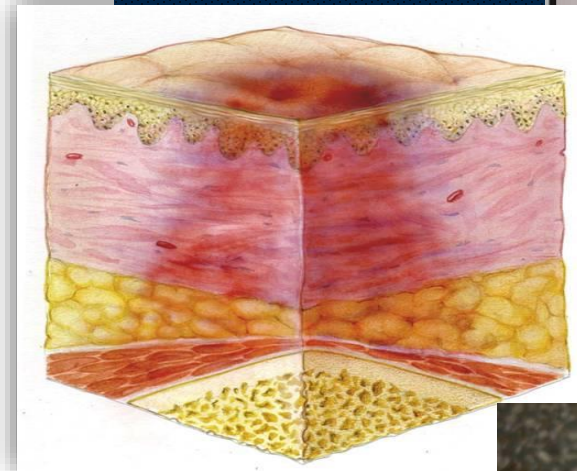
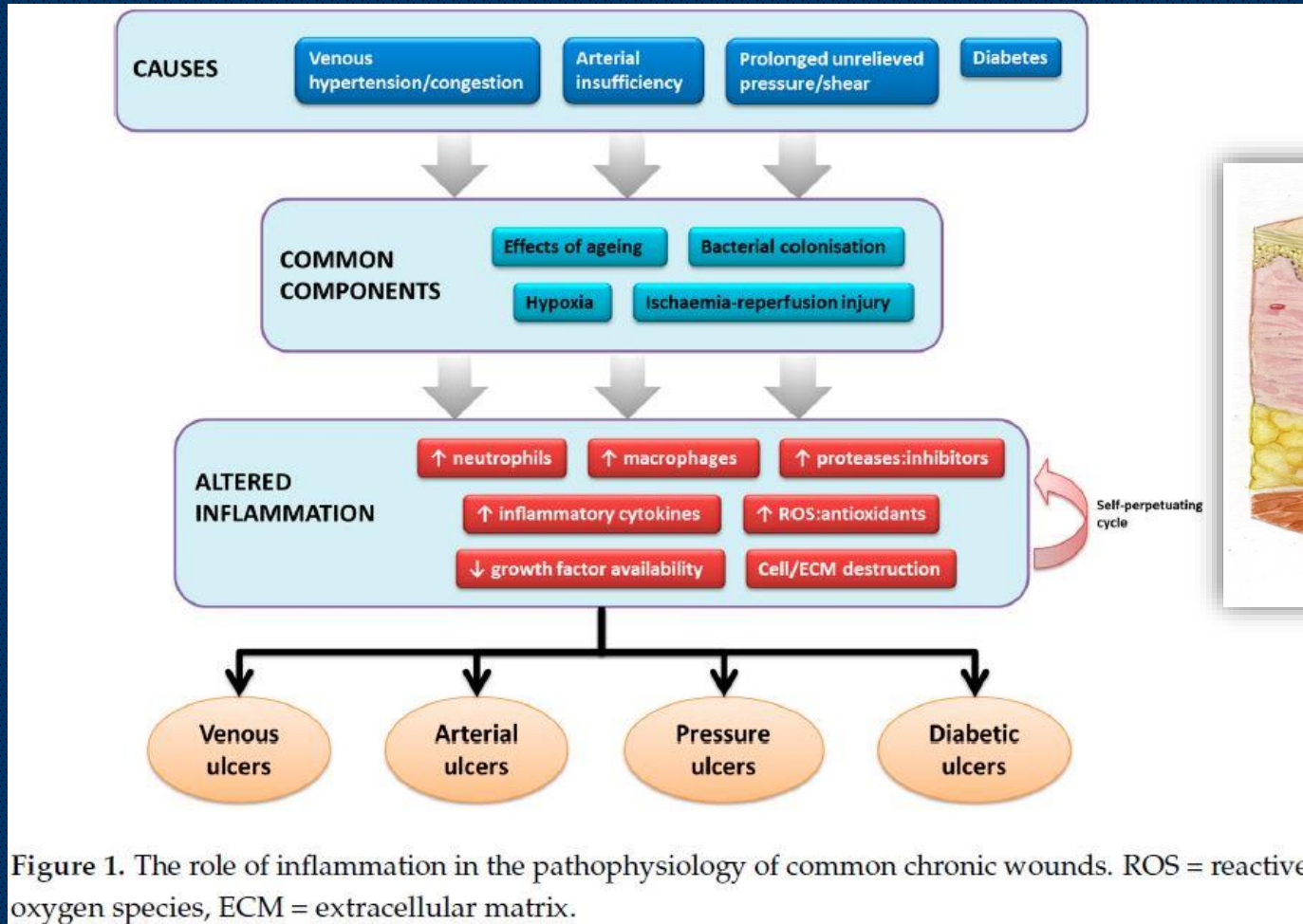


Figure 1. The role of inflammation in the pathophysiology of common chronic wounds. ROS = reactive oxygen species, ECM = extracellular matrix.



# Objective 1:

Distinguish between:

- ◆ High bioburden
- ◆ Inflammation, and
- ◆ Infection



# High Bioburden $\neq$ Infection!

- ◆ Bacteria in large numbers ( $>10^5$ , even  $>10^7$ ) don't always slow healing (7,9,10,11,71)
- ◆ What are the bacteria doing? Invasive? Commensal? Synergistic? (6a,6b,7,8)
- ◆ Highly virulent bacteria (e.g., Strep) in moderate numbers ( $>10^3$ ) (7,14)
- ◆ More than four species in high numbers – marker for slow healing (7)
- ◆ Quantitative swabs (Levine Method) OR biopsies *when symptomatic* (3, 13, 14)
- ◆ Biofilms & artificial conditions make culturing wounds unreliable (10, 12)

“The germ is nothing. It is the terrain in which it is found...” – Pasteur, 1860 (12)

[3, 6a-14, 71, 96, 97] **Infection is a *clinical* diagnosis**



# Inflammation $\neq$ Infection!

- ◆ Inflammation: Redness, heat, edema, pain, loss of function
- ◆ Moderate inflammation is adaptive: cleans, protects, recruits
- ◆ Excess inflammation (edema, pain) predisposes to infection
- ◆ Slough and callus are results of inflammation, not infection
- ◆ Inflammation is blunted in immunosuppressed patients

Slough, indicating inflammation, not necessarily infection →



# Infection = Micro-organisms Overwhelming Host

Increasing, not diminishing, inflammation, and/or (any of these):

- ◆ Darker exudate
- ◆ Thicker exudate
- ◆ Strong or foul odor
- ◆ Slowed or stalled healing
- ◆ Lymphangitis, lymphadenopathy
- ◆ Increasing wound size
- ◆ Crepitus

Like a stagnant pond

[14-17]



Photo by Colin Smith (Creative Commons)



# Kill or wipe away all the microbes?

- ◆ Alexander Fleming, in vivo & in vitro in WW1
- ◆ Rodeheaver and many others in the 1970s - 80s
- ◆ The FLOW Investigators, open fractures in 2015

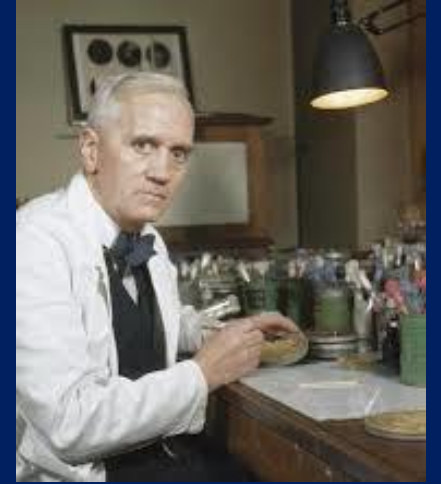


Photo TR1468, Imperial War Museum

All led to the exact same findings:

Antiseptics ***increased***  
wound infections because they

- 1) kill human tissue
- 2) disable the immune cells

[4, 18, 28, 39]



Photo from Wiki Commons

# Balance the Ecosystem

“...the medical conservative stands in awe of the human body.”

– Mandrola, et al. 2019

**WE** (health care professionals)  
**DO NOT HEAL WOUNDS.  
EVER.**

Only the patient's own body  
can heal the wound.

We remove barriers and  
provide supports.

**Don't kill the HUMAN.**

[12, 72-76, 86]

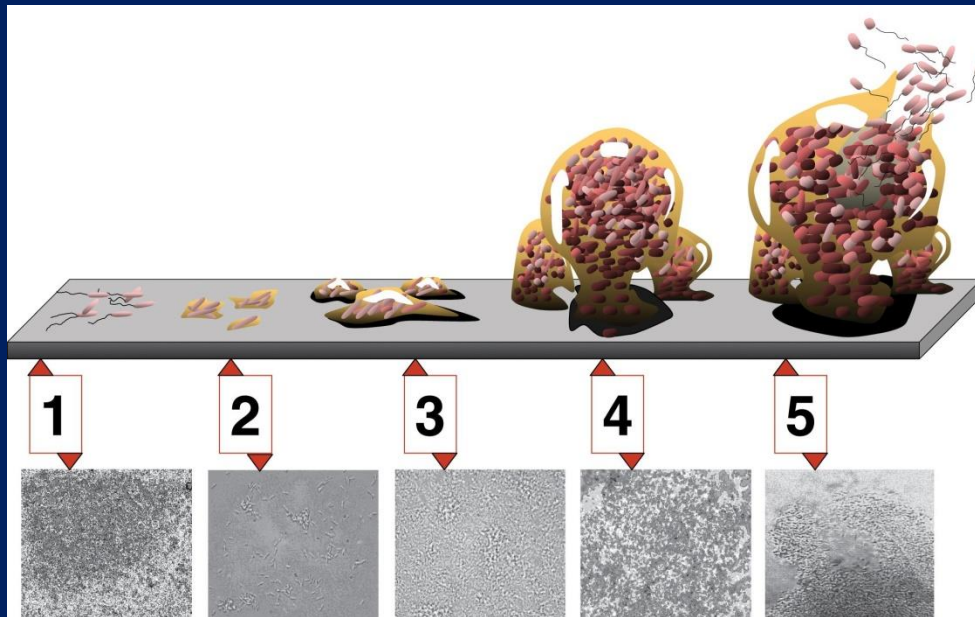


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# What about Biofilms?

Biofilms behave completely differently when the host's phagocytes are present



By D. Davis [CC BY 2.5 (<https://creativecommons.org/licenses/by/2.5>)]

Impressive growth: “mushroom-shaped”

*P. aeruginosa* biofilm on a petri dish

[4, 77-80, 86]

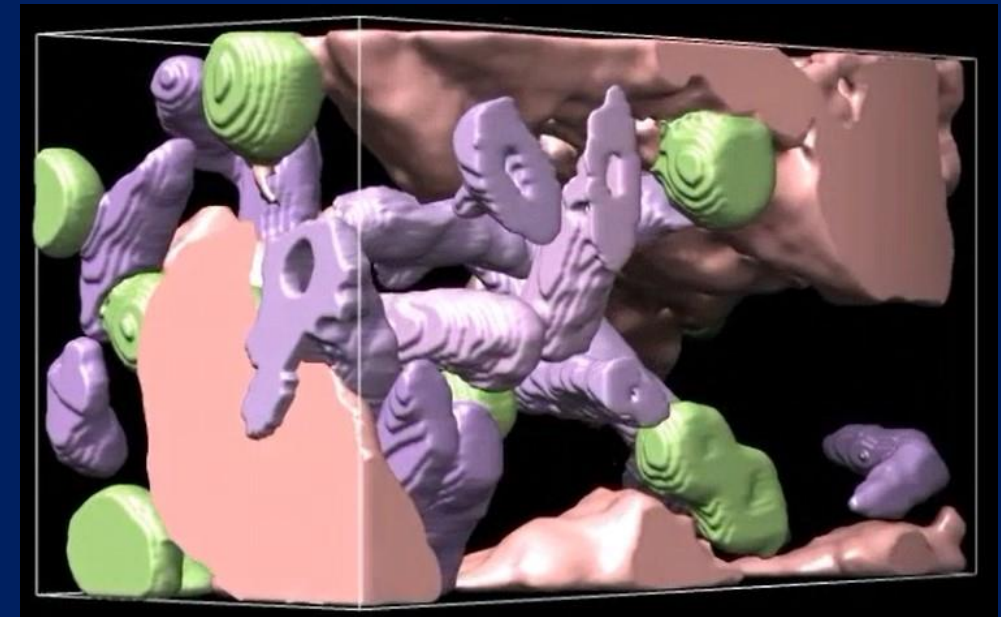


Image from Dr. Chandan Sen, used with permission

Phagocytes destroying a mature biofilm  
(*P. aeruginosa* and *A. baumannii*)

# Objective 2

Identify at least one  
wound management protocol  
that recent research shows  
actually increases  
the risk of infection

# Practices that Increase Infection Risk

## 1. Using antiseptics in open wounds. (Almost) Ever.

- ◆ Cannot kill every microbe
  - ◆ Are quickly deactivated
  - ◆ Creates a layer of dead tissue
  - ◆ Impairs leukocyte function
  - ◆ Increases infection rates vs saline
- Hypochlorous acid and/or  
conventional silver? Also toxic!

Note: This is NOT an open wound →



This IS →

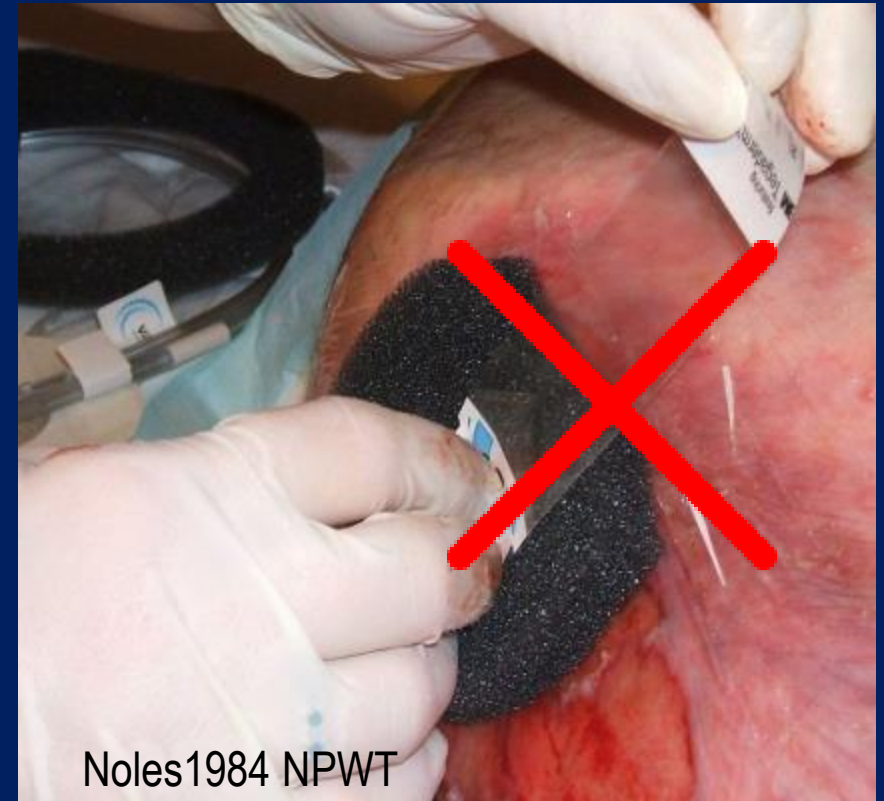




# Practices that Increase Infection Risk

## 2. Using conventional negative pressure wound therapy (NPWT)

- ◆ Compared with what?
  - Saline-soaked gauze!!!
- ◆ Pain, cortisol, stress response
- ◆ Dramatic protein losses (WBCs?)
- ◆ Reviews of studies show
  - ◆ Increased infection rates
  - ◆ Increase in costs
  - ◆ Decrease in quality of life
  - ◆ No increase in healing rates



# Practices that Increase Infection Risk

## 3. Using *high pressure* irrigation on wounds (> 15 psi)

- ◆ *Appears* to effectively debride
- ◆ Drives microbes into tissue  
(increases deep infection rate)
- ◆ Damages bone, delays healing
- ◆ Overall, infection rates are higher

**Trust the patient's body!**



Do NOT use high pressure!

# Practices that Increase Infection Risk

4. ALL forms of mechanical debridement (wet-to-dry, whirlpool, *Scrubbing* the wound bed, even with a soft sponge)

- ◆ Wounds appear cleaner, however,
- ◆ Tears cell membranes; bacteria enter
- ◆ Pushes microbes deeper into crevices
- ◆ Pain leads to stress response
- ◆ Higher infection rates with scrubbing  
(All mechanical debridement)

Serial (e.g., weekly) sharp debridement???

Also NO improvement in healing

[3, 4, 15, 39, 40, 56]





# Practices that Increase Infection Risk

## 5. Using non-occlusive dressings or “open to air”

- ◆ Bacteria can easily penetrate many layers of gauze
- ◆ Infection rates are > twice as high with dry wounds
- ◆ Cells die in dry wound beds (necrotic tissue leads to infection)
- ◆ Wet-to-dry is especially traumatic – soak if adhered



## 6. Failure to Address Edema

- ◆ Edema is a major precipitator of soft tissue infection – pooled fluid
- ◆ Edema leads to circulatory compromise → hampers the immune response
- ◆ Edema impairs cell migration from wound edges, slowing wound closure
- ◆ Edema is a sign of inflammation – try to address the cause (venous disease?)



(**How** to control edema is in the best practices section)

# Objective 3

Summarize  
current best practices  
for  
wound management  
protocols



# What *should* we do instead?

## 1. Low pressure irrigation with *copious* quantities of:

- ◆ Saline (unless pseudomonas)
- ◆ Drinkable water, or
- ◆ A nontoxic *nonionic* surfactant
- ◆ Body temperature
- ◆ Goal is 4 – 15 psi, turbulent flow
- ◆ May require 3 liters+ for major trauma
- ◆ Irrigate before and after initial sharp debridement



Preferred irrigation technique

**No need to kill the microbes – just remove them**

# Initial Sharp Debridement (NOT serial sharp debridement)

## 2. Initial sharp debridement – spare all viable skin & tissue

- ◆ Sharp steel → fewer infections than tearing
  - ◆ Cut just enough to allow irrigation in all cavities
  - ◆ Remove clearly nonviable tissue (some will rehydrate)
  - ◆ Trust autolytic debridement to complete the task
- ◆ Sharp debridement is *essential* for closed abscesses



# Best Practices for Reducing Infections

## 3. Use moisture-retentive, conforming dressings

- ◆ Decreases overall infection rates: >100 human studies by 1990
- ◆ Maintains a moist warm wound environment for new cells to grow
- ◆ Supports autolytic debridement
- ◆ Seals completely against pathogens
- ◆ Decreases pain (which ↓s stress response)
  - ◆ Occlusion alone decreases pain
  - ◆ PMDs directly alter the nociceptor response
- ◆ Increases healing rates (no wound, no wound infection)



[3, 6, 8, 15, 17, 19, 42-44, 46, 47, 89]



# Best Practices for Reducing Infections

## 4. Address Edema (↑ lymphatic drainage & circulation)

- ◆ Compression and elevation for extremity wounds (walking is 2<sup>nd</sup> best)
- ◆ NPWT with saline instillation – promising in high drainage wounds? Maybe...
  - ◆ NO antiseptics!!!
- ◆ Polymeric membrane dressings
  - ◆ Gently pull fluid from the body into the wound bed (3mm Hg pressure)
  - ◆ Subdue, focus inflammation
  - ◆ Dramatic decrease in swelling
- ◆ Honey dressings
  - ◆ Mild osmotic pull

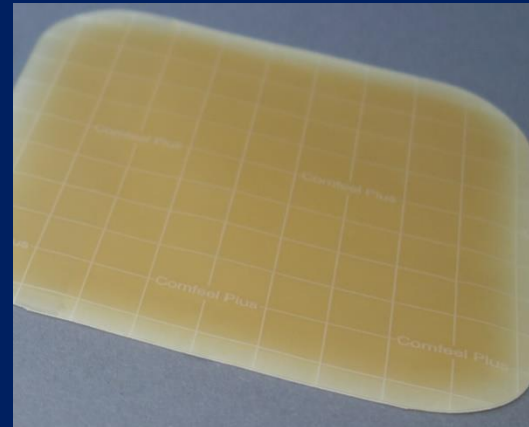


Photo from James Heilman, MD WikiCommons

# Best Practices for Reducing Infections

## 5. Use dressings which fight infection while in place

- ◆ Polymeric membrane dressings: cleanse
- ◆ Bacteria binding dressings (???)
- ◆ Hydrocolloids: low pH
- ◆ Honey-containing dressings: low pH
- ◆ Moisture promotes autolytic debridement – even plastic wrap or petrolatum
- ◆ Dressings with locked-in antimicrobials



# Does autolytic debridement really work?

Tropical environment, VERY basic dressings: THREE DAYS



Evening: 22 Dec



Morning: 23 Dec



Evening 25 Dec

[46-48]



# What about immunosuppressed patients?

Diabetes (or Hepatitis, HIV+, Chemotherapy)?

Outcomes (and guidelines) are unchanged: sharp debridement, then moist dressings.

(HIV+ on ART: CD4 > 100;  
Others, ANC > 100 - 500)  
Watch for fungal infections



Initial, before and after debridement



[91-95]



6.5 wks of moist, non-toxic treatment (closed at 8 wks) (no offloading available)



# Best Practices for Reducing Infections

## 6. Sparing (limited) Use of Antimicrobials

- ◆ Antimicrobial dressings **are** useful in limited circumstances
  - ◆ Limit to 2 weeks for critical colonization, local, or deep wound infection
  - ◆ Use only dressings with **locked-in** antimicrobial (less toxicity)
- ◆ Antibiotic or antiseptic ointments? Sensitization, resistance...
  - ◆ Dilute antimicrobial wash if circulation is severely compromised (scars)
  - ◆ In truly immunosuppressed patients, with recalcitrant biofilms
- ◆ Add systemic antibiotics for **deep tissue** infections
  - ◆ Cellulitis, Osteomyelitis, Sepsis – evidence-based recommendations next slide
  - ◆ Highly virulent microbes: Strep A and Strep pyogenes

[19, 26, 59-61, 97]

# Managing Deep Tissue Infections: CDC.gov

Oral antibiotics often as effective as IV

Older antibiotics often as effective as newer

- ◆ No antibiotics for simple abscesses – just drain and irrigate well
- ◆ Osteomyelitis: either flucloxacillin and sodium fusidate, or ciprofloxacin and clindamycin, for 5 weeks
- ◆ Bites (human or animal): amoxicillin/clavulanate for 5 – 10 days
- ◆ CA-MRSA: oral TMP/SMX, clindamycin, linezolid, or teicoplanin, or a tetracycline; or IV vancomycin
- ◆ Beta-hemolytic strep (with coverage for possible CA-MRSA): clindamycin or linezolid alone; or TMP/SMX or a tetracycline (doxycycline or minocycline) plus amoxicillin

(NOTE: Teicoplanin and polymyxin B neutralize endotoxins)

Triple-strength saline soaks BID to eradicate fungal infections



# Pseudomonas A. in Chronic Wounds

If pseudomonas is overwhelming the host: 1% white vinegar

- ◆ pseudomonas prefers slightly salty environment (saline rinses)
- ◆ pseudomonas does not tolerate acidic environment (vinegar restores low pH)
- ◆ Twice daily until green (and distinctive odor) is gone for two days



1 July



3 July



5 July



12 July



15 July

Rarely, a pseudomonas biofilm is best addressed with dilute white vinegar (acetic acid diluted in water 5:1) – BID for 3 – 5 days

[82, 83, 108, 109]



MRSA acquired in a jail, many admissions for IV antibiotics before PMDs



Community-acquired MRSA, recurrent. Oral antibiotics, no surgical intervention. Two elbow wounds. Began using PMD rope. Third (cheek) was last.

## Recurrent MRSA Infections



Officer in juvenile detention with recurrent MRSA ulcers requiring I&D and packing. Debilitating pain with conventional packing of leg MRSA ulcer. NO pain with PMDs. PMD rope led to quick resolution of cheek MRSA ulcer.

# First Aid to Prevent Wound Infections

Goal is to prevent more DAMAGE

- ◆ Stop bleeding: direct pressure, wide tourniquet - only if needed
- ◆ Irrigate with tap water to cool and clean
  - ◆ For burns, cool water at **LEAST 20 min**
  - ◆ Other wounds, body temperature
  - ◆ Low pressure, high volume (until clear)
- ◆ Dress to maintain moisture & warmth
  - ◆ Plastic food wrap (clean, nonadherent)
  - ◆ Can improvise with inside of clean plastic bag
- ◆ Immobilize/Splint if needed
- ◆ Compress/elevate if trip to facility is long



By Jenny Downing (glass half-full) via Wikimedia Commons

[47, 57, 62, 68]



# Initial Wound Management: Surgical Preps

- ◆ Presurgical showering: soap & water?
- ◆ Clean off visible dirt first
- ◆ No shaving hair: Clip
- ◆ Scrub (don't just paint) sites three times
- ◆ Use at least two different solutions
- ◆ Saline performed as well as antiseptics
- ◆ Allow povidone-iodine time to dry
- ◆ Use at recommended concentrations
- ◆ Final scrub solution can remain (esp if saline)







# Summary

For ALL wounds:

- ◆ Very conservative initial sharp debridement – if feasible
- ◆ Irrigate with NON-TOXIC fluids at low pressure
- ◆ Copious irrigation until the resultant fluid runs clear
- ◆ Dress for success: use a conforming dressing that retains moisture
- ◆ Address edema (compression, certain dressings, elevation, ...)
- ◆ Add systemic antibiotics IFF there are signs of deep infection
- ◆ Trust the patient's body to heal the wound



# References

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1. Szeto B, Kaba F, Herzig CTA, Befus M, Lowy FD, Miko BA, et al. Drug Use Is Associated With Purulent Skin and Soft Tissue Infections in a Large Urban Jail: 2011–2015. *Open Forum Infect Dis* [Internet]. 2017 Jul 1 [cited 2019 Aug 19];4(3). Available from: <https://academic.oup.com/ofid/article/4/3/ofx135/4063253>
2. Jackson KA. Invasive Methicillin-Resistant *Staphylococcus aureus* Infections Among Persons Who Inject Drugs — Six Sites, 2005–2016. *MMWR Morb Mortal Wkly Rep* [Internet]. 2018 [cited 2019 Sep 13];67. Available from: <https://www.cdc.gov/mmwr/volumes/67/wr/mm6722a2.htm>
- 3a. <https://www.bop.gov/resources/pdfs/wounds.pdf>
- 3b. Pirie W. On the use of carbolic acid in burns. *Lancet*. 1867; ii: 575.
4. Fleming A. The action of chemical and physiological antiseptics in a septic wound. *Br J Surg*. 1919;7(25):99-129. doi:10.1002/bjs.1800072508.
5. S. Hiroyasu, Z. T. Colburn, J. C. R. Jones. A hemidesmosomal protein regulates actin dynamics and traction forces in motile keratinocytes. *The FASEB Journal*, 2016; 30 (6): 2298 DOI: 10.1096/fj.201500160R
- 6a. Hutchinson JJ, McGuckin M. Occlusive dressings: a microbiologic and clinical review. *Am J Infect Control*. 1990;18(4):257-268.
- 6b. Hutchinson JJ, Lawrence JC. Wound infection under occlusive dressings. *J Hosp Infect*. 1991;17(2):83-94.
7. Tuttle MS. Association Between Microbial Bioburden and Healing Outcomes in Venous Leg Ulcers: A Review of the Evidence. *Advances in Wound Care*. 2014;4(1):1-11. doi:10.1089/wound.2014.0535.
8. Eaglstein WH. Effect of occlusive dressings on wound healing. *Clin Dermatol*. 1984;2(3):107-111.
9. Nunan R, Harding KG, Martin P. Clinical challenges of chronic wounds: searching for an optimal animal model to recapitulate their complexity. *Disease Models & Mechanisms*. 2014;7(11):1205-1213. doi:10.1242/dmm.016782.
10. Saye DE. Recurring and antimicrobial-resistant infections: considering the potential role of biofilms in clinical practice. *Ostomy Wound Manage*. 2007;53(4):46-48, 50, 52 passim.
11. Handfield-Jones SE, Grattan CE, Simpson RA, Kennedy CT. Comparison of a hydrocolloid dressing and paraffin gauze in the treatment of venous ulcers. *Br J Dermatol*. 1988;118(3):425-427.
12. Thomson PD, Smith DJ. What is infection? *Am J Surg*. 1994;167(1A):7S-10S; discussion 10S-11S.
13. Rondas AALM, Schols JMGA, Halfens RJG, Stobberingh EE. Swab versus biopsy for the diagnosis of chronic infected wounds. *Adv Skin Wound Care*. 2013;26(5):211-219. doi:10.1097/01.ASW.0000428984.58483.aa.
14. Gardner SE, Frantz RA. Wound bioburden and infection-related complications in diabetic foot ulcers. *Biol Res Nurs*. 2008;10(1):44-53. doi:10.1177/1099800408319056.
15. Boulton AJ, Meneses P, Ennis WJ. Diabetic foot ulcers: A framework for prevention and care. *Wound Repair and Regeneration*. 1999;7(1):7-16. doi:10.1046/j.1524-475x.1999.00007.x.

# References

16. Cutting KF, White R. Defined and refined: criteria for identifying wound infection revisited. *Br J Community Nurs*. 2004;9(3):S6-15. doi:10.12968/bjcn.2004.9.Sup1.12495.
17. Field FK, Kerstein MD. Overview of wound healing in a moist environment. *Am J Surg*. 1994 Jan;167(1A):2S–6S.
18. Rodeheaver G. Controversies in topical wound management. *Wounds: A Compendium of clinical research and practice*. 1989 Apr:19-27.
19. Cho CY, Lo JS. Dressing the part. *Dermatol Clin*. 1998;16(1):25-47.
20. Armstrong DG et al. 2015. Expert Recommendations for the Use of Hypochlorous Solution: Science and Clinical Application | WOUNDS. <http://www.woundsresearch.com/content/expert-recommendations-use-hypochlorous-solution-science-and-clinical-application>. Accessed September 1, 2016.
21. Wilson JR, Mills JG, Prather ID, Dimitrijevic SD. A toxicity index of skin and wound cleansers used on in vitro fibroblasts and keratinocytes. *Adv Skin Wound Care*. 2005;18(7):373-378.
22. Rani SA, Hoon R, Najafi RR, Khosrovi B, Wang L, Debabov D. The in vitro antimicrobial activity of wound and skin cleansers at nontoxic concentrations. *Adv Skin Wound Care*. 2014;27(2):65-69. doi:10.1097/01.ASW.0000443255.73875.a3.
23. Owens BD, White DW, Wenke JC. Comparison of irrigation solutions and devices in a contaminated musculoskeletal wound survival model. *J Bone Joint Surg Am*. 2009;91(1):92-98. doi:10.2106/JBJS.G.01566.
24. Menton DN, Brown M. The effects of commercial wound cleansers on cutaneous wound healing in guinea pigs. *Wounds*. 1994;6(1):21-27.
25. Burd A, Kwok CH, Hung SC, et al. A comparative study of the cytotoxicity of silver-based dressings in monolayer cell, tissue explant, and animal models. *Wound Repair Regen*. 2007;15(1):94-104. doi:10.1111/j.1524-475X.2006.00190.x.
26. Bolton LL. Evidence Corner: Silver Dressings on Partial-Thickness Burns. *Wounds*. 2013;25(12):355-357.
27. Paddle-Ledinek JE, Nasa Z, Cleland HJ. Effect of different wound dressings on cell viability and proliferation. *Plast Reconstr Surg*. 2006;117(7 Suppl):110S-118S; discussion 119S-120S. doi:10.1097/01.prs.0000225439.39352.ce.
28. FLOW Investigators, Bhandari M, Jeray KJ, et al. A Trial of Wound Irrigation in the Initial Management of Open Fracture Wounds. *N Engl J Med*. 2015;373(27):2629-2641. doi:10.1056/NEJMoa1508502.
29. Patmo ASP, Krijnen P, Tuinebreijer WE, Breederveld RS. The Effect of Vacuum-Assisted Closure on the Bacterial Load and Type of Bacteria: A Systematic Review. *Adv Wound Care (New Rochelle)*. 2014;3(5):383-389. doi:10.1089/wound.2013.0510. rsmb0mbande5 rsmb0mbande5
30. Wade C, Wolf SE, Hourigan L, Linfoot JA, et al. Loss of protein, immunoglobulins, and electrolytes in exudates from negative pressure wound therapy. *Nutr Clin Pract*. 2010;25(5):510-516. doi:10.1177/0884533610379852.

# References

31. Skrinjar E, Duschek N, Bayer GS, Assadian O, Koulas S, Hirsch K, et al. Randomized controlled trial comparing the combination of a polymeric membrane dressing plus negative pressure wound therapy against negative pressure wound therapy alone: The WICVAC study. *Wound Rep and Reg*. 2016 Jul 1;n/a-n/a.
32. Li Z, Yu A. Complications of negative pressure wound therapy: a mini review. *Wound Repair Regen*. 2014;22(4):457-461. doi:10.1111/wrr.12190.
33. Fagerdahl A-M, Boström L, Ottosson C, Ulfvarson J. Patients' experience of advanced wound treatment-a qualitative study. *Wounds*. 2013;25(8):205-211.
34. Ottosen B, Pedersen BD. Patients' experiences of NPWT in an outpatient setting in Denmark. *J Wound Care*. 2013;22(4):197-198, 200-202, 204-206. doi:10.12968/jowc.2013.22.4.197.
35. Lambert KV, Hayes P, McCarthy M. Vacuum assisted closure: a review of development and current applications. *Eur J Vasc Endovasc Surg*. 2005;29(3):219-226. doi:10.1016/j.ejvs.2004.12.017.
36. Harries RL, Bosanquet DC, Harding KG. Wound bed preparation: TIME for an update. *Int Wound J*. 2016;13(S3):8-14. doi:10.1111/iwj.12662.
37. Hannigan GD, Pulos N, Grice EA, Mehta S. Current Concepts and Ongoing Research in the Prevention and Treatment of Open Fracture Infections. *Advances in Wound Care*. 2014;4(1):59-74. doi:10.1089/wound.2014.0531.
38. Gabriel A. Wound Irrigation: Overview, Preparation, Technique. April 2016. <http://emedicine.medscape.com/article/1895071-overview>. Accessed September 1, 2016.
39. Rodeheaver GT, Kurtz L, Kircher BJ, Edlich RF. Pluronic F-68: a promising new skin wound cleanser. *Ann Emerg Med*. 1980;9(11):572-576.
40. Bolton L. Serial Debridement Under Scrutiny. *Wounds* [Internet]. 2015 Aug;27(8):236–8. Available from: <http://www.woundsresearch.com/article/evidence-corner-serial-debridement-under-scrutiny>
41. Varghese MC, Balin AK, Carter DM, Caldwell D. Local environment of chronic wounds under synthetic dressings. *Arch Dermatol*. 1986;122(1):52-57.
42. Witkowski JA, Parish LC. Cutaneous ulcer therapy. *Int J Dermatol*. 1986;25(7):420-426.
43. Bloom H. â€œCELLOPHANE â€œDRESSING FOR SECOND-DEGREE BURNS. *The Lancet*. 1945 Nov 3;246(6375):559.
44. Mertz PM, Marshall DA, Eaglstein WH. Occlusive wound dressings to prevent bacterial invasion and wound infection. *Journal of the American Academy of Dermatology*. 1985;12(4):662-668. doi:10.1016/S0190-9622(85)70091-6.
45. Buchan IA, Andrews JK, Lang SM, Boorman JG, Harvey Kemble JV, Lamberty BGH. Clinical and laboratory investigation of the composition and properties of human skin wound exudate under semi-permeable dressings. *Burns*. 1981;7(5):326-334. doi:10.1016/0305-4179(81)90005-X.
46. Powers JG, Morton LM, Phillips TJ. Dressings for chronic wounds. *Dermatol Ther*. 2013;26(3):197-206. doi:10.1111/dth.12055.
47. Benskin LL. Polymeric Membrane Dressings for topical wound management of patients with infected wounds in a challenging environment: A protocol with 3 case examples. *Ostomy Wound Management*. 2016;62(6):42-62.



# References

48. Benskin LLL. A review of the literature informing affordable, available wound management choices for rural areas of tropical developing countries. *Ostomy Wound Manage*. 2013 Oct;59(10):20–41.
49. Kim PJ, Attinger CE, Steinberg JS, et al. The impact of negative-pressure wound therapy with instillation compared with standard negative-pressure wound therapy: a retrospective, historical, cohort, controlled study. *Plast Reconstr Surg*. 2014;133(3):709-716. doi:10.1097/01.prs.0000438060.46290.7a.
50. Brinkert D, Ali M, Naud M, Maire N, Trial C, Téot L. Negative pressure wound therapy with saline instillation: 131 patient case series. *Int Wound J*. 2013 Dec;10 Suppl 1:56–60.
51. Rahman S, Shokri A. Total Knee Arthroplasty (TKA) Infections Eliminated and Rehabilitation Improved Using Polymeric Membrane Dressing Circumferential Wrap Technique: 120 Patients at 12-month Follow-up. Poster presented at European Wound Management Association (EWMA) Copenhagen, Denmark, May 2013.
52. Feliciano, Castillo. Blast injuries successfully managed with polymeric membrane dressing. Poster presented at Philippine Wound Care Society (PWCS), Manila, Philippines, Oct 22-23, 2015.
53. Benskin LLL. PolyMem(®) Wic(®) Silver(®) Rope: A Multifunctional Dressing for Decreasing Pain, Swelling, and Inflammation. *Adv Wound Care (New Rochelle)*. 2012;1(1):44-47. doi:10.1089/wound.2011.0285.
54. Pereira RF, Bártolo PJ. Traditional Therapies for Skin Wound Healing. *Adv Wound Care (New Rochelle)*. 2016;5(5):208-229. doi:10.1089/wound.2013.0506.
55. Dabiri G, Damstetter E, Phillips T. Choosing a Wound Dressing Based on Common Wound Characteristics. *Advances in Wound Care*. 2014;5(1):32-41. doi:10.1089/wound.2014.0586.
56. Ovington LG. Hanging Wet-to-Dry Dressings Out to Dry. *Advances in Skin & Wound Care*. 2002 Apr;15(2):84–6.
57. Dawson, Lewis C, Boch R. Total Joint Replacement Surgical Site Infections Eliminated by Using Multifunctional Dressing. 900 Cases Report over 4 years. Poster presented at Australian College of Operating Room Nurses (ACORN) Perth, Australia, May 2010.
58. Genuino GAS, Baluyut-Angeles KV, Espiritu APT, Lapitan MCM, Buckley BS. Topical petrolatum gel alone versus topical silver sulfadiazine with standard gauze dressings for the treatment of superficial partial thickness burns in adults: a randomized controlled trial. *Burns*. 2014;40(7):1267-1273. doi:10.1016/j.burns.2014.07.024.
59. Beckett A, Tien H. What's new in operative trauma surgery in the last 10 years. *Curr Opin Crit Care*. 2013;19(6):599-604. doi:10.1097/MCC.0000000000000033.
60. Norman G, Dumville JC, Mohapatra DP, Owens GL, Crosbie EJ. Antibiotics and antiseptics for surgical wounds healing by secondary intention. *Cochrane Database Syst Rev*. 2016;3:CD011712. doi:10.1002/14651858.CD011712.pub2.
61. Storm-Versloot MN, Vos CG, Ubbink DT, Vermeulen H. Topical silver for preventing wound infection. *Cochrane Database Syst Rev*. 2010;(3):CD006478. doi:10.1002/14651858.CD006478.pub2.
62. Tactical Combat Casualty Care Guidelines. 9 February 2015 . <http://www.itstactical.com/medcom/tccc-medcom/cotccc-tactical-combat-casualty-care-guidelines-february-2015-update/>
63. Kamel C, McGahan L, Polisena J, Mierzwinski-Urban M, Embil JM. Preoperative skin antiseptic preparations for preventing surgical site infections: a systematic review. *Infect Control Hosp Epidemiol*. 2012;33(6):608-617. doi:10.1086/665723.

# References

64. Kalantar-Hormozi AJ, Davami B. No need for preoperative antiseptics in elective outpatient plastic surgical operations: a prospective study. *Plast Reconstr Surg*. 2005 Aug;116(2):529–31.
65. World Health Organization. Ten essential objectives for safe surgery: review of the evidence and recommendations: Objective 6, Subsection: Presurgical skin disinfection [Internet]. World Health Organization; 2009. Geneva. [cited 2016 Nov 29]. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK143246/>
66. Dumville JC, McFarlane E, Edwards P, Lipp A, Holmes A, Liu Z. Preoperative skin antiseptics for preventing surgical wound infections after clean surgery. In: *Cochrane Database of Systematic Reviews*. John Wiley & Sons, Ltd; 2015. <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003949.pub4/abstract>. Accessed August 31, 2016.
67. Pullar JM, Vissers MC, Winterbourn CC. Living with a killer: the effects of hypochlorous acid on mammalian cells. *IUBMB Life*. 2000 Nov;50(4–5):259–66.
68. Goodwin N. “Mixed messages” — Ongoing confusion with hydrogel dressings in burn 1st aid. Commentary on the trial report from Holbert et al. 2018/19. *Burns* [Internet]. 2019 Jul 25 [cited 2019 Sep 10]; Available from: <http://www.sciencedirect.com/science/article/pii/S0305417919304462>
69. Benskin LLL. Discovering the Current Wound Management Practices of Rural Africans [Internet]. 2013 [cited 2013 Aug 22]. Available from: <http://www.nursinglibrary.org/vhl/handle/10755/299522>
70. Zhao R, Liang H, Clarke E, Jackson C, Xue M. Inflammation in Chronic Wounds. *Int. J. Mol. Sci*. 2016;17:2085
71. Hansson C, Hoborn J, Möller A, Swanbeck G. The microbial flora in venous leg ulcers without clinical signs of infection. Repeated culture using a validated standardised microbiological technique. *Acta Derm Venereol*. 1995 Jan;75(1):24–30.
72. Lingaas E, Fagernes M. Development of a method to measure bacterial transfer from hands. *J Hosp Infect*. 2009 May;72(1):43–9.
73. Mandrola J, Cifu A, Prasad V, Foy A. The Case for Being a Medical Conservative. *The American Journal of Medicine* [Internet]. 2019 Aug 1 [cited 2019 Sep 11];132(8):900–1. Available from: [https://www.amjmed.com/article/S0002-9343\(19\)30167-6/abstract](https://www.amjmed.com/article/S0002-9343(19)30167-6/abstract)
74. Argenta A, Satish L, Gallo P, Liu F, Kathju S. Local Application of Probiotic Bacteria Prophylaxes against Sepsis and Death Resulting from Burn Wound Infection. *PLoS One* [Internet]. 2016 Oct 25 [cited 2019 Sep 13];11(10). Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5079594/>
75. Kao M-S, Huang S, Chang W-L, Hsieh M-F, Huang C-J, Gallo RL, et al. Microbiome precision editing: Using PEG as a selective fermentation initiator against methicillin-resistant *Staphylococcus aureus*. *Biotechnol J*. 2017 Apr;12(4).
76. Shu M, Wang Y, Yu J, Kuo S, Coda A, Jiang Y, et al. Fermentation of *Propionibacterium acnes*, a Commensal Bacterium in the Human Skin Microbiome, as Skin Probiotics against Methicillin-Resistant *Staphylococcus aureus*. *PLoS One* [Internet]. 2013 Feb 6 [cited 2019 Sep 25];8(2). Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3566139/>
77. Deng B, Barki KG, Ghartak S, Roy S, McComb DW, Sen CK. THREE-DIMENSIONAL STRUCTURE OF THE WOUND BIOFILM. Poster # presented at: Wound Healing Society section of the SAWC (Symposium on Advances of Wound Care); 2015 May 29; San Antonio, Texas.
78. Hansis M. Pathophysiology of infection--a theoretical approach. *Injury*. 1996;27 Suppl 3:SC5-8.
79. Johani K, Malone M, Jensen SO, Dickson HG, Gosbell IB, Hu H, et al. Evaluation of short exposure times of antimicrobial wound solutions against microbial biofilms: from in vitro to in vivo. *J Antimicrob Chemother*. 2018 01;73(2):

# References

80. Yeo CK, Vikhe YS, Li P, Guo Z, Greenberg P, Duan H, et al. Hydrogel Effects Rapid Biofilm Debridement with ex situ Contact-Kill to Eliminate Multidrug Resistant Bacteria in vivo. *ACS Appl Mater Interfaces* [Internet]. 2018 Jun 20 [cited 2019 Sep 9];10(24):20356–67. Available from: <https://doi.org/10.1021/acsami.8b06262>
81. Molan PC. The role of honey in the management of wounds. *J Wound Care*. 1999 Sep;8(8):415–8.
82. Madhusudhan VL. Efficacy of 1% acetic acid in the treatment of chronic wounds infected with *Pseudomonas aeruginosa*: prospective randomised controlled clinical trial. *Int Wound J*. 2016 Dec;13(6):1129–36.
83. Nagoba BS, Selkar SP, Wadher BJ, Gandhi RC. Acetic acid treatment of pseudomonal wound infections – A review. *Journal of Infection and Public Health*. 2013 Dec;6(6):410–5.
84. Rodeheaver G, Bellamy W, Kody M, Spatafora G, Fitton L, Leyden K, et al. Bactericidal Activity and Toxicity of Iodine-Containing Solutions in Wounds. *Arch Surg* [Internet]. 1982 Feb 1 [cited 2019 Sep 25];117(2):181–6. Available from: <https://jamanetwork-com.rsm.idm.oclc.org/journals/jamasurgery/fullarticle/588176>
85. Connell S. A two-part quality assurance project addressing infection rates of wounds sutured in the emergency department. *J Emerg Nurs*. 1991 Aug;17(4):212–4.
86. Johnson TR, Gómez BI, McIntyre MK, Dubick MA, Christy RJ, Nicholson SE, et al. The Cutaneous Microbiome and Wounds: New Molecular Targets to Promote Wound Healing. *Int J Mol Sci* [Internet]. 2018 Sep 11 [cited 2019 Sep 13];19(9). Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6164292/>
87. Bolton LL. Guest Editorial: Wound Infection: Myths and Microbes. *Wound Management & Prevention* [Internet]. 2018 Aug;64(8):6,8. Available from: <https://www.o-wm.com/article/guest-editorial-wound-infection-myths-and-microbes>
88. Bolton L. Operational definition of moist wound healing. *J Wound Ostomy Continence Nurs*. 2007 Feb;34(1):23–9.
89. Fife CE, Farrow W, Hebert AA, Armer NC, Stewart BR, Cormier JN, et al. Skin and Wound Care in Lymphedema Patients: A Taxonomy, Primer, and Literature Review. *Adv Skin Wound Care*. 2017 Jul;30(7):305–18.
90. Gefen A. Managing inflammation by means of polymeric membrane dressings in pressure ulcer prevention. *Wounds International*. 2018;9(1):22–8.
91. Wong ME, Jaworowski A, Hearps AC. The HIV Reservoir in Monocytes and Macrophages. *Front Immunol* [Internet]. 2019 Jun 26 [cited 2019 Sep 20];10. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6607932/>
92. Pugliese A, Vidotto V, Beltramo T, Torre D. Phagocytic Activity in Human Immunodeficiency Virus Type 1 Infection. *Clin Diagn Lab Immunol* [Internet]. 2005 Aug 1 [cited 2019 Sep 14];12(8):889–95. Available from: <https://cvi.asm.org/content/12/8/889>
93. Weledji EP, Kamga HLF, Assob JC, Nsagha DS. A Critical Review on HIV/AIDS and Wound Care. *African Journal of Clinical and Experimental Microbiology* [Internet]. 2012 Jan 1 [cited 2019 Sep 20];13(2):66-73–73. Available from: <https://www.ajol.info/index.php/ajcem/article/view/74691>



# References

94. McMeeking A, Kim I, Ross F, Ayello EA, Brem H, Linton P, et al. Wounds in patients with HIV. *Adv Skin Wound Care*. 2014 Sep;27(9):396–9.
95. Chilunda V, Calderon TM, Martinez-Aguado P, Berman JW. The Impact of Substance Abuse on HIV-Mediated Neuropathogenesis in the Current ART Era. *Brain Res*. 2019 Aug 29;146426.
96. Harper CM, Dowlatshahi AS, Rozental TD. Challenging Dogma: Optimal Treatment of the “Fight Bite.” *Hand (N Y)*. 2019 Feb 27;1558944719831238.
97. Ki V, Rotstein C. Bacterial skin and soft tissue infections in adults: A review of their epidemiology, pathogenesis, diagnosis, treatment and site of care. *Can J Infect Dis Med Microbiol [Internet]*. 2008 Mar [cited 2019 Aug 19];19(2):173–84. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2605859/>
98. Liu C, Bayer A, Cosgrove SE, Daum RS, Fridkin SK, Gorwitz RJ, et al. Clinical practice guidelines by the infectious diseases society of america for the treatment of methicillin-resistant *Staphylococcus aureus* infections in adults and children. *Clin Infect Dis*. 2011 Feb 1;52(3):e18-55.
99. Periti P, Tonelli F, Mini E. Selecting antibacterial agents for the control of surgical infection: mini-review. *J Chemother*. 1998 Apr;10(2):83–90.
100. Wright A, Fleming A, Colebrook L. The Conditions UNDER WHICH THE STERILISATION OF WOUNDS BY PHYSIOLOGICAL AGENCY CAN BE OBTAINED. *The Lancet [Internet]*. 1918 Jun 15 [cited 2019 Sep 25];191(4946):831–8. Available from: [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(01\)27037-8/abstract](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(01)27037-8/abstract)
101. Coull AF, Atherton I, Taylor A, Watterson AE. Prevalence of skin problems and leg ulceration in a sample of young injecting drug users. *Harm Reduct J [Internet]*. 2014 Aug 13 [cited 2019 Sep 26];11:22. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4136408/>
102. Nelzén O. Fifty percent reduction in venous ulcer prevalence is achievable - Swedish experience. *Journal of Vascular Surgery [Internet]*. 2010 Nov 1 [cited 2019 Sep 26];52(5):39S-44S. Available from: [https://www.jvascsurg.org/article/S0741-5214\(10\)01595-8/abstract](https://www.jvascsurg.org/article/S0741-5214(10)01595-8/abstract)
103. Bailey E, Kroshinsky D. Cellulitis: diagnosis and management. *Dermatol Ther*. 2011 Apr;24(2):229–39.
104. McGuinness W, Vella E, Harrison D. Influence of dressing changes on wound temperature. *J Wound Care*. 2004 Oct;13(9):383–5.
105. Tippet A. Factors in Wound Cleansing That May Impair Healing [Internet]. *WoundSource*. 2015 [cited 2019 Oct 14]. Available from: <http://www.woundsource.com/blog/cleaning-wound>
106. Page T. The impact of exposure time on biophysical parameters of the wound environment and patient comfort during dressing changes: a descriptive study. [Internet] [Dissertation]. [Adelaide, SA, Australia]: The University of Adelaide; 2015. Available from: <https://www.semanticscholar.org/paper/The-impact-of-exposure-time-on-biophysical-of-the-a-Page/3cd71d4ab0d7e31776f4dd691cbef39c23a880b6>
107. Acharya S, Soliman M, Egun A, Rajbhandari SM. Conservative management of diabetic foot osteomyelitis. *Diabetes Res Clin Pract*. 2013 Sep;101(3):e18–20.
108. Bjarnsholt T, Alhede M, Jensen PØ, Nielsen AK, Johansen HK, Homøe P, et al. Antibiofilm Properties of Acetic Acid. *Advances in Wound Care*. 2015 Jul 1;4(7):363.
109. Halstead FD, Rauf M, Moiemens NS, Bamford A, Wearn CM, Fraise AP, et al. The Antibacterial Activity of Acetic Acid against Biofilm-Producing Pathogens of Relevance to Burns Patients. *PLoS ONE*. 2015 Sep 9;10(9):e0136190.