## Biofilms

Virtually all wounds contain bacteria but the type and number of bacteria, their phenotype, as well as the way they are organized determine to what extent they may be harmful to a (skin) lesion and its healing process. Biofilms are of particular interest in that respect[1,2].

When tissues have reduced defenses, planktonic bacteria, entering the wound, attach to the wound surface: unless the host immune system swiftly clears the bacteria the formation of micro-colonies is initiated and a biofilm starts developing[3]. "Quorum-sensing" (a way of communication among bacteria, using specific molecules) is used to determine whether a sufficient number of bacteria is present[4,5]. If so, the microorganisms take the biofilm phenotype[5] and start exuding the exopolymeric matrix[6] which is primarily composed of polysaccharides and proteins[7], but also include other compounds such as certain lipids and DNA[8]. The matrix comprises of up to 90% of the organic matter in a biofilm[9,10] and serves as an encasement, helping the microbial community protect itself from the host immune system.

A biofilm is a major contributor to the chronicity of lesions such as venous leg ulcers and diabetic foot ulcers[11,12]: it attracts excess neutrophils, which are accompanied by proteases and pro-inflammatory cytokines. This (among other factors) contributes to the (hyper) inflammatory wound environment which results in non-healing lesions that become chronic[13-17]. In at least 60% of all patients with lesions such as venous leg ulcers and diabetic foot ulcers biofilms are estimated to play an major, if not crucial, role in chronicity[11,12]. Indeed, the detrimental influence of biofilm on wound healing has been analyzed and proven in many studies[4,12,16,18-21].

Therefore, management (removal) of a wound biofilm by debridement is essential since it has a positive effect on the healing trajectory[21], as is reflected in algorithms such as "TIME" and "DIME"[22,23]. Among the many methods of debridement (see "Debridement"), DEBRICHEM provides the unique option if a one-time, non-mechanical, application, which has been shown to lead to rapidly dislodging a biofilm and necrosis, the presence of which also hampers healing[24-28]. This is a crucial step into the development of granulation tissue, an essential phase in wound healing, particularly for lesions healing by secondary intention[29].

## References

1. Percival SL, Vuotto C, Donelli G, et al. Biofilms and Wounds: An Identification Algorithm and Potential Treatment Options. Adv Wound Care (New Rochelle) 2015;4(7):389-97. doi: 10.1089/wound.2014.0574
2. Percival SL, McCarty SM, Lipsky B. Biofilms and Wounds: An Overview of the Evidence. Adv Wound Care (New Rochelle) 2015;4(7):373-81. doi: 10.1089/wound.2014.0557
3. Harrison-Balestra C, Cazzaniga AL, Davis SC, et al. A wound-isolated Pseudomonas aeruginosa grows a biofilm in vitro within 10 hours and is visualized by light microscopy. Dermatol Surg 2003;29(6):631-5.
4. Clinton A, Carter T. Chronic Wound Biofilms: Pathogenesis and Potential Therapies. Lab Med 2015;46(4):277-84. doi: 10.1309/LMBNSWKUI4JPN7SO
5. Omar A, Wright JB, Schultz G, et al. Microbial Biofilms and Chronic Wounds. Microorganisms 2017;5(1) doi: 10.3390/microorganisms5010009
6. Staudt C, Horn H, Hempel DC, et al. Volumetric measurements of bacterial cells and extracellular polymeric substance glycoconjugates in biofilms. Biotechnol Bioeng 2004;88(5):585-92. doi: 10.1002/bit.20241 [published Online First: 2004/10/08]
7. Salisbury AM, Woo K, Sarkar S, et al. Tolerance of Biofilms to Antimicrobials and Significance to Antibiotic Resistance in Wounds. Surg Technol Int 2018;33:59-66.
8. Kavanaugh JS, Flack CE, Lister J, et al. Identification of Extracellular DNA-Binding Proteins in the Biofilm Matrix. mBio 2019;10(3) doi: 10.1128/mBio.01137-19 [published Online First: 2019/06/27]
9. Donlan RM. Biofilms: microbial life on surfaces. Emerg Infect Dis 2002;8(9):881-90. doi: 10.3201/eid0809.020063 [published Online First: 2002/08/27]
10. Donlan RM, Costerton JW. Biofilms: survival mechanisms of clinically relevant microorganisms. Clin Microbiol Rev 2002;15(2):167-93. doi: 10.1128/cmr.15.2.167-193.2002 [published Online First: 2002/04/05]
11. Wolcott RD, Rhoads DD, Bennett ME, et al. Chronic wounds and the medical biofilm paradigm. J Wound Care 2010;19(2):45-6, 48-50, 52-3. doi: 10.12968/jowc.2010.19.2.46966
12. Wolcott RD, Rhoads DD, Dowd SE. Biofilms and chronic wound inflammation. J Wound Care 2008;17(8):333-41. doi: 10.12968/jowc.2008.17.8.30796
13. Dobaczewski M, Gonzalez-Quesada C, Frangogiannis NG. The extracellular matrix as a modulator of the inflammatory and reparative response following myocardial infarction. J Mol Cell Cardiol 2010;48(3):504-11. doi: 10.1016/j.yjmcc.2009.07.015
14. Loo WT, Sasano H, Chow LW. Pro-inflammatory cytokine, matrix metalloproteinases and TIMP-1 are involved in wound healing after mastectomy in invasive breast cancer patients. Biomed Pharmacother 2007;61(9):548-52. doi: 10.1016/j.biopha.2007.08.012
15. Utz ER, Elster EA, Tadaki DK, et al. Metalloproteinase expression is associated with traumatic wound failure. J Surg Res 2010;159(2):633-9. doi: 10.1016/j.jss.2009.08.021
16. Percival SL, Hill KE, Williams DW, et al. A review of the scientific evidence for biofilms in wounds. Wound Repair Regen 2012;20(5):647-57. doi: 10.1111/j.1524-475X.2012.00836.x
17. Malone M, Bjarnsholt T, McBain AJ, et al. The prevalence of biofilms in chronic wounds: a systematic review and meta-analysis of published data. J Wound Care 2017;26(1):20-25. doi: 10.12968/jowc.2017.26.1.20
18. Schierle CF, De la Garza M, Mustoe TA, et al. Staphylococcal biofilms impair wound healing by delaying reepithelialization in a murine cutaneous wound model. Wound Repair Regen 2009;17(3):354-9. doi: 10.1111/j.1524-475X.2009.00489.x [published Online First: 2009/08/08]

19. Seth AK, Geringer MR, Gurjala AN, et al. Treatment of Pseudomonas aeruginosa biofilm-infected wounds with clinical wound care strategies: a quantitative study using an in vivo rabbit ear model. Plast Reconstr Surg 2012;129(2):262e-74e. doi: 10.1097/PRS.0b013e31823aeb3b
20. Rajpaul K. Biofilm in wound care. Br J Community Nurs 2015;Suppl Wound Care:S6, S8, S10-1. doi: 10.12968/bjcn.2015.20.Sup3.S6 [published Online First: 2015/03/12]
21. Schultz G, Bjarnsholt T, James GA, et al. Consensus guidelines for the identification and treatment of biofilms in chronic nonhealing wounds. Wound Repair Regen 2017;25(5):744-57. doi: 10.1111/wrr.12590
22. Ayello EA, Dowsett C, Schultz GS, et al. TIME heals all wounds. Nursing 2004;34(4):36-41; quiz, 41-2. [published Online First: 2004/07/13]
23. Snyder RJ, Fife C, Moore Z. Components and Quality Measures of DIME (Devitalized Tissue, Infection/Inflammation, Moisture Balance, and Edge Preparation) in Wound Care. Adv Skin Wound Care 2016;29(5):205-15. doi: 10.1097/01.ASW.0000482354.01988.b4 [published Online First: 2016/04/19]
24. Ayello EA, Cuddigan JE. Conquer chronic wounds with wound bed preparation. Nurse Pract 2004;29(3):8-25; quiz 26-7. doi: 10.1097/00006205-200403000-00002 [published Online First: 2004/03/17]
25. Gethin G, Cowman S, Kolbach DN. Debridement for venous leg ulcers. Cochrane Database Syst Rev 2015(9):CD008599. doi: 10.1002/14651858.CD008599.pub2 [published Online First: 2015/09/15]
26. Manna B, Morrison CA. Wound Debridement. StatPearls. Treasure Island (FL)2020.
27. Mosti G. Wound care in venous ulcers. Phlebology 2013;28 Suppl 1:79-85. doi: 10.1177/0268355513477015 [published Online First: 2013/03/27]
28. Turns M. Diabetic foot ulcer management: the podiatrist's perspective. Br J Community Nurs 2013;Suppl:S14, S16-9. doi: 10.12968/bjcn.2013.18.sup12.s14 [published Online First: 2014/05/07]
29. Bernstein G. Healing by secondary intention. Dermatol Clin 1989;7(4):645-60. [published Online First: 1989/10/01]