

The Importance of Regenerex[®] Antimicrobial Activity



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Almost all biomaterials are foreign objects that are introduced into the body in the form of an implantable device; the area near the implant becomes immunologically compromised and is a nidus for infection.¹ The role of the biomaterial may be crucial to preventing or reducing the severity of a device-associated infection. Over the last decade, the number of materials implanted into patients as either catheters or devices has skyrocketed.² This has created a critical need for biomaterials that possess antimicrobial activity to prevent the prevalence of biomaterials-associated infections. A combination of factors has led to this growing concern:

Science and Technology

- An increasing number of people live longer and are demanding more implantable devices to keep them alive and in better health.
- Medical technology has developed a diverse array of devices that has expanded the ability to treat patients in an improved safer manner. For example, cardiac pacemakers, patches, stents, and central venous catheters all would benefit from an antimicrobial biomaterial that could prevent a number of infections currently associated with these devices.
- Novel surgical techniques allow sicker and older patients to receive these biomaterials.

Increased life span with decreased immunologic competence

- People now live longer with chronic diseases such as diabetes and cancer which makes it more difficult for them to fight off infections. They lack the ability to mount the normal immunological defenses found in healthy, young people and frequently do not have the ability to prevent a biomaterials-associated infection.³
- This population has an increased need for implantable devices for treating such problems as hip replacements, indwelling urinary catheters, cardiac stents, patches, pacemakers, etc.
- Since this population has a decreased ability to fight off infection, they are prone to developing chronic wounds from conditions such as:
 - Decubitus ulcers
 - Diabetic foot ulcers
 - Surgical wounds
 - Trauma
 - Venous leg ulcers



Health Care-Associated Infections

The treatment of these patients has further been complicated by the increased incidence of microorganisms resistant to antibiotics, caused by the overuse of antibiotics. It is now much more difficult to treat chronic infected wounds.

Hospital acquired infections are a large part of the health care-associated infections that affect implanted devices. A Center for Disease Control Study (CDC) found “Device-associated infections (i.e., ventilator-associated pneumonia, catheter-associated urinary tract infection, and central-catheter-associated bloodstream infection) accounted for 25.6% of all health care-associated infections; together, device-associated infections and surgical-site infections (21.8%) accounted for 47.4% of all health care-associated infections (239 of 504 infections).”⁴

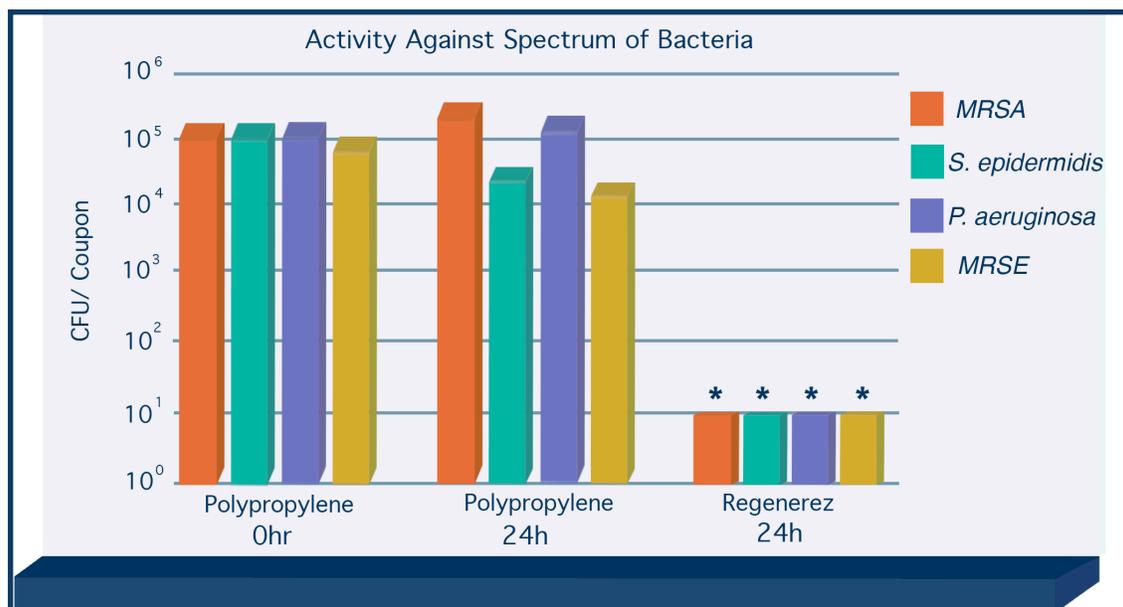
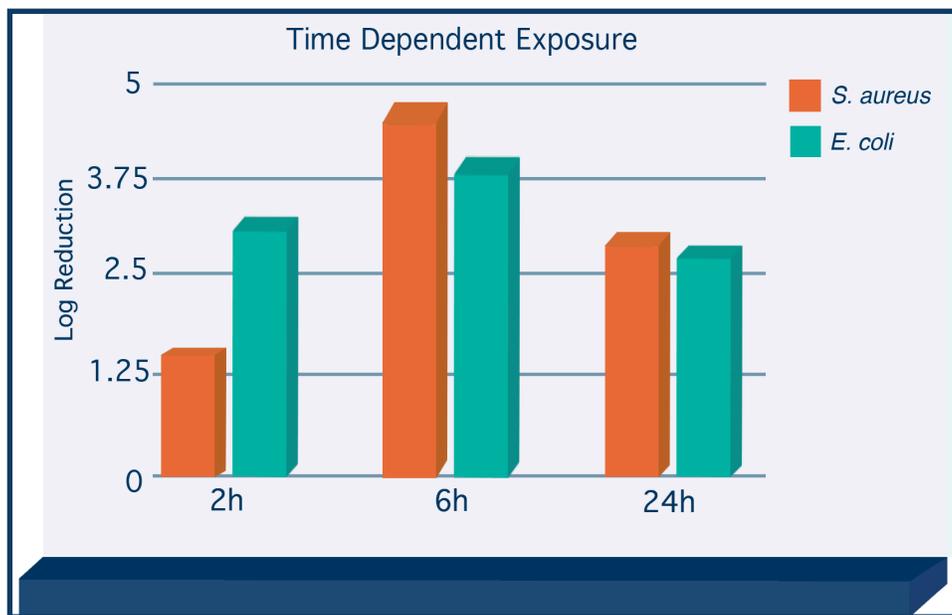
Table 1. Estimates of Costs and LOS Attributed to the 5 Major Health Care-Associated Infections for the US Adult Inpatient Population at Acute Care Hospitals ^a (Adapted from Zimlichman E. and et al: JAMA 2013)		
Health Care- Associated Infection Type	Cost, 2012 \$US	LOS (as Total, ICU), d
Surgical Site Infections	20 785	11.2 (10.5-11.9) ^b
MRSA	42 300	23.0 (14.3-31.7) ^b
Central line-associated bloodstream infections	45 814	10.4, 6.9 (6.9-15.2,3.5-9.6) ^{b,c}
MRSA	58 614	15.7 (7.9-36.5) ^c
Catheter-associated urinary tract infections	896	NR
Ventilator-associated pneumonia	40 144	13.1, 8.4 (11.9-14.2, 7.8-9.0) ^{b,c}
Clostridium difficile infections	11 285	3.3 (2.7-3.8) ^b
<p>Abbreviations: ICU, intensive care unit; LOS, length of hospital stay; MRSA, methicillin-resistant <i>Staphylococcus aureus</i>; NR, not reported</p> <p>^a Data are reported as mean (95%CI) values.</p> <p>^b Estimates obtained from literature and 100 000-trial Monte Carlo simulations using triangular distribution.</p> <p>^c Estimates obtained from literature and 100 000-trial Monte Carlo simulations, using general distribution.</p>		



Antimicrobial Activity

Regenerez has potential for prophylactic or therapeutic intervention of infection and has a large range of antibacterial activity without having the disadvantage of developing antibiotic resistance.⁵ Regenerez is comprised of polyglycerol sebacate (PGS) and is synthesized from natural metabolites (ie, glycerol and sebacic acid). The degradation products of PGS resemble medium-chain fatty acids (MCHA) and their monoglyceride derivatives. As well-known antimicrobials, MCFAs possess the ability to disrupt the bacterial cell membrane, disrupt the cell wall⁶, and generate toxic peroxidation and auto-11 oxidation products⁷.

Regenerez has demonstrated antimicrobial activity through industry tests standards: the JIS Z 2801 Test for Antibacterial Activity, the ASTM E2315 Suspension Time Kill (STK) test and a Minimum Inhibitory Concentration (MIC) test. The results of the JIS Z 2801 Test for Antibacterial Activity are shown below.



* Values were below the detection limit of the assay at <10 CFU/coupon



These results show excellent activity against a broad spectrum of microbes, both gram negative and positive bacteria. This innate antimicrobial activity expands Regenerex's potential biomedical applications that also include its anti-inflammatory, anti-fibrotic, and flexible elastomeric properties.

Studies on Regenerex have also shown a reduction in inflammation by a decrease in the expression of proinflammatory markers iNOS, TNF α and CD86 as well as the increase in pro-healing markers PPAR γ , IL-10 and CD206.⁸ The down regulation of M1 and upregulation of M2 macrophage markers suggest the immunomodulatory properties of Regenerex.

As the need for advanced implantable biomaterials grows, Regenerex has shown to be an excellent technology platform for use in the following applications:

- A surgical implant coating/component to help prevent infection
- A wound care agent
- Tissue engineering scaffold with innate antimicrobial properties
- Indwelling catheters for preventing urinary tract infection
- Preventing central-catheter-associated bloodstream infection

References

1. Rockford E. Richard R. and Moriarty T: Influence of the material on device associated infections. CMI, 18:1162-1167
2. Umscheid M, Mitchel M, Doshi J, and et al: Estimating the proportion of health care- associated infections that are reasonable preventable and the related mortality and costs. Infection Control Hosp Epidemiol. 2011; 32: 101-114
3. David L. Fern´andez-Hidalgo. Chauhan A. and et al: Management of infections related to totally implantable venous-access ports: challenges and perspectives. Lancet Infectious Diseases, Elsevier, 2014, 14:146 - 159. .
4. Dudkeck M. Weiner L. Allen-Bridsen K. and et al: National Safety Healthcare Network Report Data Summary for 2012 Device Associated Module, Am J Infec Control, 2013; 41-1148-1166
5. Data on file
6. Fischer C. Drake D. Blanchet D, and et al: Antibacterial activity of sphingoid bases against gram positive and negative bacteria. Antimicrob. Agents Chemother. 2012: 1157-1161
7. Kenny J, Ward D. Josefson E. and et al: The staphylococcus aureus response to unsaturated long chain fatty acids: survival mechanisms and virulence implications. PLoS ONE, 2009: 4344.
8. Data on file



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