

Azzopardi EA. Characteristic gram-negative bacteria and a clinically viable mechanism for selective drug targeting. In: Perks G, Ed. British Association of Plastic Reconstructive & Aesthetic Surgeons Winter Meeting. London.2014. <https://www.bapras.org.uk/docs/default-source/bapras-event-documents/scientific-meetings/final-conference-guide-for-website.pdf?sfvrsn=4>

Infection is recognised as one of the most pressing challenge facing surgeons in plastic surgery, burns and physicians in all specialties. Our work is the first to describe the characteristic spectrum of Gram-negative bacteria to infect burn wounds (Azzopardi E et al. PLoS One, 2014). Given the rapid availability of a Gram-stain, our work significantly increases appropriate targeting of antimicrobial prescriptions.

We also describe a method whereby passive targeting of molecules and “smart” activation at an infected site can be achieved (Azzopardi E. et al. Lancet, 2014). This method can be translated to the delivery of most bioactive molecules to soft tissue infection, reducing toxicity at undesired sites whilst increasing activity at the target area.

#### Title

Characteristic Gram-negative bacteria and a clinically viable mechanism for selective drug targeting.

Background and aims Gram negative infection is a major determinant of morbidity and survival. Traditional teaching suggests that burn wound infections in different centres are caused by differing sets of causative organisms. We established whether there is a characteristic spectrum of Gram-negative bacteria that infect burn wounds, and whether a common targeting mechanism for drug delivery can be established.

Methods Metanalysis of standardised bacterial incidence rates from studies published (limits: 2000-2010, adult, civilian patients) was performed. A common biochemical cascade instigated by these bacteria sought (limits: 1945- current, bacteria, biochemistry).

#### Primary Findings

Gram-negative infections predominate in burn surgery. *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Enterobacter* spp., *Proteus* spp. and *Escherichia coli* emerged as characteristic Gram-negative burn wound pathogens. Their incidence did not differ significantly between burn centres ( $F(4, 20) = 1.1$ ,  $p = 0.3797$ ;  $r^2 = 9.84$ ). A common, widespread and clinically useful bradykinin-controlled mechanism for enhancing vascular permeability was discovered.

#### Interpretation

This study is the first to establish the pathogens responsible for the majority of Gram-negative burn wound infections. 1 The bradykinin-controlled vascular permeability enhancement elicited by the

majority of Gram-negative bacteria can be used to target bioactive molecules through an Enhanced Permeability and Retention effect. 2

1. Azzopardi E. et al. PloS One. 2014, 9: e95042.

.2 Azzopardi E, et al. The Lancet. 2014, 383: S9.