Reactive Oxygen – a novel antimicrobial agent?

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Disclosures

- Consulting or lecture honoraria from Bayer, Wyeth, Janssen-Cilag, Pfizer, Astra Zeneca, Cubist, Merk, Motif Bio and Matoke

- Investigator on antibiotic trials for Bayer, Pfizer, Basilea, Wyeth, Astra Zeneca

- On Executive committee of ISAC & past General Secretary of British Society of Antimicrobial Chemotherapy
Chief Medical Officer: Drug resistance could take healthcare back to the 1800s

last updated Mon 11 Mar 2013

Antibiotic resistance is exacerbated by patients not completing their prescribed courses. Photo:

The government's top medical advisor has warned that antibiotic resistance could bring about a return to the hospital conditions of the nineteenth century when patients risked dying of infections from routine operations.
Antibiotic alternatives

- Bacteriophages
- Probiotics
- Antibiotic resistance breaker molecules
- Bioelectronics
- Reactive oxygen
Reactive Oxygen – an antibiotic alternative or an antibiotic?

Modification of a natural product derived from another organism, able to kill and inhibit most bacteria (and viruses and fungi)

Current licensed agent is a topical treatment based on engineered honey (SHRO) which is:

- Safe and non-toxic
- Highly Antimicrobial
- Sustained release
What is Reactive Oxygen (RO)?

- RO can attack a variety of targets to exert antimicrobial activity
- Most RO is formed by partial reduction of molecular oxygen
- Four major RO are recognized comprising: superoxide ($O_2^-$), hydrogen peroxide ($H_2O_2$), hydroxyl radical (-OH), and singlet oxygen ($^1O_2$), but they display very different kinetics and levels of activity.
- An RO mechanism exists in many bactericidal antibiotics
- Engineered honey (Surgihoney) produces sustained release of RO
- Coupling chemistry between $H_2O_2$ and polyphenols, rather than $H_2O_2$ alone, may exert the oxidative effect causing bacterial growth arrest and DNA degradation

Technology allows for accurate delivery of low levels of H$_2$O$_2$ (Reactive Oxygen Species) at a controlled antimicrobial potency and therapeutic dose to the wound site for a sustained period of time.
Criteria for any new therapy

- Is it effective?
- Is it safe?
- Is it worth it?
The antimicrobial activity of prototype modified honeys that generate reactive oxygen species (ROS) hydrogen peroxide.
Engineered honey: In vitro antimicrobial activity of a novel topical wound care treatment

Matthew Dryden a,*, Gemma Lockyer a, Kordo Saeed a, Jonathan Cooke b,c

Abstract
Surgihoney is a novel engineered organic honey product for wound care. Its antimicrobial activity can be controlled and adjusted by the engineering process, allowing preparation of three different potencies, labelled Surgihoney 1–3. Susceptibility testing of a range of wound and ulcer bacterial isolates to Surgihoney by the disc diffusion method, minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) determination, and time–kill measurements by time suspension tests were performed. Surgihoney demonstrated highly potent inhibitory and cidal activity against a wide range of Gram-positive and Gram-negative bacteria and fungi. MICs/MBCs were significantly lower than concentrations likely to be achieved in topical clinical use. The topical concentration of Surgihoney in wounds was estimated at ca. 500 g/L. MICs/MBCs for Staphylococcus aureus were 32/125 g/L for Surgihoney 1 and 0.12/0.25 g/L for Surgihoney 3. Cidal speed depended on potency, being 48 h for Surgihoney 1 and 30 min for Surgihoney 3. Maintenance of the Surgihoney inoculum preparation for up to a week demonstrated complete cidal activity and no bacterial persistence. Surgihoney has wide potential as a highly active topical treatment combining the effects of the healing properties of honey with the potent antimicrobial activity of the engineered product for skin lesions, wounds, ulcers and cavities. It is highly active against multidrug-resistant bacteria. It is more active than other honeys tested...
RO Surgihoney active against Gram positive and negative bacteria tested

Inhibitory zone sizes with Medihoney and different potencies of Surgihoney (S1–3).

<table>
<thead>
<tr>
<th>Organism (no. of strains)</th>
<th>Mean (range) inhibitory zone size (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S1</td>
</tr>
<tr>
<td>Meticillin-susceptible <em>Staphylococcus aureus</em> (12)</td>
<td>36.2 (32–38)</td>
</tr>
<tr>
<td>Meticillin-resistant <em>S. aureus</em> (6)</td>
<td>35.6 (31–38)</td>
</tr>
<tr>
<td>β-Haemolytic streptococci (6)</td>
<td>40.0 (35–42)</td>
</tr>
<tr>
<td><em>Enterococcus</em> spp. (5)</td>
<td>38.0 (34–39)</td>
</tr>
<tr>
<td><em>Escherichia coli</em> (6)</td>
<td>33.4 (30–37)</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em> (2)</td>
<td>34.2 (30–38)</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em> (4)</td>
<td>25.8 (20–28)</td>
</tr>
<tr>
<td><em>Acinetobacter lwoffi</em> (1)</td>
<td>32.1</td>
</tr>
<tr>
<td><em>Bacteroides fragilis</em> (1)</td>
<td>22.3</td>
</tr>
<tr>
<td><em>Propionibacterium acnes</em> (1)</td>
<td>19.7</td>
</tr>
<tr>
<td><em>Candida</em> spp. (3)</td>
<td>9 (8–10)</td>
</tr>
<tr>
<td><em>Aspergillus fumigatus</em> (1)</td>
<td>8</td>
</tr>
</tbody>
</table>

Time kill curves for SHRO against MSSA, MRSA, VRE, E.coli and Ps. aeruginosa
Effect of RO on chronic wound biofilm
SHRO prevents and reduces biofilm production by Pseudomonas sp and Acinetobacter sp.

- SHRO can prevent biofilm formation and reduce the seeding of pre-formed biofilms.
- SHRO is a promising topical antimicrobial agent with potent anti-biofilming activity against key Gram-negative pathogens of burn wounds.

Figure 1: Production of ROS during *Xenopus* tadpole tail regeneration.

From

*Amputation-induced reactive oxygen species are required for successful *Xenopus* tadpole tail regeneration*

Nick R. Love, Yaoyao Chen, Shoko Ishibashi, Paraskevi Kritsiligkou, Robert Lea, Yvette Koh, Jennifer L. Gallop, Karel Dorey & Enrique Amaya

*Nature Cell Biology* 15, 222–228 (2013) | doi:10.1038/ncb2659

Received 18 June 2012 | Accepted 26 November 2012 | Published online 13 January 2013

(a) Bright-field and fluorescence micrographs of a tadpole derived from the F1 generation of a transgenic *X. laevis* line that expresses the H$_2$O$_2$ sensor HyPerYFP ubiquitously$^{10}$. (b) HyPerYFP transillumination (Trans) imaging of a representative regenerating tadpole tail. H$_2$O$_2$ is derived from the excitation ratio of HyPer YFP and HyPerGFP. A 1:1 HyPer YFP:GFP ratio and transillumination threshold were used to generate images. Scale bars: 400 μm. 1,000 μm.
Clinical experience

• Is it effective *in-vivo*?

• Licensed agent is Surgihoney RO

• Antimicrobial and controls biofilm
Bacterial bioburden and biofilm
Antibiotics do not work well

- Chronic wounds
- Ulcers
- Wound infection prevention
- Chronic sinusitis
- Chronic wet ear
- Chronic respiratory diseases
  - COPD
  - Cystic fibrosis
  - Bronchiectasis
- Chronic recurrent cystitis
- Prosthetic material infection
- MASSIVE DISEASE BURDEN
Topical treatment with SHRO in wounds
Observational study: 114 skin and soft tissue lesions

- Hospital
  - Diabetic foot ulcers
  - Ischaemic ulcers
  - Varicose ulcers
  - Intravascular catheter line sites in oncology
  - Surgical wounds

- Primary care
  - Diabetic foot ulcers
  - Ischaemic ulcers
  - Varicose ulcers

- Developing world
  - Surgical, traumatic, tropical and non-healing lesions.

Chronic wounds

91 year old independently mobile lady, lived with nephew – progressively severe and painful venous leg ulcers.

Reactive oxygen treatment over 14 days reduced the inflammation and pain, reduced bioburden and slough.

This could all have been managed in the community, saving a hospital admission.

77 year old man

Peripheral vascular disease

Large ischaemic ulcers

Non healing

Heavily colonised with MRSA, VRE, coliforms and Pseudomonas aeruginosa.

## 114 chronic wounds: treatment with Surgihoney RO – Patient demographics

<table>
<thead>
<tr>
<th>Wound type</th>
<th>Number of patients</th>
<th>Average age (years)</th>
<th>Mean wound duration (months)</th>
<th>Mean number comorbidity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leg ulcers</td>
<td>37</td>
<td>76 (32-91)</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Pressure ulcers</td>
<td>19</td>
<td>76 (45-97)</td>
<td>5.4</td>
<td>3.8</td>
</tr>
<tr>
<td>Surgical wounds</td>
<td>14</td>
<td>54 (0-76)</td>
<td>1.9</td>
<td>4.7</td>
</tr>
<tr>
<td>Diabetic ulcers</td>
<td>9</td>
<td>67 (53-87)</td>
<td>4.2</td>
<td>4</td>
</tr>
<tr>
<td>Central Catheter Site Infections</td>
<td>2</td>
<td>44</td>
<td>n/a</td>
<td>3</td>
</tr>
<tr>
<td>Suprapubic catheter site</td>
<td>1</td>
<td>61</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Traumatic wounds</td>
<td>12</td>
<td>72.8 (21-90)</td>
<td>2</td>
<td>3.2</td>
</tr>
<tr>
<td>Other topical infections</td>
<td>3</td>
<td>63 (22-95)</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Developing world</td>
<td>17</td>
<td>40.5 (23-82)</td>
<td>3.6</td>
<td>2.2</td>
</tr>
</tbody>
</table>

### Clinical response of 114 chronic wounds to treatment with Surgihoney RO.

*ALL cases (100%) showed improvement in either healing criteria or bacterial load. Adverse effects – 2.6% reported stinging.

<table>
<thead>
<tr>
<th>Wound type*</th>
<th>Reduction in bacterial load %</th>
<th>&gt;20% Reduction in wound size %</th>
<th>% Improvement in healing criteria (Dx, slough, inflammation)</th>
<th>Mean duration of treatment (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leg ulcers</td>
<td>88</td>
<td>68</td>
<td>92</td>
<td>24 (8-130)</td>
</tr>
<tr>
<td>Pressure ulcers</td>
<td>100</td>
<td>63</td>
<td>89</td>
<td>27.4 (14-80)</td>
</tr>
<tr>
<td>Surgical wounds</td>
<td>87</td>
<td>71</td>
<td>86</td>
<td>34.5 (14-62)</td>
</tr>
<tr>
<td>Diabetic ulcers</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>35.5 (10-131)</td>
</tr>
<tr>
<td>Central Catheter Site Infections</td>
<td>100</td>
<td>n/a</td>
<td>100</td>
<td>9</td>
</tr>
<tr>
<td>Suprapubic catheter site</td>
<td>100</td>
<td>n/a</td>
<td>100</td>
<td>12</td>
</tr>
<tr>
<td>Traumatic wounds</td>
<td>100</td>
<td>58</td>
<td>100</td>
<td>32.3 (7-90)</td>
</tr>
<tr>
<td>Other topical infections</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>37.3 (8-94)</td>
</tr>
<tr>
<td>Developing world</td>
<td>n/a</td>
<td>88</td>
<td>94</td>
<td>19.6 (8-64)</td>
</tr>
</tbody>
</table>

Mr RL 66yr old

- Accountant
- Enlarging scabby lesion on upper lip
- Slowly got bigger over 2 months
- Been to GP
- Swab ++ commensals
- Given several courses of antibiotics
- Flucloxacillin, co amoxiclav, clindamycin
- No effect

- Referred to dermatology
- Swabs and fungal tests NAD
- Biopsy – folliculitis
- Nothing unusual in history, no travel, no bites, no animal contact.
Treated with daily topical Surgihoney RO for 2 weeks
**Necrotising Fasciitis with Multi-Drug Resistant Colonisers**

A Suebsaeng1, L Wingate-Saul1, M Dryden2,3

1. Royal Hampshire County Hospital, Winchester, 2. Department of Microbiology and Infection, Hampshire Hospitals NHS Foundation Trust; 3. Rare and Imported Pathogens Department, Public Health England, Porton Down, UK

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**Case Presentation**

- 77 year old male presented with a painful right leg on return from holiday
- He had been treated for gastroenteritis with IV fluids at a hospital in India

**Examination**

- Afebrile, stable
- Right lower leg: tender, swollen and erythematous. Two dusky areas (on the lateral aspect and on the dorsum of the foot) which were open and purulent

**Investigations**

- CRP and WCC elevated
- US and MRI: 2 x subcutaneous collections at the dorsum of the foot (5 x 7 x 2 cm) and lateral margin of right leg (> 9cm long)
- Wound swabs:
  - *S. aureus* - fully sensitive
  - *Group A Streptococcus* – fully sensitive
  - *Enterobacter cloacae*
  - *E. coli*
  - *Acinetobacter spp.*

*Carbapenemase-Producing Enterobacteriaceae (CPE): resistant to amoxicillin, co-amoxiclav, ceftriaxone, ciprofloxacin, co-trimoxazole, gentamicin, piperacillin/tazobactam, temocillin; and sensitive only to fosfomycin, tigecycline and polymyxin

**Diagnosis & Management**

- Necrotising fasciitis diagnosed on the basis of clinical picture; radiology; and microbiology
- Necrotising fasciitis is a surgical emergency
- Urgent debridement
- IV flucloxacillin (2g QDS) and clindamycin (1.2g QDS)
- Isolation
- Daily Surgihoney RO (Reactive Oxygen) dres
- Later: reconstructive surgery

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**Necrotising Fasciitis**

- Potentially lethal soft tissue infection – mortality 10-40%1,2
- Rare: incidence 4 per 100,0001,2
- Inflammation and necrosis of muscle fascia which can then spread to muscle and subcutaneous fat3
- Progression can be very rapid with skin necrosis occurring only after extensive destruction of underlying structures1,4

**Type 1**: polymicrobial – anaerobic bacteria2
**Type 2**: monomicrobial – most commonly GAS; also other staphylococcal / streptococcal species2

**Clinical features1,5:**
- Swelling and erythema
- Rapid progression
- Disproportionate pain
- Bullae / crepitus / frank cutaneous gangrene
- Overlying skin initially spared
- Patient systemically unwell

**Microbiology**

- *Group A Streptococcus* most likely pathogen +/- *S. aureus*,3
- The Gram negative organisms were likely colonisers
- These were Carbapenemase-Producing Enterobacteriaceae
- Carbapenemase is an extended spectrum beta-lactamase enzyme which confers extensive resistance6
- CPE commonly nosocomial – and an epidemiological link with the Indian subcontinent6,7,8
- Their eradication was important in case they caused infection in this patient or in others
- They were not sensitive to flucloxacillin or clindamycin and were not targeted with antibiotics – but they were eradicated
- Wound swabs were consistently sterile 10 days after debridement and treatment with daily Surgihoney RO dressings

**Surgihoney RO (Reactive Oxygen)**

Surgihoney RO is pharmaceutical grade honey that has been engineered to increase its antimicrobial activity. It works by several mechanisms: its low pH, osmotic dehydration, and the continuous release of highly antimicrobial oxygen radicals. It is a novel therapy for open soft tissue lesions and may prove an important therapy in lesions with a high bacterial bioburden and biofilm, to eradicate or reduce heavy bacterial loads, and promote healing. Surgihoney RO is the first agent available for clinical use that employs novel Reactive Oxygen technology. It works as a powerful antimicrobial in vitro against Gram positive and Gram negative organisms, including multi-drug-resistant strains.9-11 It is effective in acute and chronic wound infection and in the prevention of surgical wound infection.11,12

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**References**

3. Dryden M, Lockyer G (2014); 2: 3, 168-172
4. Dryden M, Dickinson A (2016); 5
6. Greenwood D, Barer M (2005) Enterobacteriaceae and lateral margin of right leg (> 9cm long) which were open and purulent
10. Greenwood D, Barer M (2005) Enterobacteriaceae and lateral margin of right leg (> 9cm long) which were open and purulent

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**Conclusions**

This case is important as an example of:
- Necrotising fasciitis – a rare and dangerous surgical emergency
- Successful management of necrotising fasciitis through a combination of debridement and plastic surgery, antibiotics, Surgihoney RO and infection control procedures
- Multi-drug resistant organisms likely imported from abroad
- The eradication of those organisms through debridement surgery, Surgihoney RO and infection control measures

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**Day 14**

**At 2 months (i)**

**Post debridement**

**Day 7**

**At 2 months (ii)**
CA MRSA superficial infection treated with SurgihoneyRO

Day 1

Day 5

Day 10
RO in infection prevention and control
Paediatric MRSA wound colonisation / infection

The use of Surgihoney to prevent or eradicate bacterial colonisation in dressing oncology long vascular lines

**Objective:** A pilot evaluation was performed to assess the effects of Surgihoney, an engineered honey with highly active antimicrobial activity, on bacterial colonisation in long lines in oncology patients.

**Method:** This prospective service evaluation was conducted at Hampshire Hospitals NHS Foundation Trust (HHFT) in England, UK, between 2012 and 2013. The study population consisted of oncology patients with central intravenous lines who were receiving outpatient chemotherapy. All patients were offered line dressing with or without Surgihoney, applied to the line exit site.

**Results:** The primary outcome measure of the study was the presence or absence of bacterial colonisation of the line site. There were 30 patients in each arm – with or without Surgihoney. In the Surgihoney arm, 2 patients with existing line site colonisation were cleared of bacterial colonisation and none acquired colonisation during the study period. In the non-treatment arm, 6 patients were colonised at the line site prior to screening or during the evaluation. Bacterial colonisation was maintained throughout the period.

**Conclusion:** Surgihoney is an effective antimicrobial line-site dressing, significantly reducing line site colonisation and eradicating existing colonisation. It was well tolerated by the patients.

**Declaration of Interest:** Surgihoney supplies were donated by Healing Honey International (HHI) who also provided some funding to Hampshire Hospitals Foundation Trust for microbiological investigation. MD and JC have provided clinical advice in an advisory capacity to HHI.
Central line colonised with CPE

Carbapenemase-producing enterobacteriaceae (CPE) at line insertion site cleared with Reactive Oxygen treatment

Trauma wound treated with SurgihoneyRO
RO in surgical prophylaxis

Complex joint replacement surgery

- 2 current evaluations in complex surgery
  - Abdominal reconstruction
  - Cytoreductive surgery in pseudomyxoma

- Preliminary results promising
  - No infection and tolerated
Using antimicrobial Surgihoney to prevent caesarean wound infection

Caesarean section (CS) is a common operation in obstetric practice. There has been a national increase in caesarean wound infection (8–24.6%) (National Institute for Health and Care Excellence (NICE), 2011; Paranjothy et al., 2005; NHS Information Centre for Health and Social Care, 2009) and a wide variation across NHS hospitals (ranging from 13.6 to 31.9%) associated with the 147,726 cases of CS each year in the UK (Bragg et al., 2010). A recent survey showed a national average wound infection rate of 9.6% (Wloch et al., 2012a). Caesarean wound infection is a major cause of prolonged hospital stay and resource consumption, as well as other morbidity and mortality. Recovery from CS is more difficult for women who develop post-operative wound infection (Wloch et al., 2012a). In terms of the burden on health-care resources, the cost of each case of CS infection has been estimated to be between £300 and more than £17,000, depending on severity (Wloch et al., 2012b).

Surgihoney™ (Healing Honey International, UK) is a licensed sterile product which has been developed for wound care and as a prophylactic dressing. It is prepared by combining 85% (v/v) manuka honey (MGO ≥ 550) with a unique combination of biocompatible excipients. The dressing is applied directly to the wound site without any additional gauze layer. This study aimed to evaluate the clinical and cost-effectiveness of Surgihoney compared with the existing surgical site antisepsis procedures in women undergoing CS.

Abstract
Caesarean section (CS) wound infection rates are unacceptably high; around 10% according to figures from the Health Protection Agency (2012). This service evaluation assessed the effects of Surgihoney on surgical site infection rates in women undergoing caesarean section. All women presenting for CS were offered Surgihoney as a single application wound dressing at the end of the procedure. All women were followed up and examined for surgical site infection for 30 days after CS. A single application of Surgihoney dressing reduced surgical site infection (SSI) by 60.33% from a rate of 5.42% (n=590) to 2.15% (n=186) (p-value=0.042). The potential saving to the NHS of using Surgihoney as a single application achieving this level of wound infection reduction is considerable. Surgihoney offers a simple, cost-effective intervention to reduce SSI in women undergoing CS. It is applicable to practice in all health economies and could potentially save considerable surgical infective morbidity in patients undergoing surgical delivery.

Methods
Clinical Evaluation
The evaluation was an observational study with temporal comparison of CS surgical site infection (SSI) rates. It was primarily a service evaluation for the use of Surgihoney antimicrobial dressing.
SHRO prophylaxis in abdominal wall reconstruction.

- **18 patients to date**
  - 3 grade 4 ventral hernias with enterocutaneous fistulae
  - 15 grade 3 ventral hernias with contaminated stoma or wound infections
  - All healed with surgery + SHRO
  - Adverse events – 1 dehiscence, 2 subcut haematoma. NO infections on the background of a high infection rate
  - Reduced morbidity. Reduction in hospital stay and antibiotic use.

Intestinal Failure Service

The Intestinal Failure (IF) Service at UCH is a multidisciplinary service managing the complex needs of patients with gastrointestinal fistulas. The team includes consultant surgeons, anaesthetists, radiologists and nutritional gastroenterologists, as well as specialist nurses with expertise in this area. At UCH we aim to assess patients referred to us quickly and plan every aspect of their care effectively.

**Conditions treated**
- Enterocutaneous fistulas (ECFs)
- Intra-abdominal fistulas
- Abdominal wall defects and massive hernias

Personal communication S Parker & A. Wilson, Dept of Surgery UCHL
Honey as a Novel Antimicrobial Coating in Salvage Revision Total Knee Arthroplasty
Rhodri Llywelyn Williams, Wasim Khan, Amisha Mehta, Rhydian Morgan-Jones
Department of Orthopaedic Surgery, University Hospital of Wales, Cardiff UK

Aim: Honey has been used as a topical antiseptic for at least 5,000 years. SurgiHoney is a CE licensed sterile product, which has been proven to be non-toxic and effective when used topically in the treatment of chronically infected wounds. The key difference from other medical grade honey is the broad spectrum antimicrobial characteristics with activity against Gram +ve, Gram –ve and multi-resistant organisms. Its novel role against the bacterial bio burden and biofilm associated with periprosthetic infections around total knee arthroplasties (TKA’s) is therefore considered.

The Cardiff Debridement Strategy
• Surgical: Explantation & Sharp Dissection
• Mechanical: Curettage, Reraming, Lavage
• Chemical: Honey
  Repeated Cyclical Debridement

Methods: SurgiHoney was used as an implant coating immediately prior to wound closure after implantation of salvage endoprosthesis for multiply revised, infected TKA’s undergoing staged reconstruction.

Results: During application of the Surgihoney we report no systemic adverse features. Physiological parameters including heart rate, respiratory rate and blood pressure were recorded and did not change significantly during and after the application. We also report good soft tissue and wound healing. Post-operatively we did not experience any wound complications or delayed wound healing. No early recurrent infection has been identified at early follow-up (6 to 12 months)

<table>
<thead>
<tr>
<th>Operation (*previous multiple surgeries)</th>
<th>Microbe</th>
<th>Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>*2nd stage</td>
<td>Polymicrobial: Pseudomonas, Mycellial fungus, CNS, Enterobacter</td>
<td>6 months</td>
</tr>
<tr>
<td>*2nd stage</td>
<td>Polymicrobial: CNS aureus, Enterobacter, Mycellial fungus</td>
<td>8 months</td>
</tr>
<tr>
<td>*2nd stage</td>
<td>Polymicrobial: CNS aureus, Aspergillus</td>
<td>12 months</td>
</tr>
<tr>
<td>*2nd stage</td>
<td>Polymicrobial: including CNS aureus and various anaerobes</td>
<td>11 months</td>
</tr>
</tbody>
</table>

Conclusion: The use of Surgihoney as a novel anti-microbial is established in the management of complex wound infections. This is the first reported use of SurgiHoney as a deep, implant coating in the salvage of prosthetic joint infection.
Novel approach to conflict and war wounds – presented at 1st Global Conflict Medicine Congress, Beirut May 2017

- Trauma conflict wounds very high rate of MDR contamination
- Cause? Overuse of prophylactic antibiotics and poor IPC or environmental contamination?
- Solution: Improve IPC reduce broad spectrum antibiotic use. Prophylax wounds with RO.
- Needs trials but success with Manchester bombing victims

Dryden M, Antibiotic treatment of MDR wound infection, MEMA, Beirut, May 2017
Personal comm. Wong J, Plastic Surgery, Manchester 2017
Severe fungal kerion infection (T.tonsurans) treated with topical SHRO
Skin scraping results – Trichophyton tonsurans
First treatment for rhinosinusitis.
Reactive Oxygen (RO) v coamoxiclav in H. influenzae biofilm

Data from Allen R, Salib R. University of Southampton Medical School, UK 2017
ENT infections – a role for RO

Ear biofilm infections

Chronic sinusitis
Future developments in the lower respiratory tract

Nebulised RO in COPD/bronchiectasis

- Tolerated in ‘healthy’ doctor (left)
- Used in compassionate treatment in 3 patients
- Reduction in respiratory tract bacterial load
- Eradication of Mycobacterium avium in bronchiectasis patient with a 2 month follow up.
Intraperitoneal SHRO gel

- 17 year old boy with severe autism. Abdominal pain for a week but refused to allow anyone to examine him.
- Admitted to hospital 06.03.2017 with perforated appendix. High inflammatory markers CRP 340, WBC 25., PCT 47.
- Emergency surgery – four quadrant peritonitis, abdomen washed out.
- Transferred to ITU, remained sedated and ventilated to avoid him pulling out all the tubes.
- Abdomen distended with abdominal drain draining faeculent fluid. The microbiology of this grew Esch.coli, enterococci and Candida albicans. He was treated with systemic antibiotics and antifungals: co amoxiclav, gentamicin, metronidazole and fluconazole, and in addition received intraperitoneal SHRO 100mg down the abdominal drain daily.
- No further surgery carried out. SHRO well tolerated.

Tam Al-Ani, Abstract, Surgical Intensive Care Soc 2017
RO in persistent urosepsis

- 3 cases treated with RO to date on compassionate grounds
- Reduction in inflammatory markers in the urine and in bacteriuria
- No further admissions for urosepsis

Clinical register Hampshire Hospitals 2017
Reactive Oxygen - Summary of a novel antimicrobial development

- Novel technology with broad antimicrobial activity (bacteria, virus and fungal)
- Clinical availability in UK of a pharmaceutical grade product for wound care, Surgihoney
- Role for RO in infection prevention and antimicrobial stewardship
- Potential for a wide range of clinical applications for treating skin and mucosal bacterial overgrowth and biofilm production AND surgical prophylaxis
- Novel delivery mechanisms being developed: powder, gel, liquid, nebuliser, nanofibre, targeted injectables.
- Initiation and delivery of a diverse programme of clinical evaluation with highly promising results.
- Need for RCTs
Thank you

Acknowledgements.
The following colleagues have contributed to research presented here:

- **Matoke Ltd**: [www.surgihoneyro.com](http://www.surgihoneyro.com); [www.matokeholdings.com](http://www.matokeholdings.com)
- **Hampshire Hospitals Foundation NHS Trust**: Kordo Saeed, Amy Dickson, Gemma Lockyer
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- **UCHL**: Sam Parker, Mr A Wilson