Development of a Next-Generation Antimicrobial Wound Dressing- Results Count

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Making a Difference in People's Lives

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Overview

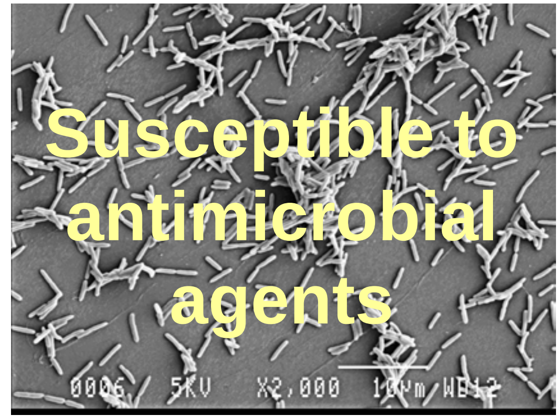
- The clinical problem
- The solution
- The evidence

The Clinical Problem – Wound Biofilm

Bacteria exist in two different life-styles

Planktonic

- Single cells / free-living
- In solution
- Fast multiplying – high metabolism



Biofilm

- Community of cells
- Attached to an surface
- Encased in a slime (exopolymeric substance, EPS)
- Slow metabolism

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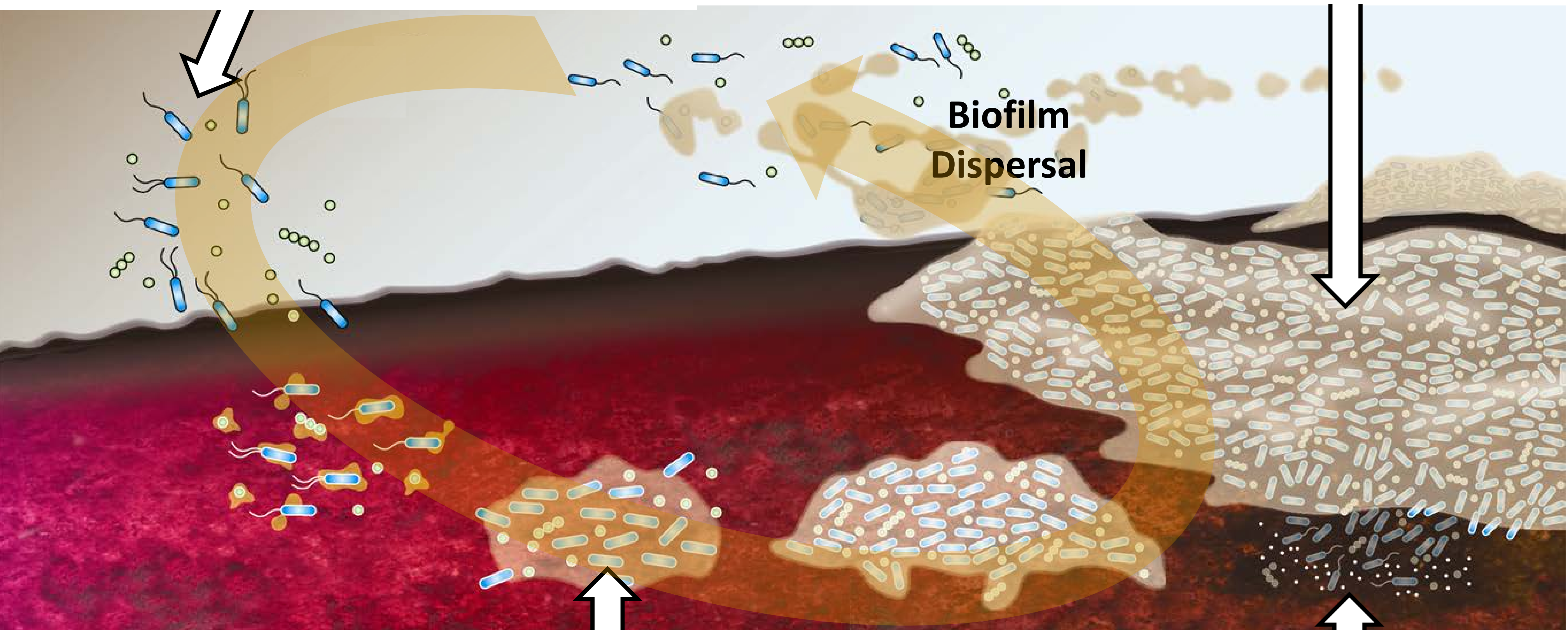
Bacteria adapt – the biofilm life cycle

Planktonic
(microscopic, invisible, single cells)

Biofilm Maturation
(multi-species, slime, may be macroscopic – visible)



Microcolony formation
(multi-species, microscopic – invisible)

Potential for invading
(planktonic) **infection**

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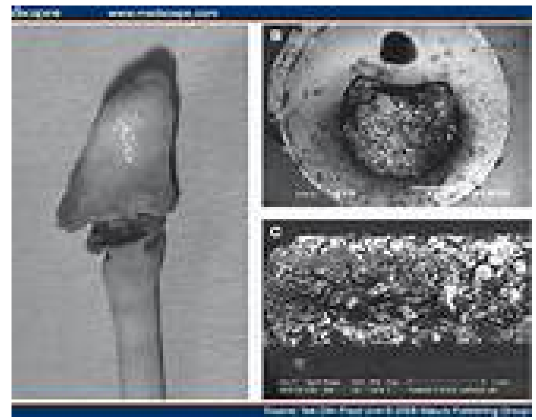
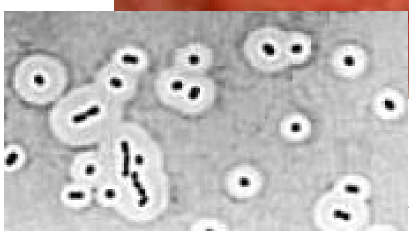
Biofilm in Nature & Disease





- 99% of bacteria in nature exist as biofilm[1]
- Biofilm accounts for >80% of all microbial infections in the body[2]

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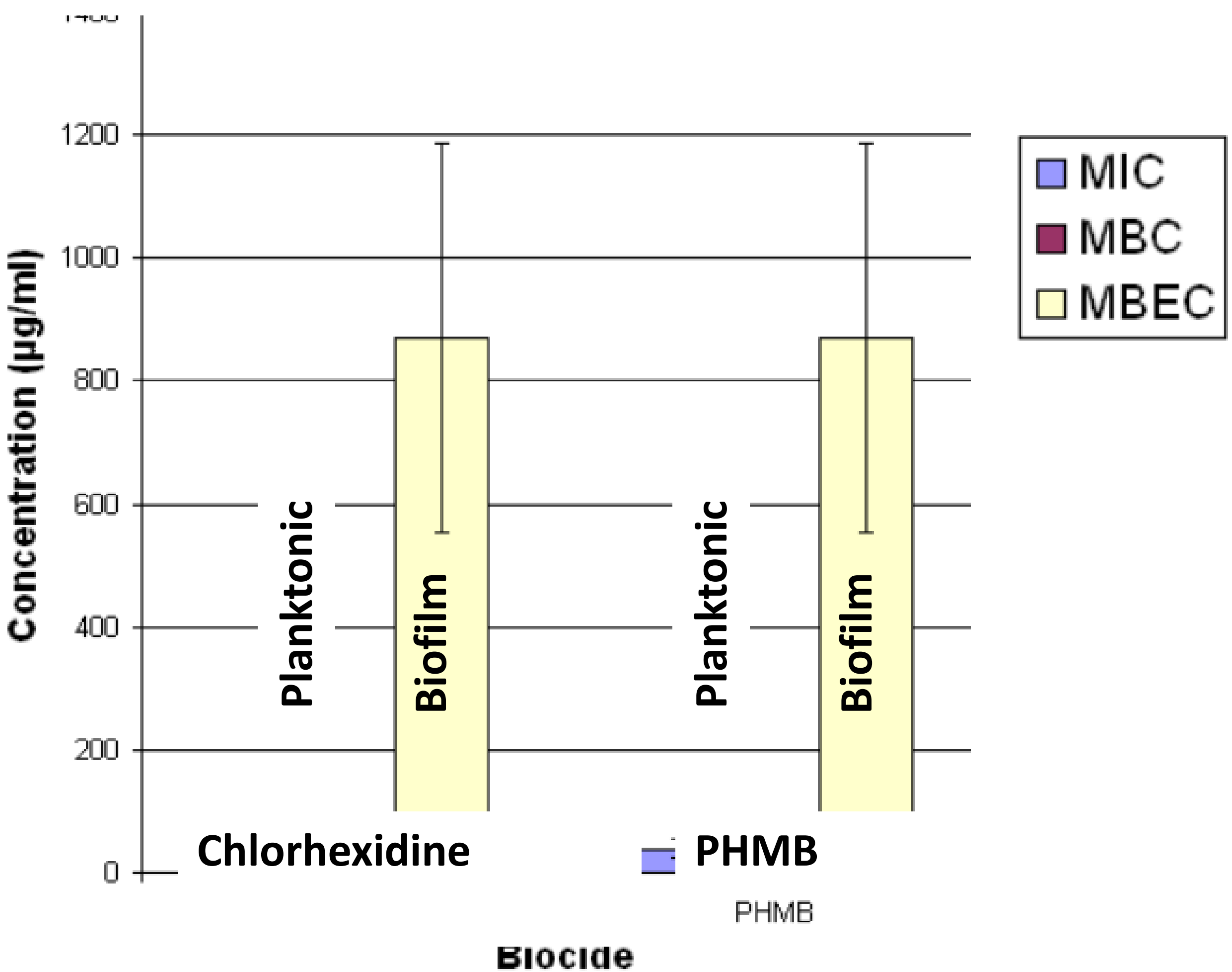
1. Costerton et al. Bacterial biofilms in nature and disease. Ann Rev Microbiol 1987; 41:435-64.
2. National Institutes of Health, 2002

Biofilm is more tolerant to antimicrobials than planktonic bacteria

Example : Biocide susceptibility testing of *Serratia marcescens*



Data Courtesy of :
Dr Andrew McBain, Manchester Pharmacy School, Univ. Manchester

MIC: **M**inimum **I**nhibitory **C**oncentration
MBC: **M**inimum **B**actericidal **C**oncentration
MBEC: **M**inimum **B**iofilm **E**radication **C**oncentration

ConvaTec's Wound Biofilm Science

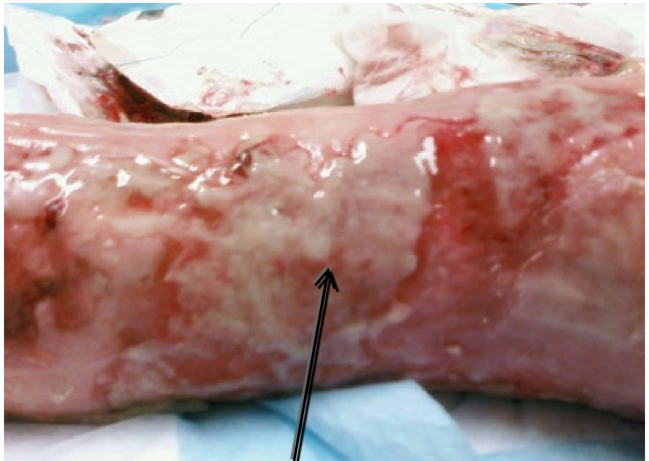
- 2003. The 10^5 bacterial growth guideline: Reassessing it's clinical relevance in wound healing. *OWM*.
- 2004. Biofilms and their potential role in wound healing. *WOUNDS*.
- 2007. Antimicrobial activity of silver-containing dressings on wound microorganisms using an *in vitro* biofilm model. *Int. Wound J*.
- 2008. Assessing the effect of an antimicrobial wound dressing on biofilms. *Wound Rep Reg.*
- 2009. Clinical experience with wound biofilm and management: A case series. *OWM*.
- 2012. Potential implication of biofilm in chronic wounds: A case series. *JWC*.
- 2013. Biofilm delays wound healing: A review of the evidence. *Burns & Trauma*.
- 2014. A clinical algorithm for wound biofilm identification. *JWC*.
- 2014. The visualization of biofilms in chronic diabetic foot wounds using routine diagnostic microscopy methods. *J Diabetes Res*.
- 2014. An *in vitro* test of the efficacy of an anti-biofilm wound dressing. *Int J Pharmaceutics*
- 2014. Clinician perceptions of wound biofilm. *Int. Wound J*.
- 2014. Impact of a novel, anti-microbial dressing on *in vivo*, *Pseudomonas aeruginosa* wound biofilm: Quantitative comparative analysis using a rabbit ear model. *Wound Rep. Reg*.
- 2015. Clinical Biofilms: A Challenging Frontier in Wound Care. *Adv Wound Care*.
- 2015. Safety and Performance Evaluation of a Next Generation Antimicrobial Dressing in Patients with Chronic Venous Leg Ulcers. *Int Wound J*.
- 2015. A real-life clinical evaluation of a next-generation antimicrobial dressing on acute and chronic wounds. *J. Wound Care.* (JWC Award winner 2015).
- 2015. Design of a next generation antimicrobial Hydrofiber dressing to combat wound biofilm (submitted to *BMJ Innovations*).
- 2015. A real-life clinical evaluation of a next-generation antimicrobial wound dressing in the United Kingdom. Submitted to *JWC*.
- 2015. Clinical safety and effectiveness of a next-generation antimicrobial wound dressing designed to manage exudate, infection & biofilm (submitted to *IWJ*).
- 2015. Management of diabetic foot ulcers using a next generation antimicrobial dressing: A case series (submitted to *J Diabetes Research*).

Biofilm Delays Wound Healing

- ***"…biofilms are the principle cause of wound chronicity "***[1]
- ***"…biofilms represent a fourth major pillar of chronic wound pathogenesis"***[2]
- Biofilm creates a sustained low-grade & ineffective inflammatory response[2]
- **Biofilm impairs epithelial migration & granulation tissue formation**[2]
- Individual bacterial species possess distinct levels of biofilm virulence[3]
- Multi-species biofilm delays healing more than single-species biofilm[4]
- Bacteria from patients with persistent infections are positive for biofilm formation[5]
- **At least 60% of chronic wounds contain biofilm**[6, 7]
- ***Biofilm delays wound healing: a review of the evidence***[8]

1. Wolcott et al. Chronic wounds and the medical biofilm paradigm. J Wound Care 2010;19:45-53
2. Gurjala et al. Development of a novel, highly quantitative *in vivo* model for the study of biofilm-impaired cutaneous wound healing. WRR 2011;19:400-10
3. Seth et al. Quantitative comparison and analysis of species-specific wound biofilm virulence using an *in vivo*, rabbit ear model. J Am Coll Surg 2012; 215:388-99
4. Seth et al. Comparative analysis of single-species and polybacterial wound biofilms using a quantitative, *in vivo*, rabbit ear model. PLoS ONE 2012;7:e42897
5. Sanchez et al. Biofilm formation by clinical isolates and the implications in chronic infections. BMC Infect Dis 2013;13:47
6. James et al. Biofilms in chronic wounds. Wound Repair Regen 2008;16:37-44
7. Kirketerp-Møller et al. Distribution, organization, and ecology of bacteria in chronic wounds. J Clin Microbiol 2008;46:2712-22
8. Metcalf & Bowler. Biofilm delays wound healing: a review of the evidence. Burns Trauma 2013; 1: 5-12.

Is Wound Biofilm Visible?



Suspected biofilm over friable granulation tissue in leg ulcer

Thick opaque biofilm? Unresponsive to antibiotics

Suspected biofilm in non-healing surgical wound

Suspected biofilm in non-healing surgical wound

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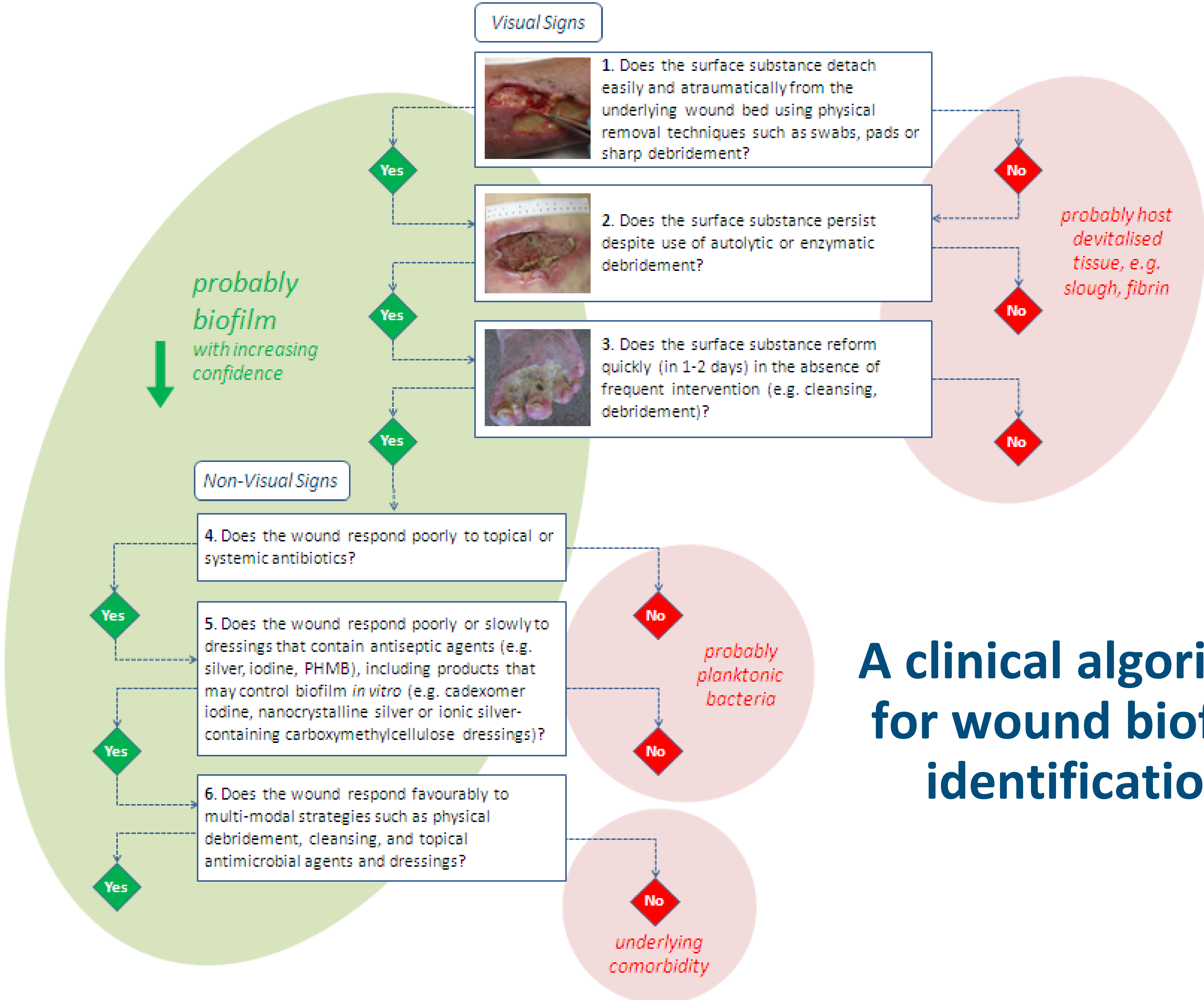


A clinical algorithm for wound biofilm identification

Metcalf DG, Bowler PG, Hurlow J. A clinical algorithm for wound biofilm identification J Wound Care 2014; 23: 137-142.

Optimum wound biofilm management today?

- Cleansing

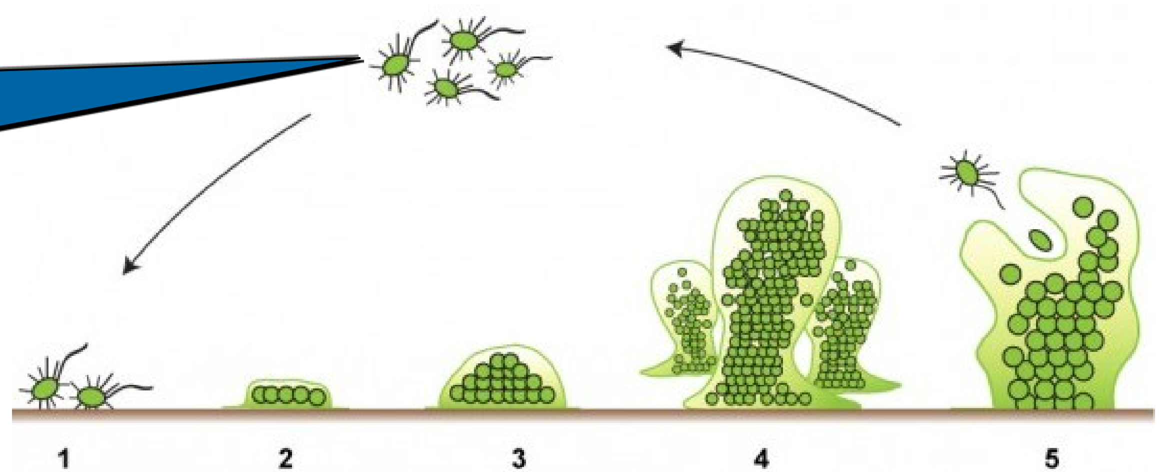
- Debridement

- Antimicrobial Agents/Dressings (anti-biofilm dressings?)

Considerations for an Anti-biofilm Wound Dressing

- **Breakdown** & **disrupt** biofilm
- **Expose** bacteria for more **effective killing** by antimicrobial agents such as ionic silver
- **Prevent biofilm reformation** in the wound

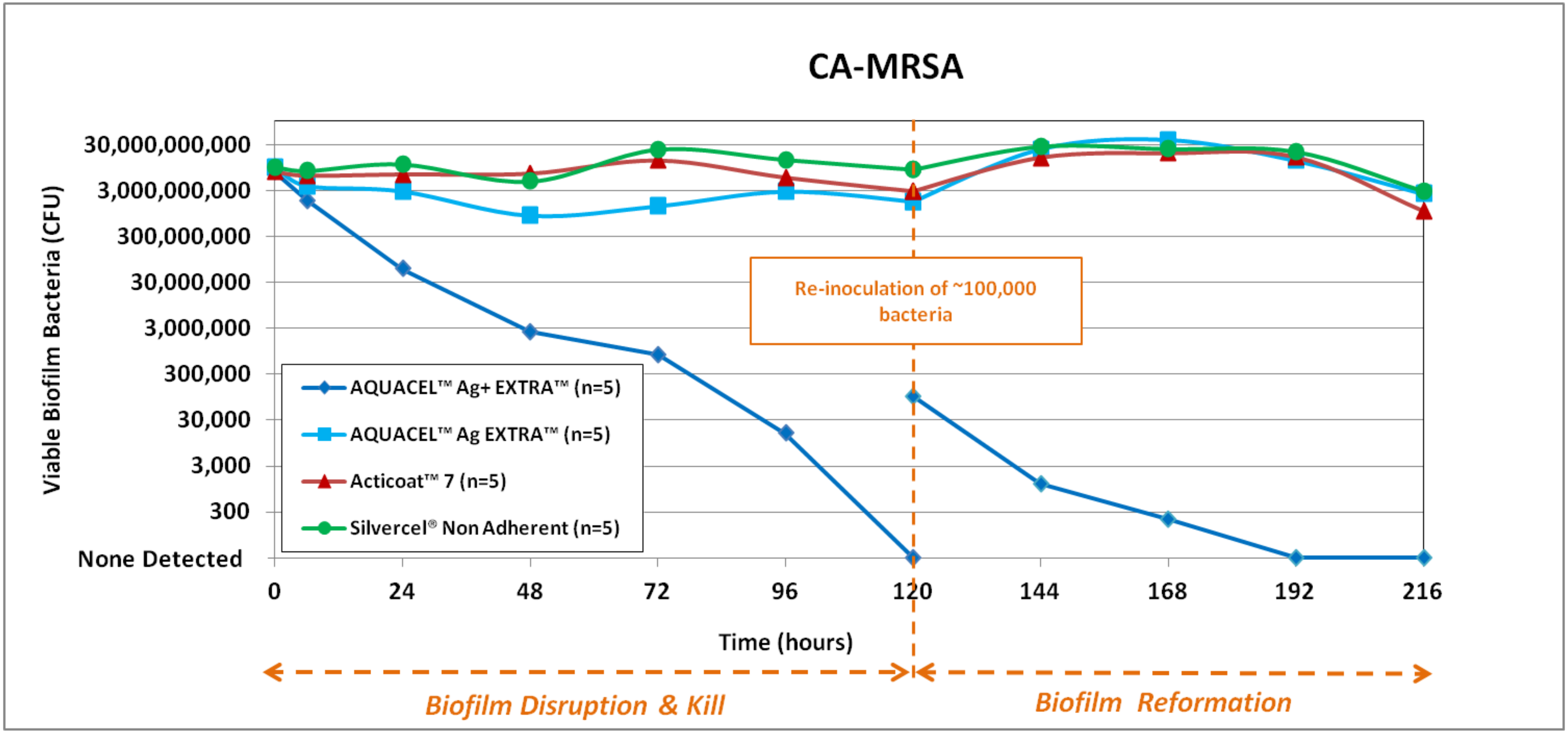
100 - 1,000 times more susceptible than biofilm bacteria



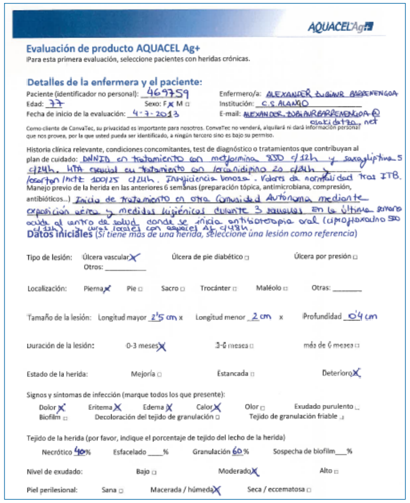
- Same base product as AQUACEL™ Ag / Extra dressings, i.e. physical attributes, 1.2% ionic silver
- Two additional components:
  1. A *metal chelator* (protects silver and destabilises biofilm)
  2. A *surfactant* (reduces surface tension and loosens biofilm surface)
- Synergistic enhancement between ionic silver, surfactant & metal chelator* (IP protected)

* Said et al. *Int J Pharm*, 2014

The Evidence:
AQUACEL™ Ag+ Extra™ Dressing vs Standard Silver Dressings



The Evidence:
Clinical evaluation of AQUACEL™ Ag+ dressing



AQUACEL Ag+

Evaluación de producto AQUACEL Ag+

Para esta primera evaluación, seleccione pacientes con heridas crónicas.

Detalles de la enfermera y el paciente:

Paciente (identificador no personal): 469759
Enfermero/a: ALEXANDER ZUBIAUR BARRENENGOA
Edad: 77
Sexo: F ☒ M ☐
Institución: C.S ALANGO
Fecha de inicio de la evaluación: 4-7-2013
E-mail: ALEXANDER.ZUBIAURBARRENENGOA@osakidetza.net

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Historia clínica relevante, condiciones concomitantes, test de diagnóstico o tratamientos que contribuyan al plan de cuidado: DMNID en tratamiento con metformina 850 c/12h y saxagliptina 5 c/24h. HTA esencial en tratamiento con lercanidipino 20 c/24h y losartan/hctz 100/25 c/24h. Insuficiencia venosa. Valores de normalidad tras ITB.

Manejo previo de la herida en las anteriores 6 semanas (preparación tópica, antimicrobiana, compresión, antibióticos...) Inicio de tratamiento en otra Comunidad Autónoma mediante exposición aérea y medidas higiénicas durante 3 semanas. En la última semana acude al centro de salud donde se inicia antibioterapia oral (ciprofloxacino 500 c/12h) y curas locales con aquacel Ag c/48h.

Datos iniciales *(Si tiene más de una herida, seleccione una lesión como referencia)*

Tipo de lesión: Úlcera vascular ☒ Úlcera de pie diabético ☐ Úlcera por presión ☐
Otros: ______

Localización: Pierna ☒ Pie ☐ Sacro ☐ Trocánter ☐ Maléolo ☐ Otras: ______

Tamaño de la lesión: Longitud mayor 2'5 cm x Longitud menor 2 cm x Profundidad 0'4 cm

Duración de la lesión: 0-3 meses ☒ 3-6 meses ☐ más de 6 meses ☐

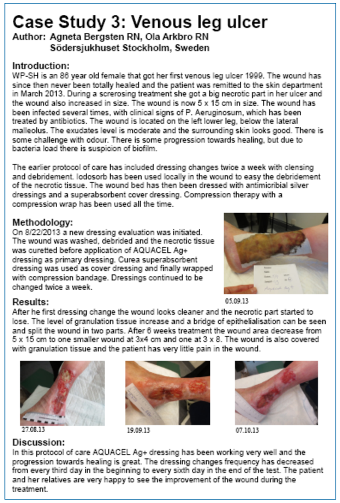
Estado de la herida: Mejoría ☐ Estancada ☐ Deterioro ☒

Signos y síntomas de infección (marque todos los que presente):
Dolor ☒ Eritema ☒ Edema ☒ Calor ☒ Olor ☐ Exudado purulento ☐
Biofilm ☐ Decoloración del tejido de granulación ☐ Tejido de granulación friable ☐

Tejido de la herida (por favor, indique el porcentaje de tejido del lecho de la herida)
Necrótico 40% Esfacelado ___% Granulación 60% Sospecha de biofilm ___%

Nivel de exudado: Bajo ☐ Moderado ☒ Alto ☐

Piel perilesional: Sana ☐ Macerada / húmeda ☒ Seca / eccematosa ☐



Case Study 3: Venous leg ulcer

Author: Agneta Bergsten RN, Ola Arkbro RN
Södersjukhuset Stockholm, Sweden

Introduction:
WP-SH is an 86 year old female that got her first venous leg ulcer 1999. The wound has since then never been totally healed and the patient was remitted to the skin department in March 2013. During a screrosing treatment she got a big necrotic part in her ulcer and the wound also increased in size. The wound is now 5 x 15 cm in size. The wound has been infected several times, with clinical signs of P. Aeruginosum, which has been treated by antibiotics. The wound is located on the left lower leg, below the lateral malleolus. The exudates level is moderate and the surrounding skin looks good. There is some challenge with odour. There is some progression towards healing, but due to bacteria load there is suspicion of biofilm.

The earlier protocol of care has included dressing changes twice a week with clensing and debridement. Iodosorb has been used locally in the wound to easy the debridement of the necrotic tissue. The wound bed has then been dressed with antimicribial silver dressings and a superabsorbent cover dressing. Compression therapy with a compression wrap has been used all the time.

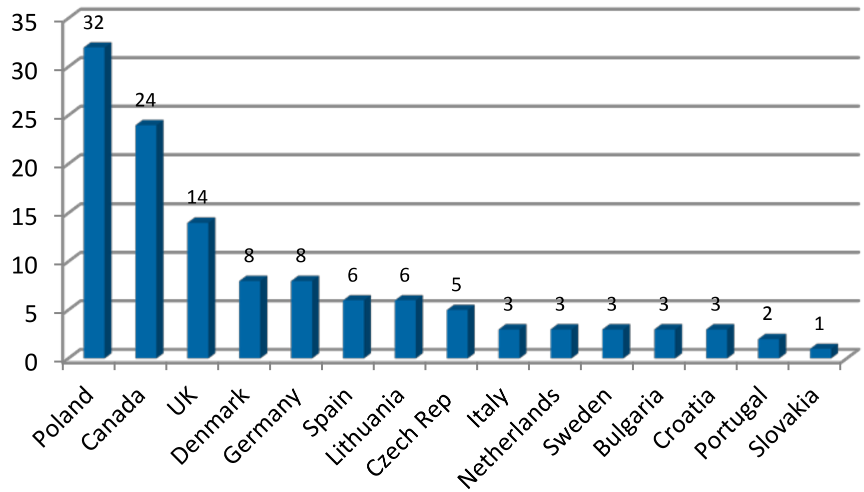
Methodology:
On 8/22/2013 a new dressing evaluation was initiated. The wound was washed, debrided and the necrotic tissue was curetted before application of AQUACEL Ag+ dressing as primary dressing. Curea superabsorbent dressing was used as cover dressing and finally wrapped with compression bandage. Dressings continued to be changed twice a week.

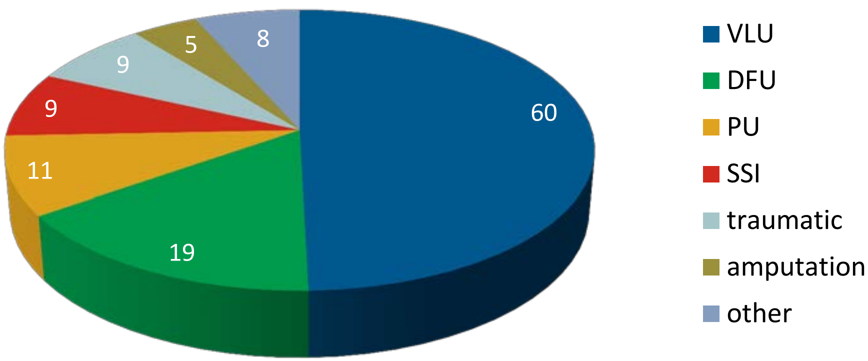
05.09.13

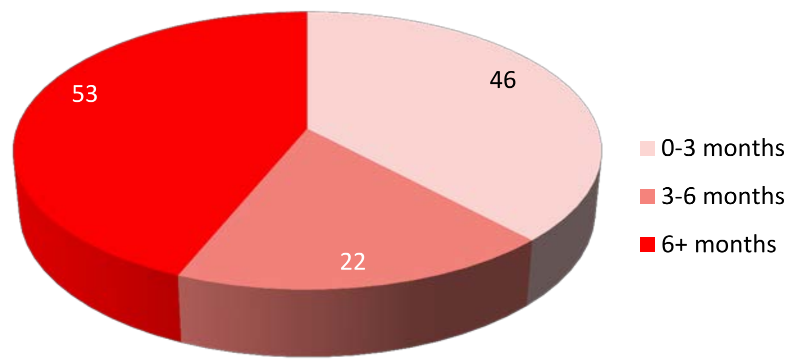
Results:
After he first dressing change the wound looks cleaner and the necrotic part started to lose. The level of granulation tissue increase and a bridge of epithelialisation can be seen and split the wound in two parts. After 6 weeks treatment the wound area decrease from 5 x 15 cm to one smaller wound at 3x4 cm and one at 3 x 8. The wound is also covered with granulation tissue and the patient has very little pain in the wound.

27.08.13 19.09.13 07.10.13

Discussion:
In this protocol of care AQUACEL Ag+ dressing has been working very well and the progression towards healing is great. The dressing changes frequency has decreased from every third day in the beginning to every sixth day in the end of the test. The patient and her relatives are very happy to see the improvement of the wound during the treatment.







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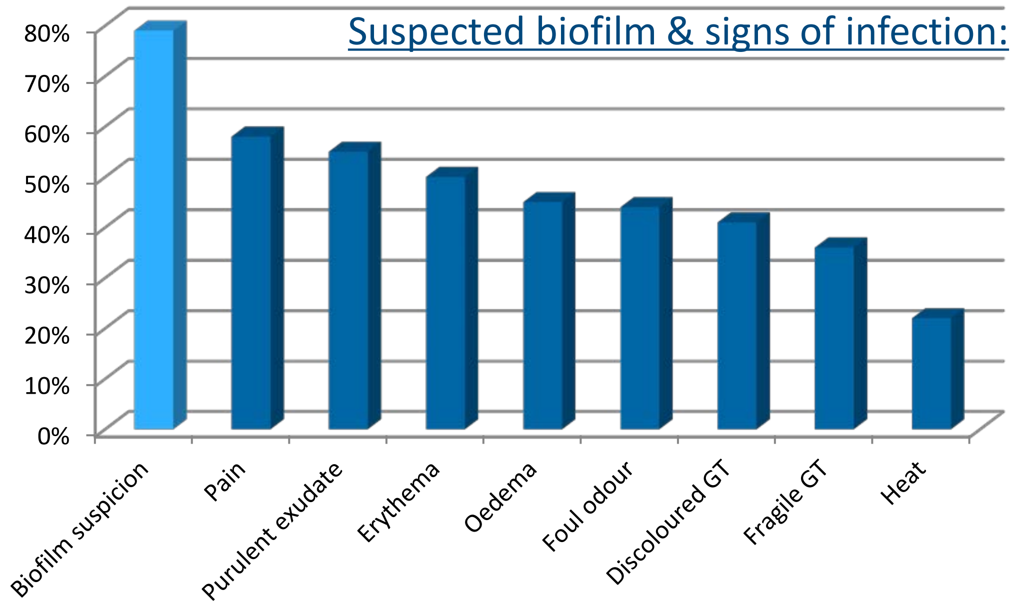
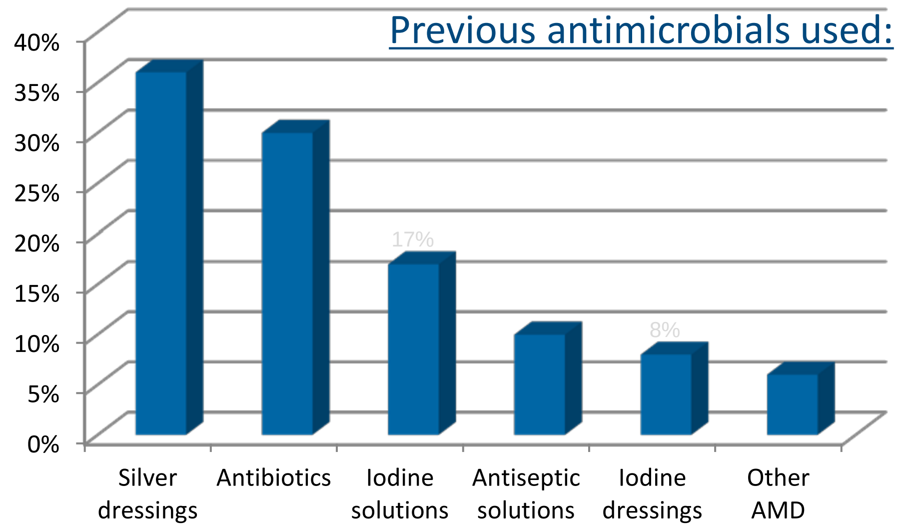
Walker et al. A real-life clinical evaluation of a next-generation antimicrobial dressing on acute and chronic wounds. *J. Wound Care.* (JWC Award winner 2015).

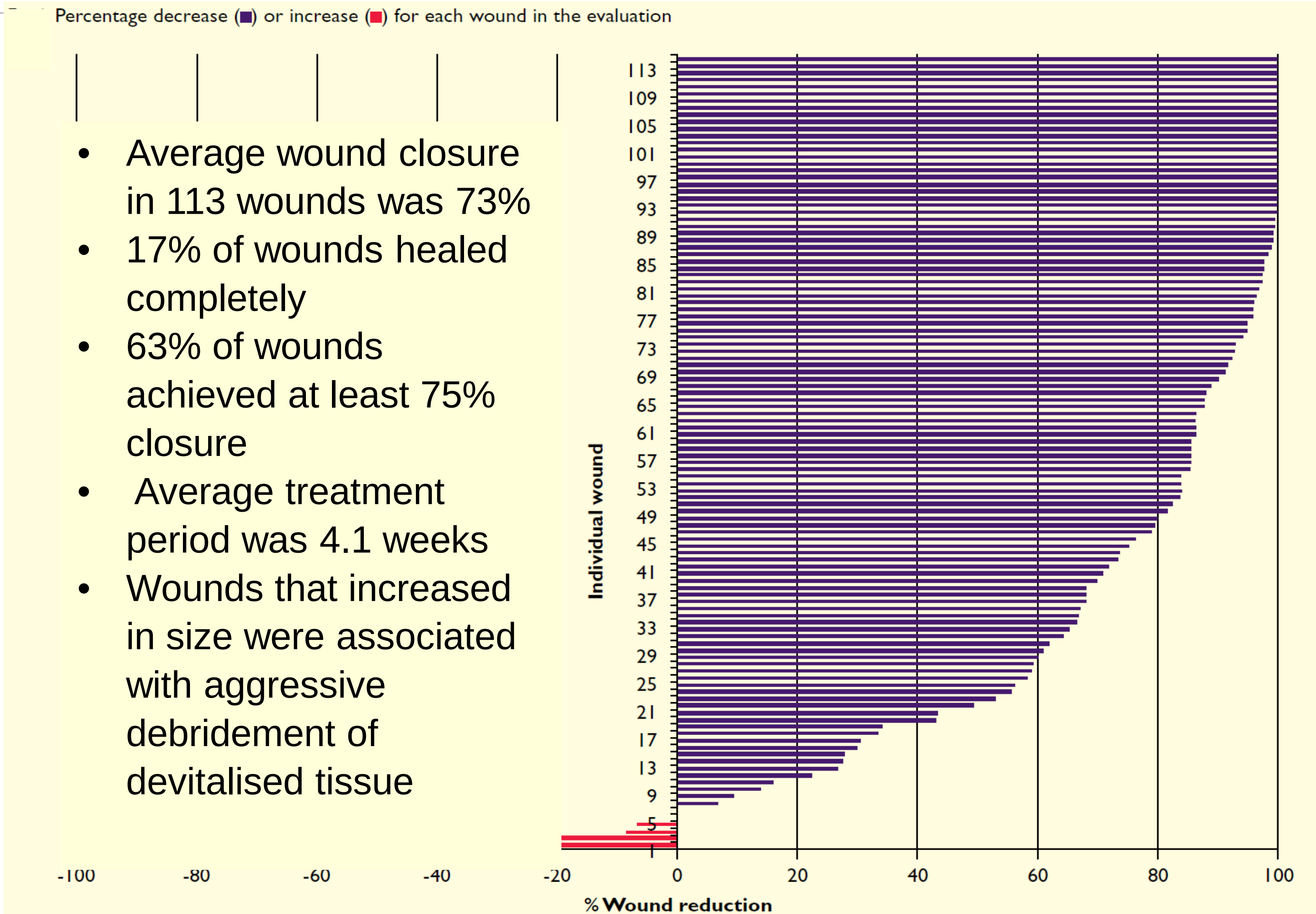
Baseline Information





Clinical Evaluation of a Next-Generation Antimicrobial Dressing on Acute and Chronic Wounds

- Average wound closure in 113 wounds was 73%
- 17% of wounds healed completely
- 63% of wounds achieved at least 75% closure
- Average treatment period was 4.1 weeks
- Wounds that increased in size were associated with aggressive debridement of devitalised tissue



- Dressing did not contain strengthening yarn or have the additional absorptive capacity of AQUACEL™ Ag+ Extra™ dressing

Walker et al. A real-life clinical evaluation of a next-generation antimicrobial dressing on acute and chronic wounds. JWC. 2015; 1.

Clinical case study examples

<u>Lithuania</u>
Post-traumatic leg wound; Purulent exudate, odor, poor granulation tissue, suspect biofilm, despite antibiotics;
AQUACEL™ Ag+: infection resolves, healed in 7 weeks


On presentation


Day 21


Day 48

<u>Netherlands, Alita Jaspar</u>
Stalled traumatic leg wound; Peri-wound maceration, malodorous exudate, despite silver sulfadiazine;
AQUACEL™ Ag+: infection resolved, great improvement


On presentation


Day 35


Day 45

<u>Portugal, Dr Vitor Santos</u>
Chronic DFU of 6+ months; Odor, exudate, slough, suspect biofilm.
AQUACEL™ Ag+: peri-wound skin improved, wound bed cleared, healed in 5 weeks


On presentation


Day 10


Day 37

* Dressing did not contain strengthening yarn or have the additional absorptive capacity of AQUACEL™ Ag+ Extra™ dressing

Concluding remarks

- Biofilm exacerbates chronicity & impedes healing in most infectious diseases
- If a wound (acute or chronic) is not healing and is unresponsive to antimicrobial therapies, biofilm is likely to be implicated
- A comprehensive protocol-of-care is likely to be most effective in overcoming wound biofilm (debridement, cleansing, antimicrobial)
- The first wound dressing designed to combat biofilm (within a protocol-of-care) is now available to patients in Europe and has been associated with outstanding clinical outcomes