

**The rational for local antibiotic use in
surgery to prevent post-operative
infection is based on myth and not
science
AGAINST THE MOTION**

2017

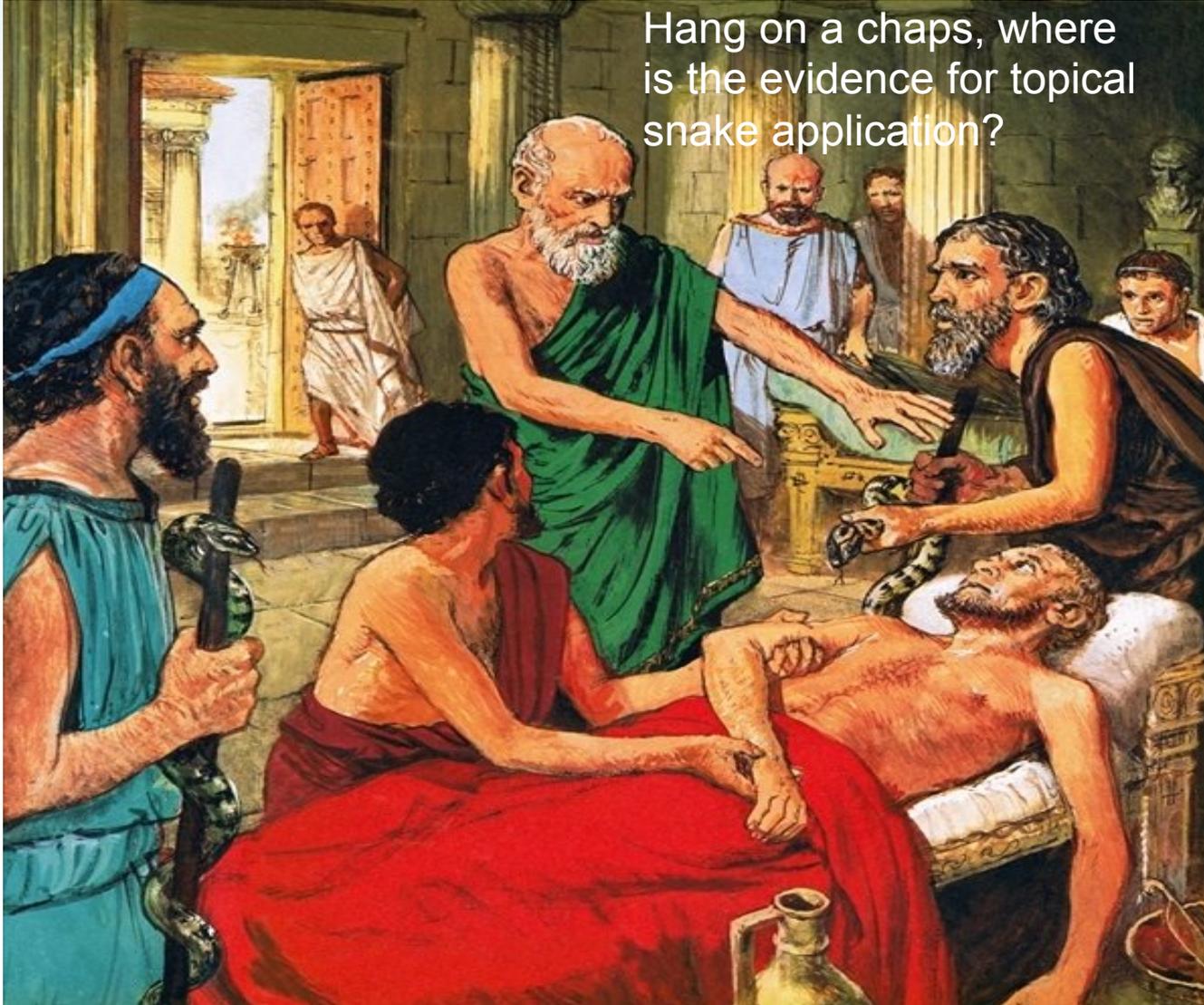
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Disclosures

- **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**

Topical antibiotic use – a lot of it about, but where is the evidence?

Hang on a chaps, where is the evidence for topical snake application?



A brief straw poll amongst colleagues

- Orthopaedic
- General surgery
- Plastics
- ENT
- Ophthalmology
- Dermatology
- Interventional cardiology
- A&E
- GPs

- Widely used
- Great geographical and specialty variation in use.

History of Medicine



I have a surgical infection.

2000 B.C. - Here, eat this root and put poultice on wound.

1000 A.D. - That root is heathen, say this prayer.

1850 A.D. - That prayer is superstition, drink this potion.

1940 A.D. - That potion is snake oil, swallow this pill.

1975 A.D. - That pill is ineffective, take this antibiotic.

2017 A.D. - That antibiotic destroys your microbiome and causes resistance. Here, eat this root and put poultice on wound.

Short-Term Antibiotic Treatment Has Differing Long-Term Impacts on the Human Throat and Gut Microbiome

Jakobsson HE et al., , March 24, 2010 <https://doi.org/10.1371/journal.pone.0009836>

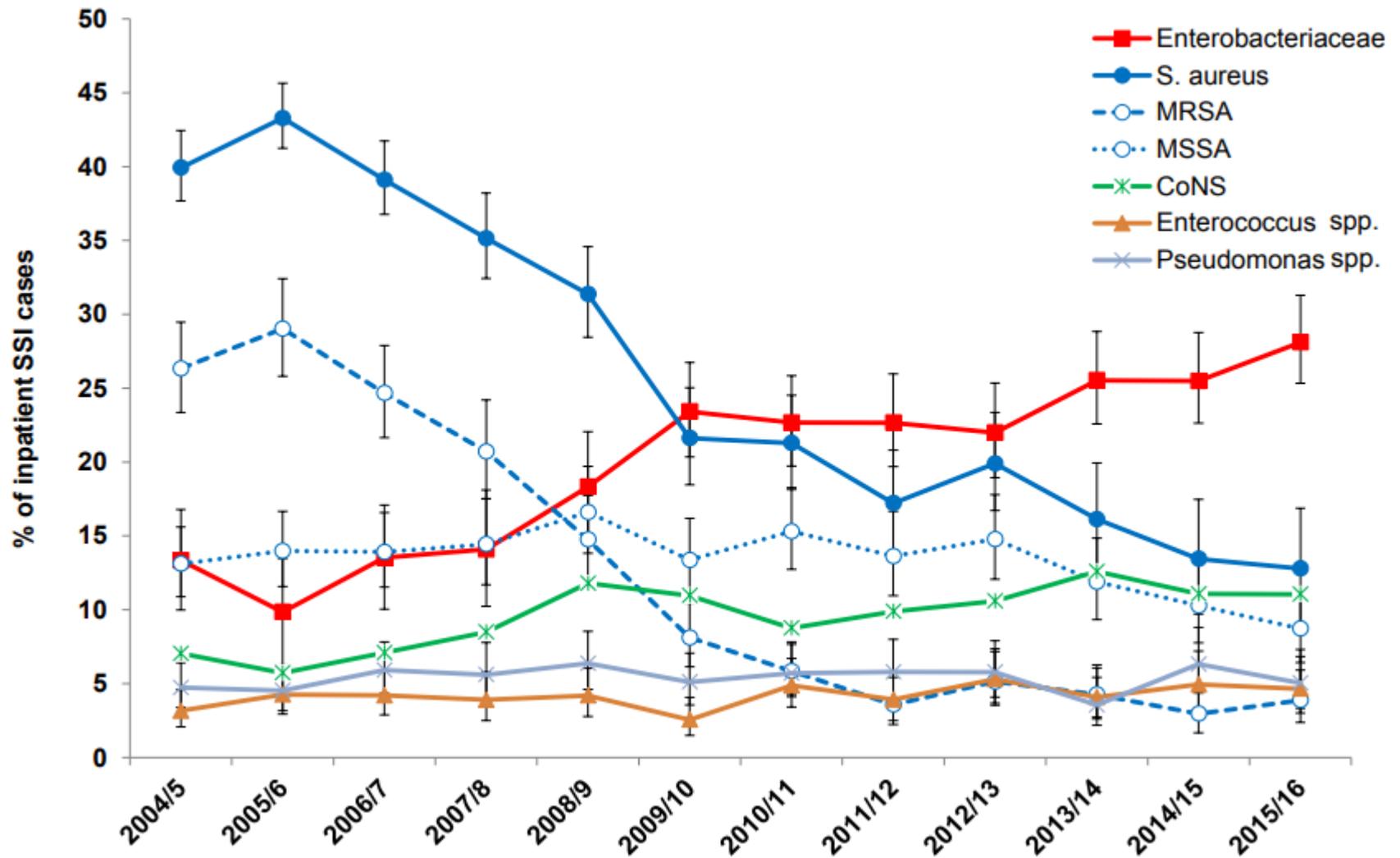
Systemic antibiotic use is like napalm – it destroys all with long-term consequences. It is ecological vandalism.



Four years after treatment high levels of the macrolide resistance gene *erm*(B) were found, indicating that antibiotic resistance, once selected for, can persist for longer periods of time than previously recognized.

This highlights the importance of a restrictive antibiotic usage in order to prevent subsequent treatment failure and potential spread of antibiotic resistance.

Trends in micro-organisms reported as causing inpatient SSIs



IV surgical prophylaxis: why do we use it?

- **To prevent surgical infection**
- **Evidence based. Really? What quality of evidence?**
- **Prior to incision**
- **Need rapid tissue levels**
- **Choice of antibiotic depends on likely contaminating microbes**
- **Single dose currently in vogue**

Topical antibiotics: why not?

- **Pros**

- High sustained local concentration
- No disruption of microbiome
- Active at the site of entry of infection
- No systemic toxicity
- No C.difficile
- May be particular benefit for high risk eg DM, smokers, ischaemic etc

- **Cons**

- contact dermatitis
- interference with wound healing
- the potential for increased antibiotic resistance
- cytotoxicity

Strategy 293121/saved

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Contents 37 of 37 results on Saved Results

1. Topical vancomycin: Does it reduce surgical site infection in bone tumors?.....	Page 3
2. Routine Use of Topical Bacitracin to Prevent Sternal Wound Infections After Cardiac Surgery	Page 3
3. Considering a new domain for antimicrobial stewardship: Topical antibiotics in the open surgical wound	Page 3
4. Hot Topics in Perioperative Antibiotics for Cataract Surgery.....	Page 4
5. Intraoperative Topical Antibiotics for Infection Prophylaxis in Pelvic and Acetabular Surgery.....	Page 4
6. Direct sternal administration of Vancomycin and Gentamicin during closure prevents wound infection	Page 4
7. Superficial Vancomycin Coating of Bone Cement in Orthopedic Revision Surgery: A Safe Technique to Enhance Local Antibiotic Concentrations.....	Page 5
8. The Effect of Antibiotic-Coated Sutures on the Incidence of Surgical Site Infections in Abdominal Closures: a Meta-Analysis.....	Page 5
9. Topical approaches to improve surgical outcomes and wound healing: A review of efficacy and safety.....	Page 6
10. Vancomycin Paste Does Not Reduce the Incidence of Deep Sternal Wound Infection After Cardiac Operations.....	Page 6
11. A review of the application of vancomycin powder to posterior spinal fusion wounds with a focus on side effects and infection. A prospective study.....	Page 7
12. Perioperative antibiotics to prevent acute endophthalmitis after ophthalmic surgery: A systematic review and meta-analysis.....	Page 7
13. The effect of vancomycin powder on the rates of infection and pseudarthrosis in lumbar spine surgery: A retrospective analysis of 453 patients.....	Page 8
14. Topical Antimicrobials and the Open Surgical Wound.....	Page 8
15. Intra-Wound Antibiotics and Infection in Spine Fusion Surgery: A Report from Washington State's SCOAP-CERTAIN Collaborative.....	Page 9
16. Topical spraying of cefazolin and gentamicin reduces deep sternal wound infections after heart surgery: a multicenter, large volume, retrospective study.....	Page 9
17. Local administration of gentamicin collagen sponge in surgical excision of sacrococcygeal pilonidal sinus disease: a systematic review and meta-analysis of the literature.....	Page 10
18. Meta-analysis of local gentamicin for prophylaxis of surgical site infections in colorectal surgery.....	Page 10
19. A Retrospective Study on the Protective Effects of Topical Vancomycin in Patients Undergoing Multilevel Spinal Fusion.....	Page 11
20. Prophylactic peri-operative local antibiotic irrigation.....	Page 11
21. Reducing surgical site infections following craniotomy: Examination of the use of topical vancomycin.....	Page 12
22. Local Application of Gentamicin in the Prophylaxis of Perineal Wound Infection After Abdominoperineal Resection: A Systematic Review.....	Page 12
23. Comparison of 1-day versus 1-hour application of topical neomycin/polymyxin-B before cataract surgery.....	Page 13
24. Topical antibiotic prophylaxis for prevention of surgical wound infections from dermatologic procedures: A systematic review and meta-analysis.....	Page 13
25. Topical intrawound application of vancomycin powder in addition to intravenous administration of antibiotics: A meta-analysis on the deep infection after spinal surgeries.....	Page 14
26. Collagen implant with gentamicin sulphate reduces surgical site infection in vascular surgery: A prospective cohort study.....	Page 14

SIGN guidance

on antibiotic prophylaxis in surgery 2008, updated 2014

- **There is evidence that supplementary application of resorbable gentamicin-impregnated collagen fleeces after abdominoperineal excision of rectal cancer or gentamicin-collagen implant between the two halves of the sternum after cardiac surgery, may minimise wound infection after surgery.**
- **Results from studies on the use of intranasal mupirocin to prevent SSI are inconsistent due to small sample size, design differences and mixed surgical groups. A meta-analysis suggests that its use should be considered in non-general surgery, for example, cardiothoracic or orthopaedic procedures**
- **BUT intranasal mupirocin should be used to prevent MRSA infection**
- **Grommet insertion – topical antibiotics recommended.**

- **Joint replacement: A large retrospective study showed that a combination of IV prophylactic antibiotic and antibiotic impregnated bone cement is more effective than IV prophylaxis alone in reducing the risk of SSI. Compared to the combined regimen, patients who received antibiotic prophylaxis only systemically had a 1.4 times higher revision rate with all reasons for revision as the end point ($p=0.001$), 1.3 times higher with aseptic loosening ($p=0.02$) and 1.8 times higher with infection as the end point ($p=0.01$).**
- **In addition to intravenous antibiotics, impregnated cement is recommended for cemented joint replacements.**
- **Intracameral antibiotic prophylaxis is recommended for cataract surgery.**
- **Intracameral or intravitreal intraocular antibiotic prophylaxis is recommended at completion of surgery for penetrating eye injuries (dependent on extent of injury and the presence or absence of an intraocular foreign body)**
- **In adults, intraventricular prophylactic antibiotic at time of insertion of a ventriculoperitoneal (VP) shunt reduced the shunt infection from 6% to 0.4% (RR 0.7, $p=0.0001$)**

Chloramphenicol

BMJ

RESEARCH

Does single application of topical chloramphenicol to high risk sutured wounds reduce incidence of wound infection after minor surgery? Prospective randomised placebo controlled double blind trial

Clare F Heal, senior lecturer,¹ Petra G Buettner, senior lecturer,² Robert Cruickshank, general practitioner,³ David Graham, general practitioner,³ Sheldon Browning, general practitioner,⁴ Jayne Pendergast, practice nurse,³ Herwig Drobetz, staff orthopaedic surgeon,⁵ Robert Gluer, medical student,¹ Carl Lisek, surgical registrar⁶

ABSTRACT

Objective To determine the effectiveness of a single application of topical chloramphenicol ointment in preventing wound infection after minor dermatological surgery.

Design Prospective randomised placebo controlled double blind multicentre trial.

Setting Primary care in a regional centre in Queensland, Australia.

Participants 972 minor surgery patients.

Interventions A single topical dose of chloramphenicol (n=488) or paraffin ointment (n=484; placebo).

Main outcome measure Incidence of infection.

Results The incidence of infection in the chloramphenicol group (6.6%; 95% confidence interval 4.9 to 8.8) was significantly lower than that in the control group (11.0%; 7.9 to 15.1) (P=0.010). The absolute reduction in infection rate was 4.4%, the relative reduction was 40%, and the relative risk of wound infection in the control group was 1.7 (95% confidence interval 1.1 to 2.5) times higher than in the intervention group. The number needed to treat was 22.8.

Conclusion Application of a single dose of topical chloramphenicol to high risk sutured wounds after minor surgery produces a moderate absolute reduction in infection rate that is statistically but not clinically significant.

Trial registration Current Controlled Trials ISRCTN73223053.

infection. Despite this, it is regularly used in areas outside its main indication. Before our study, several of the investigating general practitioners had applied it to sutured wounds as prophylaxis against wound infection. A survey of UK plastic surgeons reported that 66% used chloramphenicol eye ointment in their practice, mainly as prophylaxis against infection.⁴ The ointment has been used as an adhesive for replacement of the nail bed.⁵ A comprehensive Medline search found only one other study relating to the use of topical chloramphenicol ointment on wounds; this study investigated the application of chloramphenicol ointment to wounds after hip replacement.⁶ The incidence of wound infection in the intervention group was reduced (4% v 8%), but the sample size was small and the results were not statistically significant.

Topical ocular chloramphenicol is widely used in the United Kingdom and Australia for the treatment of conjunctivitis, but is very rarely prescribed for this indication in the United States.⁷ Some controversy previously existed about the link between aplastic anaemia and topical ocular chloramphenicol, on the basis of a small number of single case reports,⁷ but two international case-control studies provided no support for this association. Although the association between ocular chloramphenicol and aplastic anaemia cannot be excluded, the risk is less than one in a million per treatment course.⁸ No incidences of aplastic anaemia after dermatological application have been reported, despite widespread use.

- Ophthalmology
- ENT minor surgery
- Dermatology
- Plastic surgery

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Fusidic acid more effective than placebo in impetigo treatment

Primary care

Fusidic acid cream in the treatment of impetigo in general practice: double blind randomised placebo controlled trial

Sander Koning, Lisette W A van Suijlekom-Smit, Jan L. Nouwen, Cees M Verduin, Roos M D Bernsen, Arnold P Oranje, Siep Thomas, Johannes C van der Wouden

Abstract

Objective To test the hypothesis that fusidic acid would not increase the treatment effect of disinfecting with povidone-iodine alone in children with impetigo.

Design Randomised placebo controlled trial.

Setting General practices in Greater Rotterdam.

Participants 184 children aged 0-12 years with impetigo.

Main outcome measures Clinical cure and bacterial

the resistance of staphylococci to oral antibiotics such as erythromycin has increased dramatically.¹⁻¹¹ At the same time, topical antibiotic treatment with mupirocin has been shown to give results equal to or even better than oral treatment.^{1-9, 12-15} In general, children comply better with topically administered treatment than with oral treatment,¹⁵ and fewer systemic side effects occur.⁸

Fusidic acid is an antibiotic that has been available for a long time and is mainly used topically.¹⁴ It is rec-

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Fusidic acid more effective than placebo but increase in resistance with widespread use

Fusidic Acid

- **Fusidic acid is commonly prescribed for localised skin infections and to prevent infection in minor surgery**
- **Resistance to fusidic acid is rising and is approaching 50% in some areas. In particular, resistance rates are high in patients with long term dermatology problems such as eczema.**
- **The resistance induced is not stable and may fade if treatment is stopped**
- **Use only for short courses (1-2 weeks), then stop**
- **Fusidic acid should only be used on very localised lesions**
- **It should not be used regularly**

Bacitracin, Gramicidin, Tetracycline, Neomycin, Polymyxin

- **Bacitracin & zinc** – more allergic reactions – dermatitis in 8 – 15%
- ?Selection of USA300 (also neomycin res. Japan EID)
- Generally thought poorly efficacious
- Risk of resistance development to systemic antibiotics

Routine Use of Topical Bacitracin to Prevent Sternal Wound Infections After Cardiac Surgery

Chan J.L.; Diaconescu A.C.; Horvath K.A. Source Annals of Thoracic Surgery; 2017 In press

- 9 year experience of periop sternal wound bacitracin
- 0% deep infection rate!! V expected 0.29%
- 4 superficial infections
- Well tolerated. No serious adverse effects
- Readily available and inexpensive therapy, this simple intervention may be a useful adjunct strategy in preventing sternal wound infections

Vancomycin Paste Does Not Reduce the Incidence of Deep Sternal Wound Infection After Cardiac Operations.

Lander H et al. The Annals of thoracic surgery; Feb 2017; vol. 103 (no. 2); p. 497-503

- **14,492 patients reviewed retrospectively**
- **12 years**
- **Multivariate analysis**
- **Use of vancomycin paste at sternal edges not associated with a reduction in infection.**

The effect of vancomycin powder on the rates of infection and pseudarthrosis in lumbar spine surgery.

Maitra S et al. Spine Journal; Oct 2016; vol. 16 (no. 10)

- A retrospective analysis of 453 patients
- Pre and post intervention sampling
- Overall deep infection rate was 9/232 (3.9%) in the pre-vancomycin group and 4/221 (1.8%) in the vancomycin group
- No significant difference was noted in the mean levels fused or revision rates due to pseudarthrosis between the two groups

Mupirocin

- Unique mode of action, blocking protein and RNA synthesis within bacterial cells by inhibiting the enzyme isoleucyl t-RNA synthetase.
- Spectrum of antibacterial activity, including many strains of staphylococci and streptococci. Active v MRSA.
- Minimal activity against normal skin flora, and thus has no effect on the natural defences of the skin against infection.
- Mupirocin is bactericidal at clinical concentrations.
- Not used in systemic infection
- Resistance rising
- Used in skin infection, minor surgery and intranasally to prevent staphylococcal infection

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



Technology allows for accurate delivery of low levels of H_2O_2 (Reactive Oxygen Species) at a controlled antimicrobial potency and therapeutic dose to the wound site for a sustained period of time.



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 147726 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 morbidities 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 £17000, 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

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.

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SHRO prophylaxis in abdominal wall reconstruction.

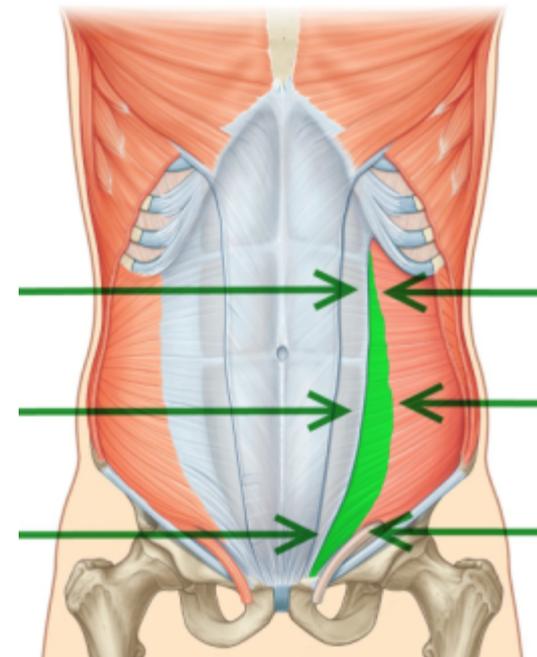
- **18 patients to date**
 - **3 grade 4 ventral hernias with enterocutaneous fistulae**
 - **15 grade 3 ventral hernias with contaminated stoma or wound infections**
 - **All healed with surgery + SHRO**
 - **Adverse events – 1 dehiscence, 2 subcut haematoma. NO infections on the background of a high 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



Prosthetic device surgery

Honey as a Novel Antimicrobial Coating in Salvage Revision Total Knee Arthroplasty

Rhodri Llywelyn Williams, Wasim Khan, Amisha Metah, 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 bioburden 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, Reaming, Levege
- 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.

Keywords: Revision, Arthroplasty, Infection, SurgiHoney



The Chemical Debridement of an Infected Endoprosthesis using SurgiHoney

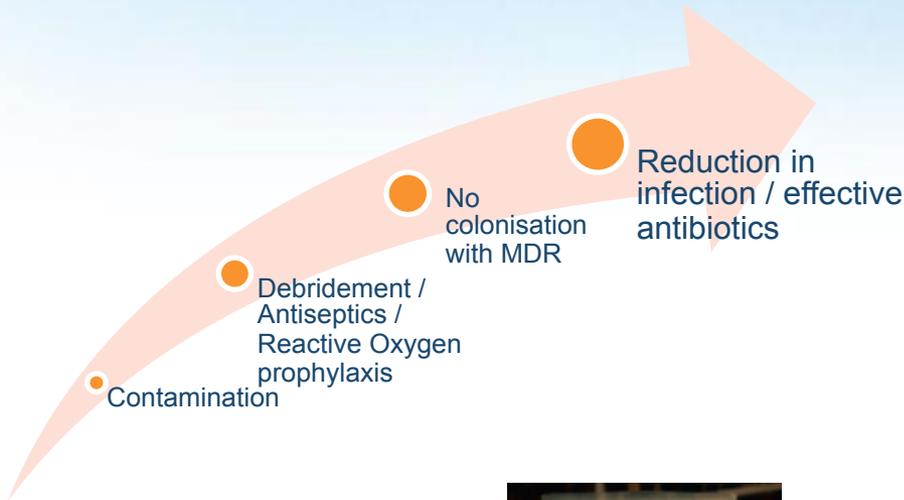
Results: During application of the Surgihoney we report no systemic adverse features. Physiological parameters including heart rate, respiratory rate and blood pressure were recorded and did not change significantly during and after the application. We also report good soft tissue and wound healing. 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)

Operation (*previous multiple surgeries)	Microbe	Follow up
*2 nd stage	Polymicrobial :Pseudomonas, Mycellial fungus, CNS, Eterobacter	6 months
*2 nd stage	Polymicrobial: , CNS aureus, Enterobacter, Mycellial fungus	8 months
*2 nd stage	Polymicrobial: CNS aureus, Aspergillus	12 months
*2 nd stage	Polymicrobial: including CNS aureus and various anaerobes	11 months

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

Traumatic explosive or penetrating injury



- 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 RO topical treatment of soft tissue injuries in Manchester bombing victims

Trauma wound treated with SurgihoneyRO





Day 1

77 year old man
Peripheral vascular
disease

Large ischaemic
ulcers



Day 4

Non healing

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



Day 10



Reactive
Oxygen™



Surgihoney™
The World's Most Powerful,
Non Toxic, Topical Antimicrobial

Considering a new domain for antimicrobial stewardship: Topical antibiotics in the open surgical wound

Edmiston CE et al American Journal of Infection Control; 2017

- **Use of topical abx often NOT monitored by stewardship programs**
- **Survey results indicate that the practice of using topical antibiotics intraoperatively, in both irrigation fluids and powders, is widespread.**
- **Given the risks inherent in their use and the lack of evidence supporting it, the practice should be monitored as a core part of ASPs**
- **Alternative agents, such as antiseptics, should be considered**

The rationale for local antibiotic use in surgery to prevent post-operative infection has logic and is based not on myth but considerable evidence in favour although that evidence is not as robust as is required by science.



Summary

- **Topical antibiotics in surgery can reduce infection rates.**
- **Jury is still out**
- **Quality of evidence is mediocre and most studies recommend RCTs**
- **Monitor and include in stewardship programmes**
- **Avoid systemically used antibiotics**
- **Consider alternative antimicrobials eg Reactive Oxygen.**