Antimicrobial copper surfaces to reduce AMR transfer and hospital infection rates worldwide

breaking the chain of infection

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Environmental Healthcare Unit

Inclusive national partnership with international reach

National Biofilms Innovation Centre

National Infrastructure and expertise, regional support

SCELSE
Singapore Centre for Environmental Life Sciences Engineering

CENTER FOR BIOFILM ENGINEERING

MONTANA STATE UNIVERSITY

COSTERTON BIOFILM CENTER

Core institutions with >100 international funded partnerships including developing countries

If one full wide bodied jet was lost each day would anyone fly?

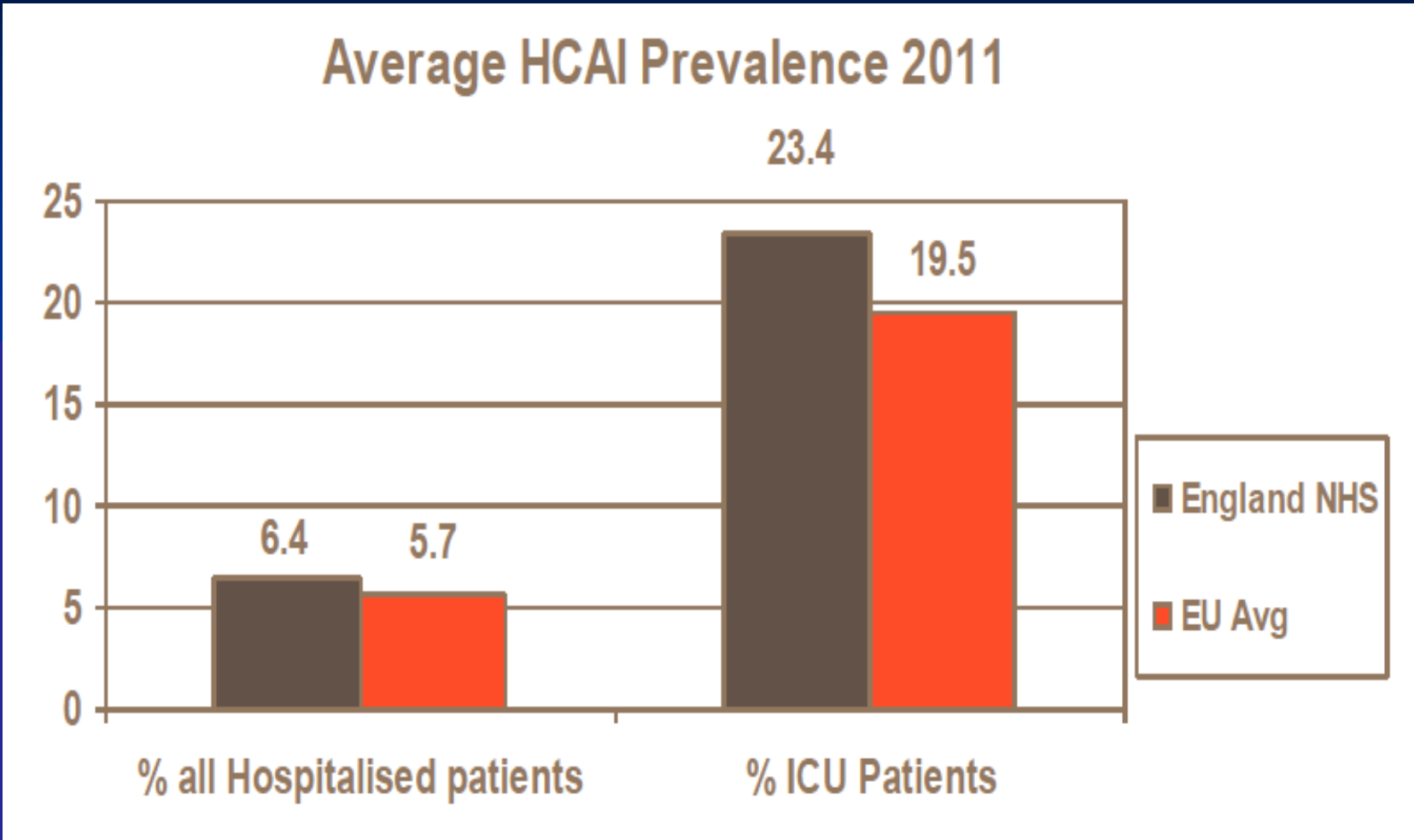
350 US patients die *every day* from HCAIs

M. Schmidt

July 2004 Report from the Infectious Disease Society of America and updates:

- 1.7- 2.0 million people infected in U.S. hospitals each year (approx 5% of those admitted)
- 99,000 of those infected die (4th leading cause of death)
  - equiv. one airliner crashing each day of the year
- In 2012 estimate cost at $47 billion per annum
- CDC estimates HCAI add 208% to hospital bill; ~ $48,000 per patient
- WHO - 7.0 million people infected worldwide; $80 billion
- Trends toward the increasing number of infections and increasing drug resistance show no signs of abating

Healthcare-Associated Infections in EU



Up to 51% prevalence in ICUs within EU countries

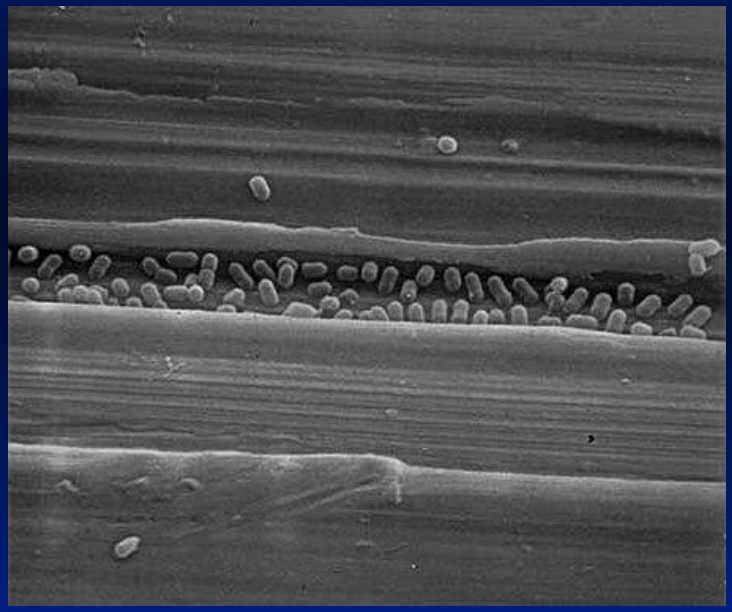
Source: WHO - The Burden of HealthCare-Associated Infection Worldwide – A Summary. 2011
WHO - European Health for All Database (HFA-DB)

Average adult touches up to 30 objects a minute

80% of infectious diseases are transferred by touch!

SURFACE CLEANING PROBLEMS

most surfaces are not smooth
- have draw marks, scratches etc where pathogens hide



Stainless steel is not easy to clean, as claimed; risk of cross-contamination

Hand hygiene compliance (e.g. hand rubs or soap) is poor, even professionals

TERMINAL CLEANING PROBLEMS

- **French, G. L., Otter, J. A., Shannon, K. P., Adams, N. M., Watling, D. & Parks, M. J. (2004).** Tackling contamination of the hospital environment by methicillin-resistant *Staphylococcus aureus* (MRSA): a comparison between conventional terminal cleaning and hydrogen peroxide vapour decontamination. *J Hosp Infect* **57**, 31-37

- Terminal cleaning (defined as environmental cleaning after discharge of an infectious patient) is ineffective in eradicating MRSA

- 74% of environmental swabs yielded MRSA before cleaning and 66% afterwards.

- Evidence indicates the need for more passive preventative measures with regards to reducing MRSA populations on commonly touched surfaces.

CAUSES OF ANTIBIOTIC RESISTANCE

HANDLE ANTIBIOTICS WITH CARE

Antibiotic resistance happens when bacteria change and become resistant to the antibiotics used to treat the infections they cause.

Over-prescribing of antibiotics

Patients not finishing their treatment

Over-use of antibiotics in livestock and fish farming

Poor infection control in hospitals and clinics

Lack of hygiene and poor sanitation

Lack of new antibiotics being developed

www.who.int/drugresistance

#AntibioticResistance

World Health Organization

Why our Interest in Copper?
Copper Symbols since Antiquity

Egyptian Ankh

Eternal Life

Chinese Medicine
increase the flow of 'chi'
(life energy)

Alchemy
planetary symbol for Venus,
protect against evil

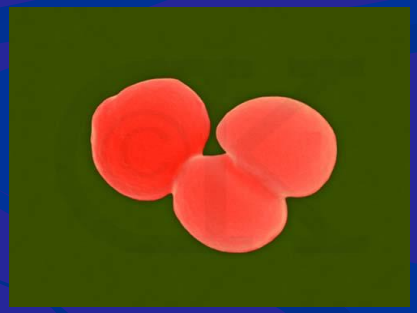
Copper Used to Protect Human Health in the Past

- Egypt (2000 BC) - Sterilize drinking water and wounds
- Greece, Hippocrates (400 BC) – Treat leg ulcers related to varicose veins
- Aztecs – Copper oxide and malachite for skin conditions
- France (1850 AD) – Copper workers found to be immune during Cholera epidemic
- USA, Phildadelphia Hospital Study (1983 AD) – Low *E. coli* count on brass doorknobs
- Punjab, India (2005 AD) – *E. coli* eliminated in 24 hours in water-filled brass containers (TamraJal used for 5000 years)

ANTIMICROBIAL COPPER

- **Water-borne pathogens in biofilms**
  - *Legionella pneumophila, Helicobacter pylori*
  - *E. coli* O157

- **Food-borne pathogens on surfaces**
  - *E. coli* O157, *Salmonella*
  - *Listeria monocytogenes*



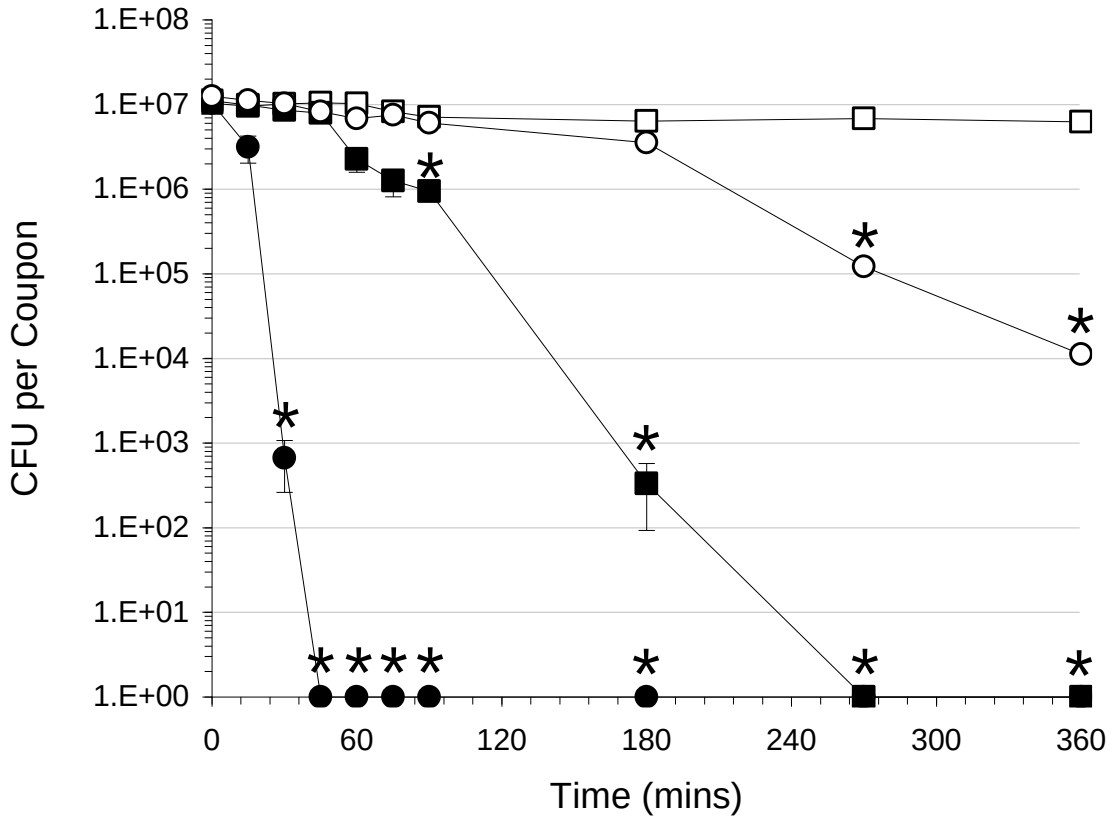
- **Hospital-acquired pathogens**
  - MRSA, VRE, *C. difficile,*
  - *A. baumannii, K. pneumoniae* NDM-1 *etc*

  - Viruses - influenza H1N1, norovirus, adenovirus
  - Fungi- *Candida*, *Aspergillus* (HVAC systems)

Moist contact model

MRSA on Stainless Steel (□), C19700 (●), C24000 (■) and C77000 (○) at 20°C

Moist test simulating coughs, sneezes etc (20 µL inoculum)



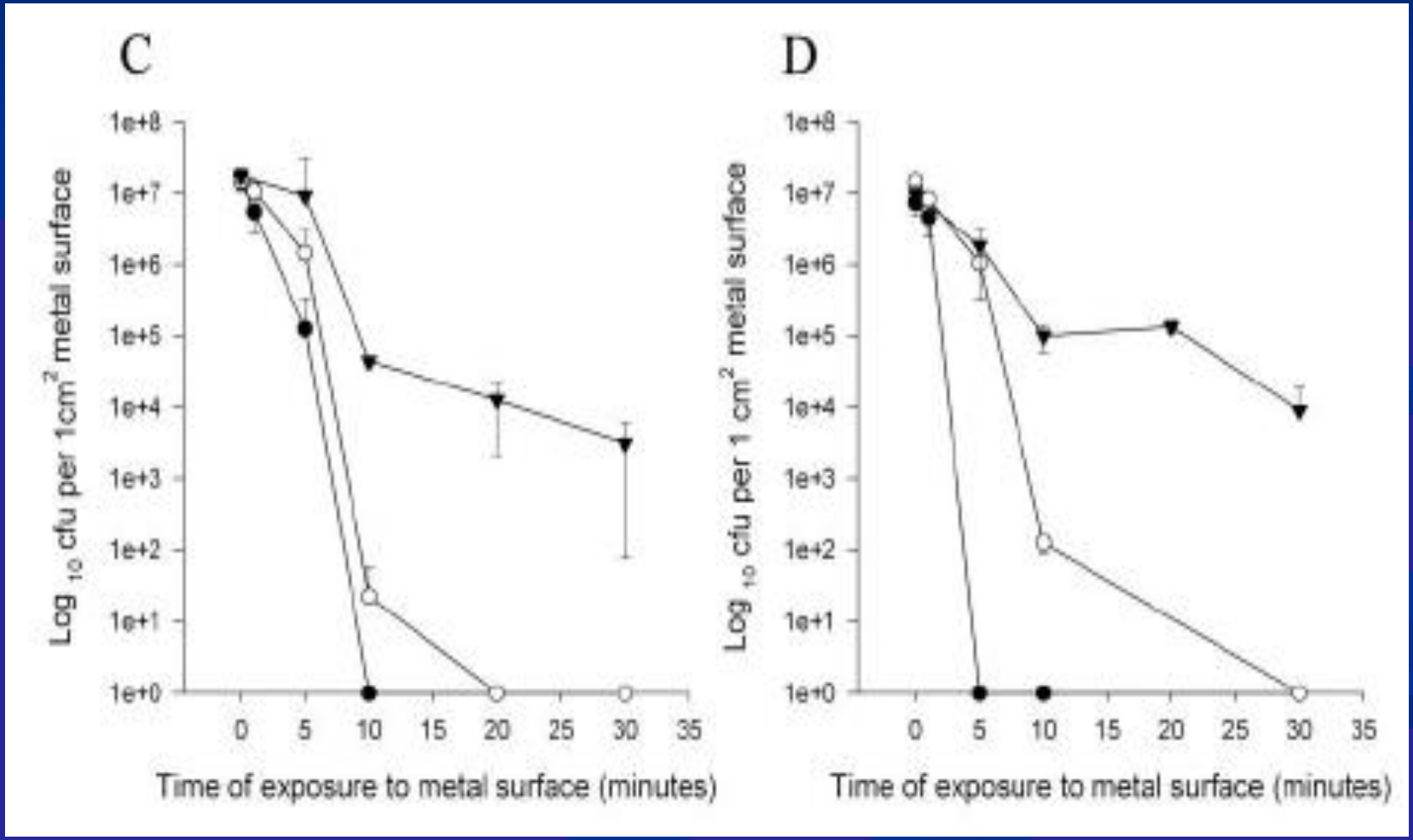
or Silver for 24h

* Indicates p=<0.05 compared to zero time controls

Noyce *et al.*, JHI 63, 289-297 (2006)

Dry touch surface model

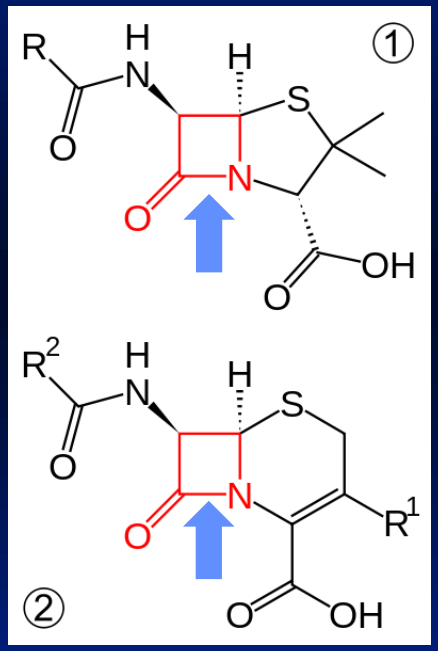
Rapid inactivation of dry challenge *E. coli* and *S. typhimurium* on copper, brass and stainless steel

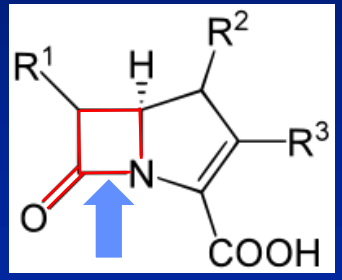


Warnes *et al.*, Environ. Microbiol. 14, 1730–1743 (2012)

Evolution of β-lactamase to carbapenamases e.g. *bla*$_{NDM-1}$

December 2009, after unsuccessful treatments in hospitals in New Delhi, a Swedish national was referred back to a Swedish hospital, where it was discovered that he had acquired an antibiotic-resistant bacterial infection during his stay in India; infected with ***Klebsiella pneumoniae*** (Gram-negative bacterium found in the normal flora of the mouth, skin, and intestines) infection.
NDM-1 gene now found in **India, Pakistan, Bangladesh, Australia, Canada, the Netherlands, United States, UK.**
Carbapenamases hydrolyse carbapenems called **'antibiotics of last resort'.**



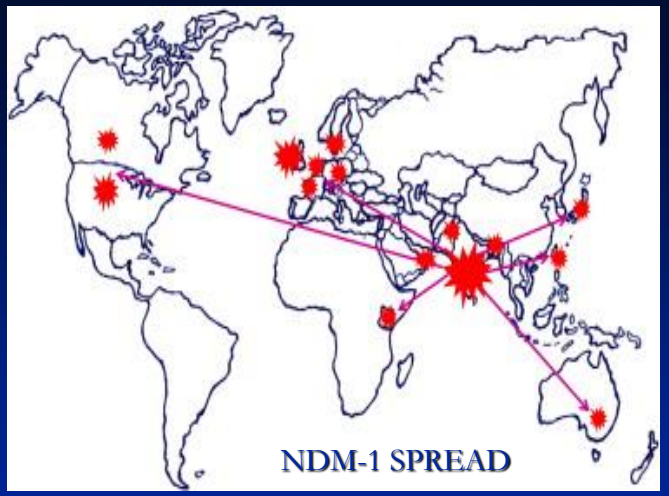


1. Penicillins
   - β-lactamases

2. Cephalosporins
   - BS β-lactamases

3. Cephalosporins e.g. cefoxatime
   - ESBL:
   - CTX, OXA, TEM

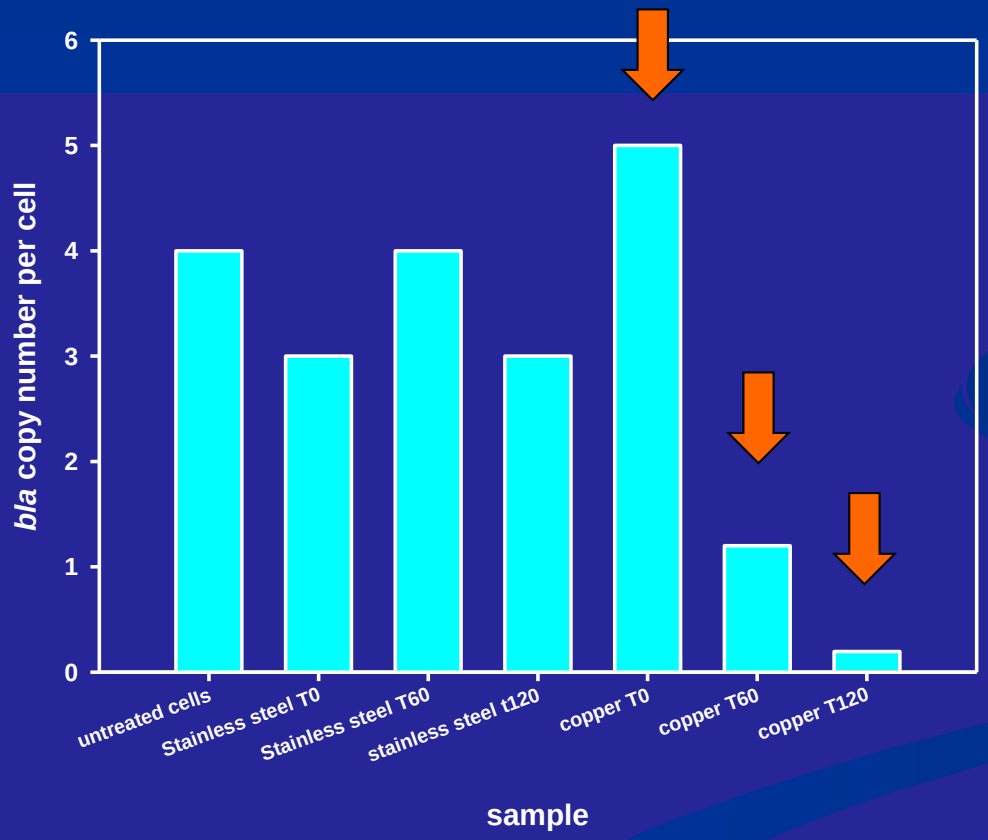
3. Carbapenems e.g. meropenem
   - KPC, NDM-1



'antibiotics of last resort'

Direct detection of the *CTX-M-15 bla* gene in the same plasmid preparations using quantitative PCR (qPCR)

Copy number of beta lactamase gene in antibiotic resistant *E. coli* (untreated cells or those exposed to copper and stainless steel surfaces at room temperature: 'wet' inoculum)



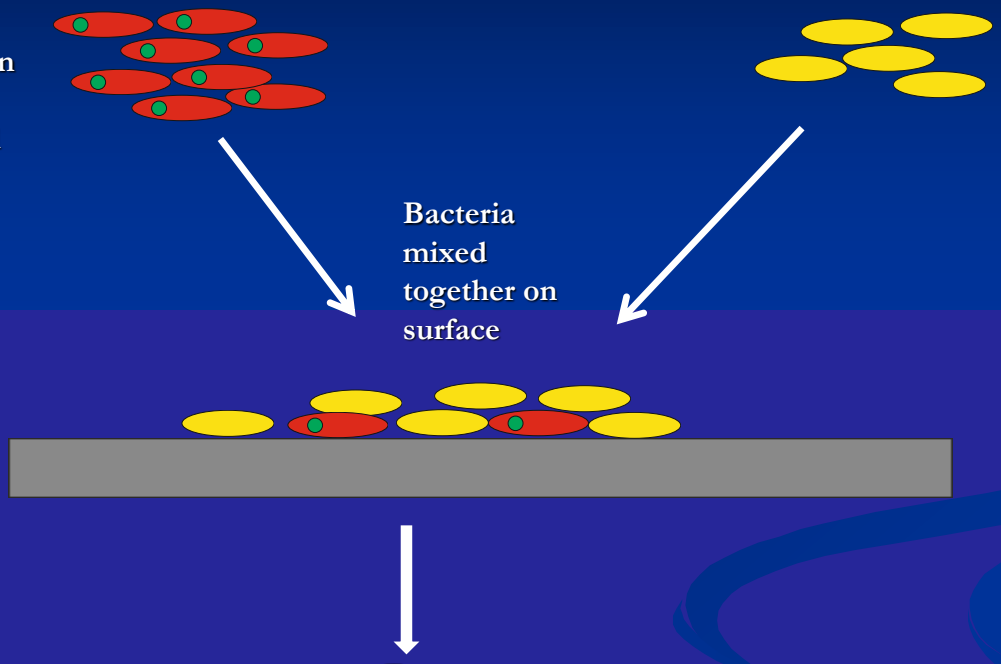
If the cT values are converted to actual gene copy number per cell it can be seen that copy number has depleted over time when exposed to copper surfaces.

Warnes *et al*. mBio 3, e00489-12 (2012)

Can antibiotic resistance genes be transferred by natural conjugation on surfaces?

Pathogen containing antibiotic resistance gene on plasmid (green)
e.g. *K. pneumoniae* NDM-1 and *E. coli* CTX-M-15
DONOR, sensitive to sodium azide

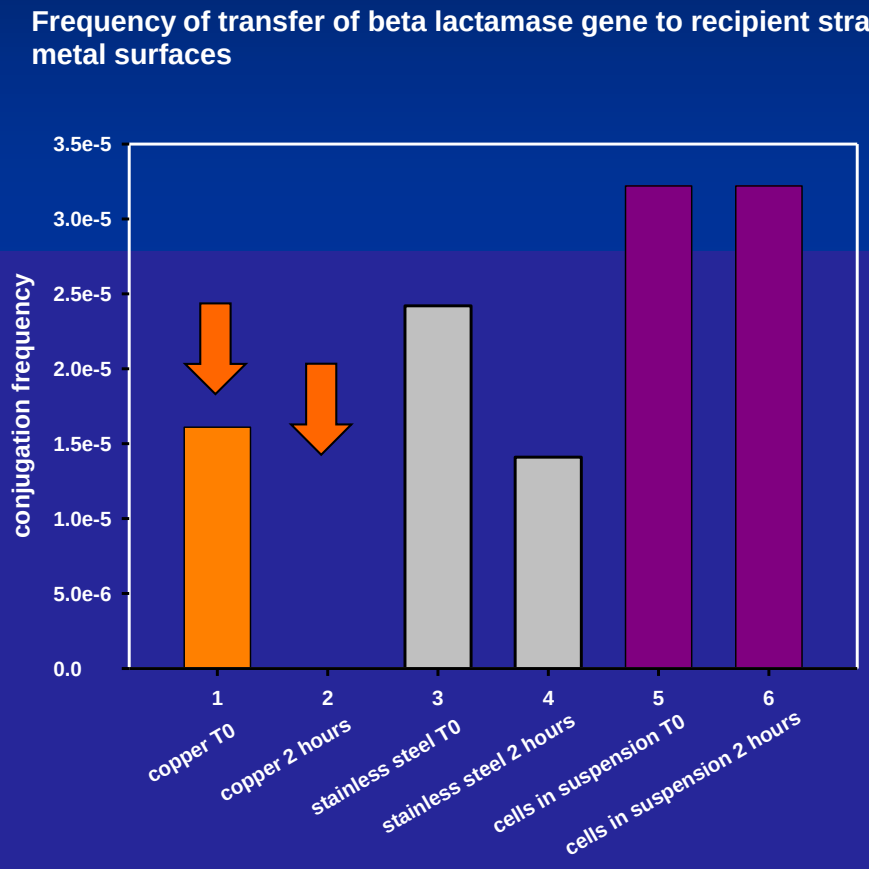
E. coli RECIPIENT strain, resistant to sodium azide but sensitive to antibiotic

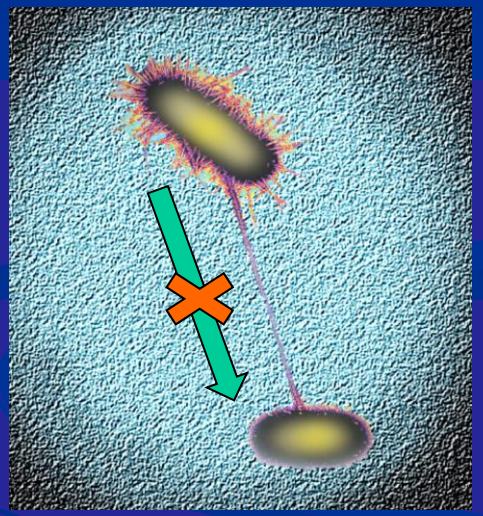


Transconjugants selected for growth on medium containing antibiotic (e.g. cefotaxime, meropenem)
AND sodium azide

Detection of *bla CTX-M-15* in possible transconjugants

(selected by ability to grow on medium containing cefoxatime cephalosporin and sodium azide)





www.flickr.com

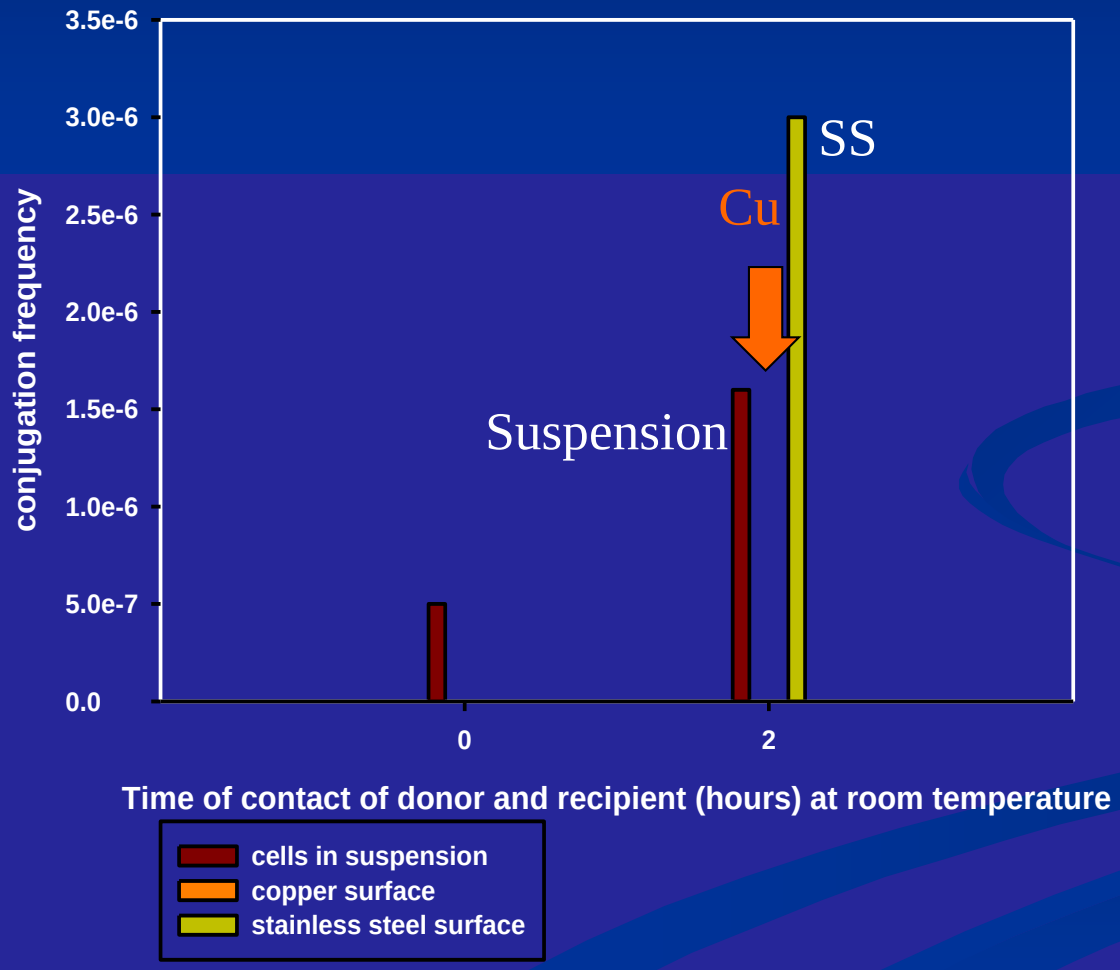
Cu prevents transfer

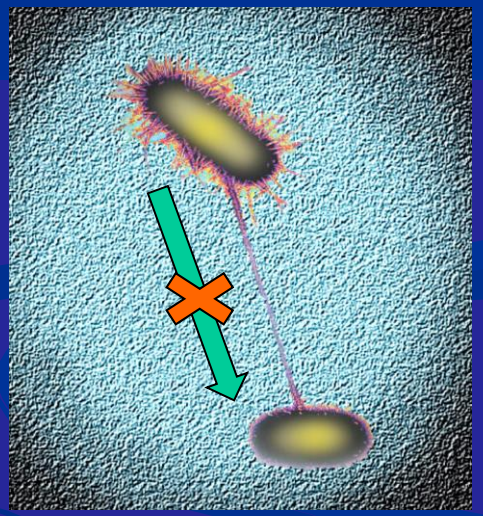
Conjugation frequency =
no. transconjugants /no. donor cells

Warnes *et al*. mBio 3, e00489-12 (2012)

Horizontal transfer of *K. pneumoniae bla* $_{NDM-1}$ occurs in suspension and on stainless steel surfaces

Frequency of transfer of *bla* $_{NDM-1}$ to recipient cells on surfaces or in suspension.



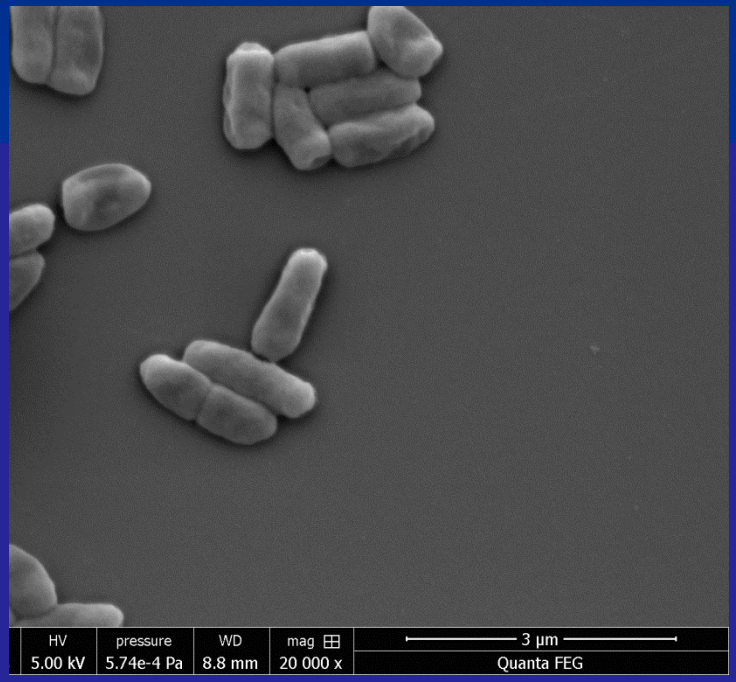


www.flickr.com

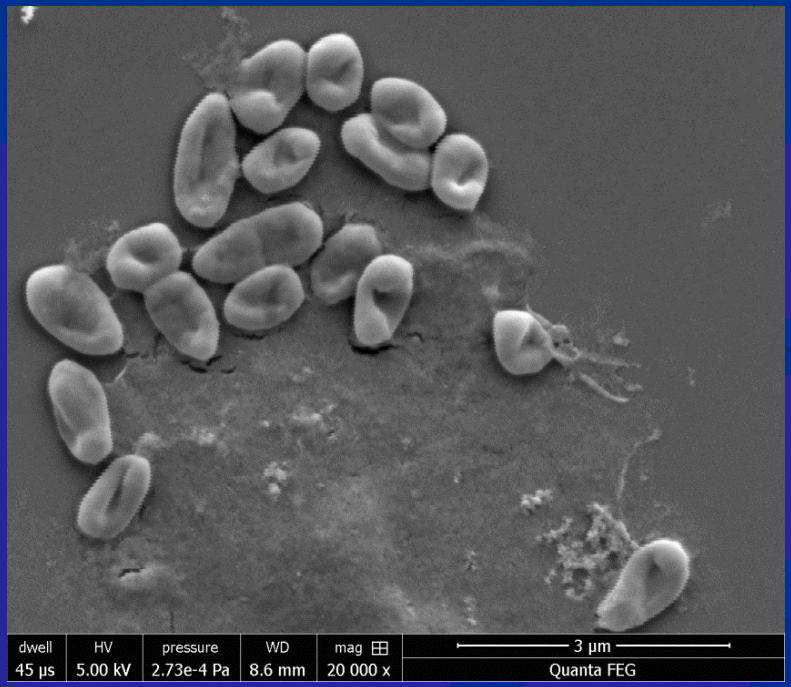
Cu prevents transfer

Warnes *et al*. mBio 3, e00489-12 (2012)

P. aeruginosa collapse on Cu



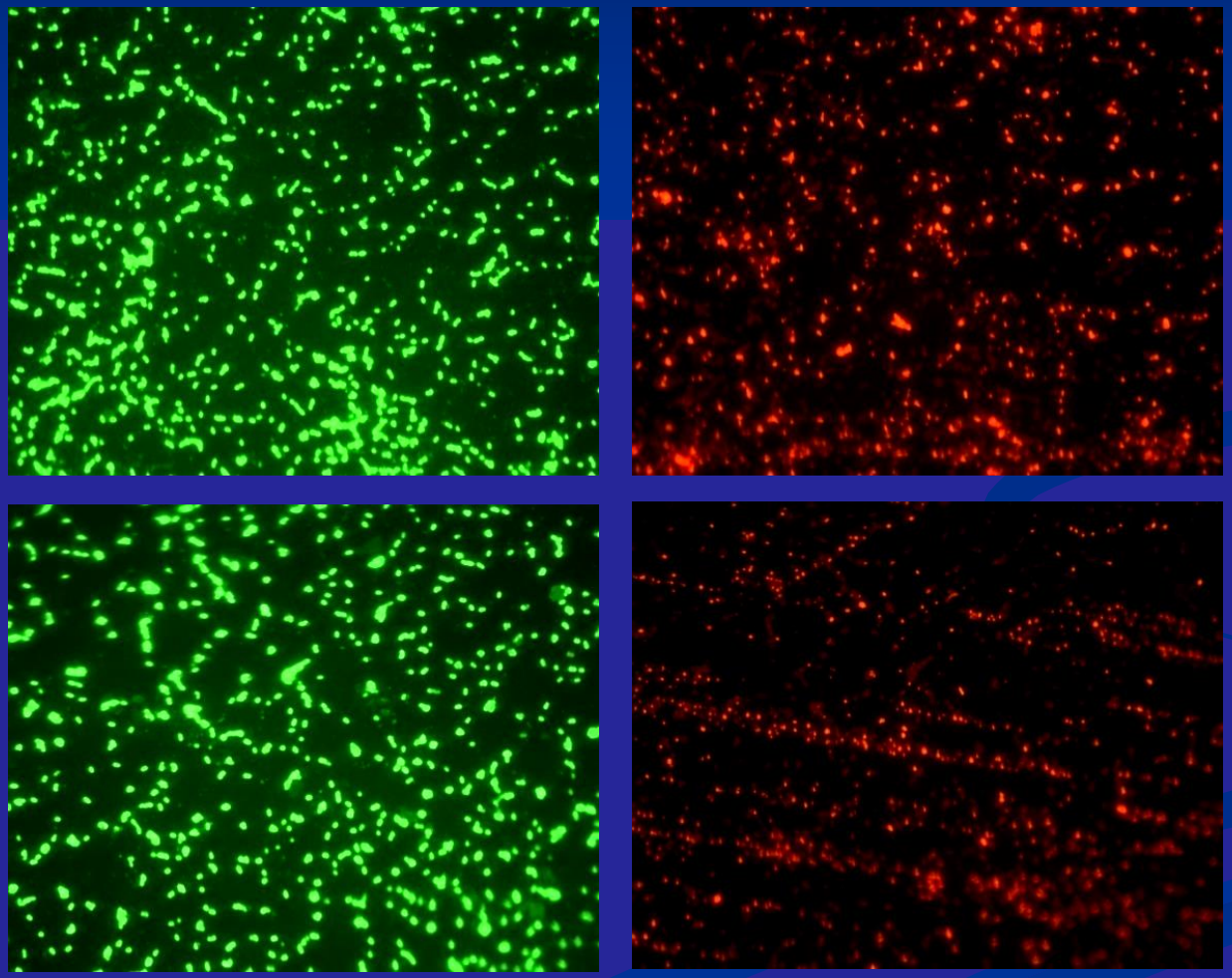
Stainless steel 1h



Copper 1h

Gram-positive VRE DNA content and respiration on stainless steel (inoculum 10^6 cfu per cm^2; 4h)

Dry test simulating hand contact (1 µL inoculum)



E. faecalis

E. faecium

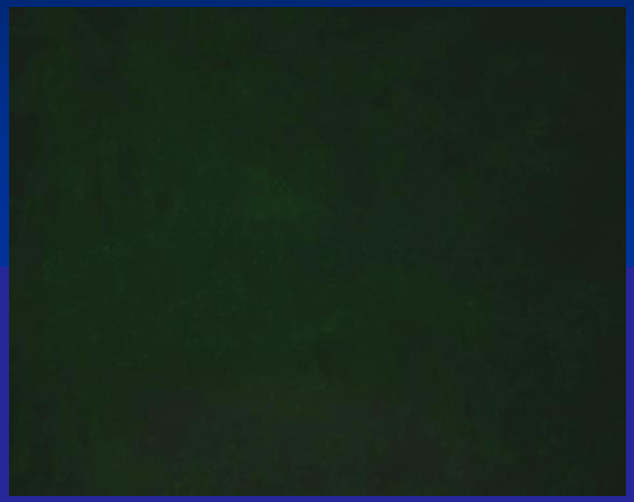
SYTO9

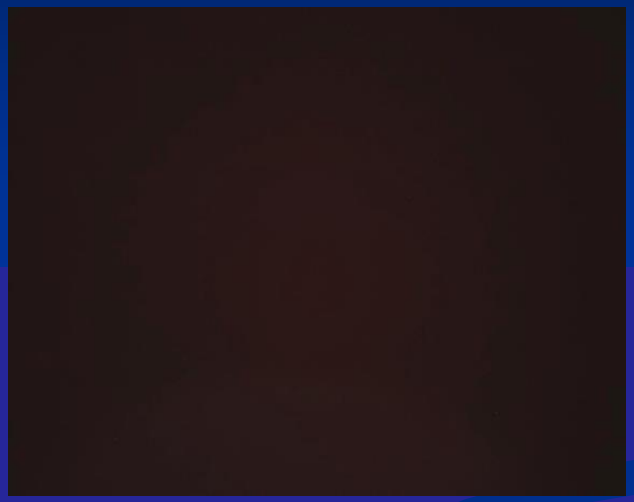
CTC

Warnes and Keevil, AEM 77, 6049-59 (2011)

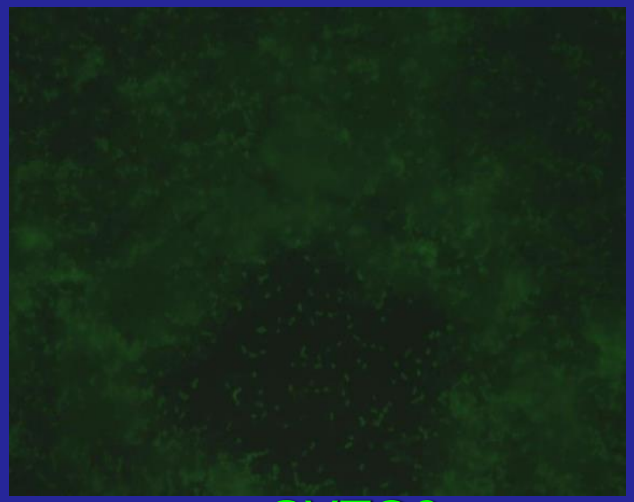
Destruction of VRE DNA and respiration on copper

(inoculum 10^6 cfu per cm^2; 10 min)





E. faecalis



E. faecium

SYTO9

CTC

Warnes and Keevil, AEM 77, 6049-59 (2011)

Copper disrupts membrane electrical potential in Gram negatives – 10 min exposure

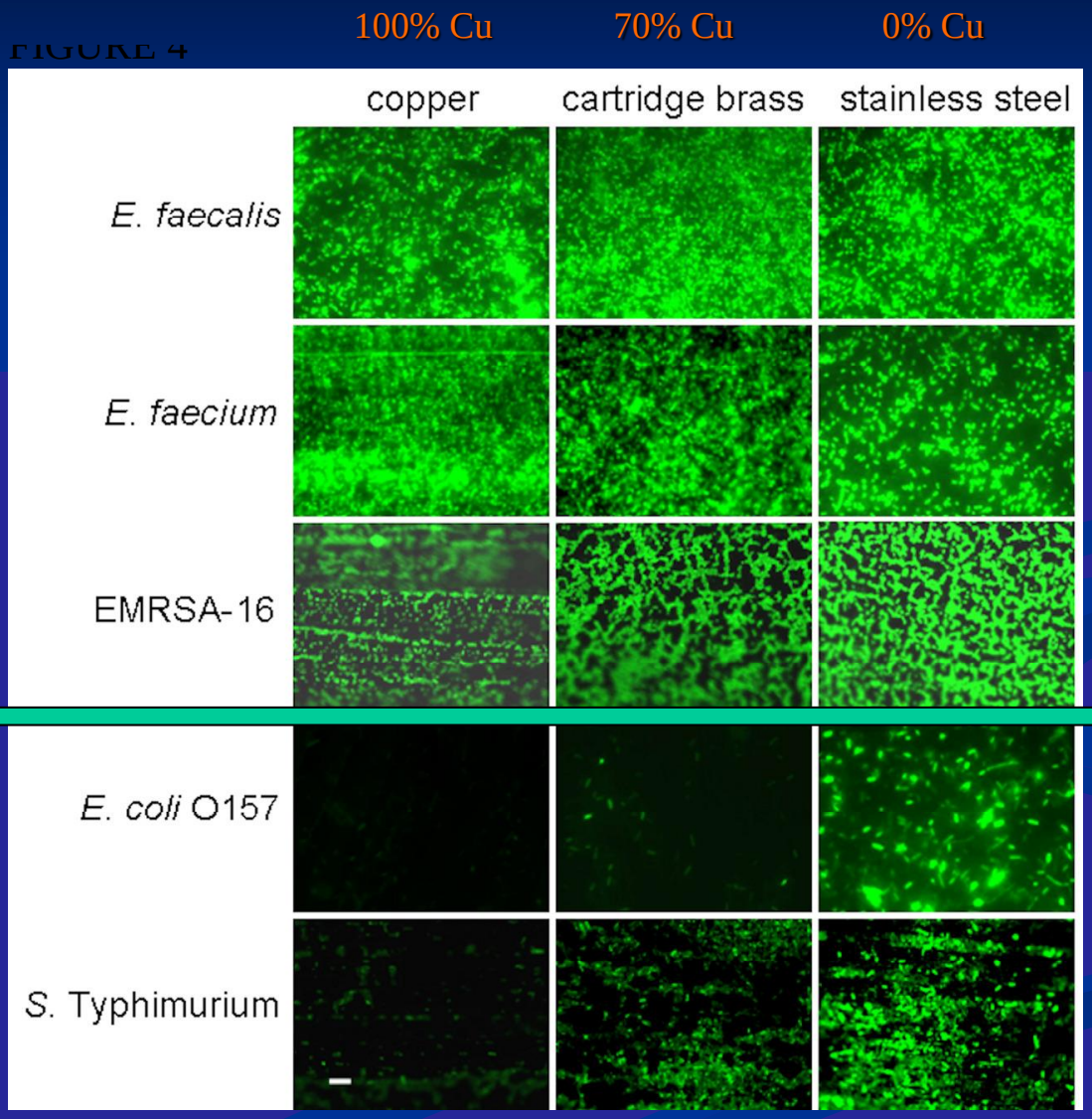
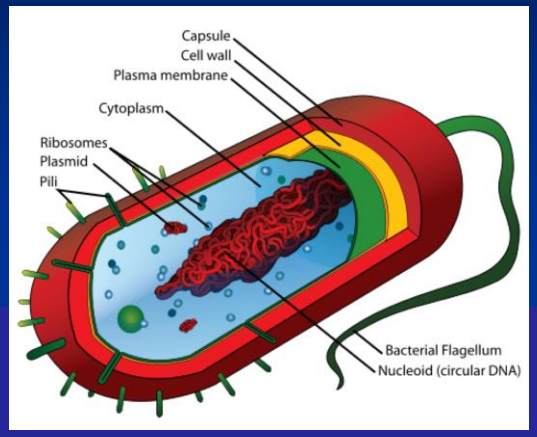


FIGURE 5

Warnes *et al*., Environmental Microbiology 14, 1730-43 (2012)

Bacterial metabolic suicide on Cu

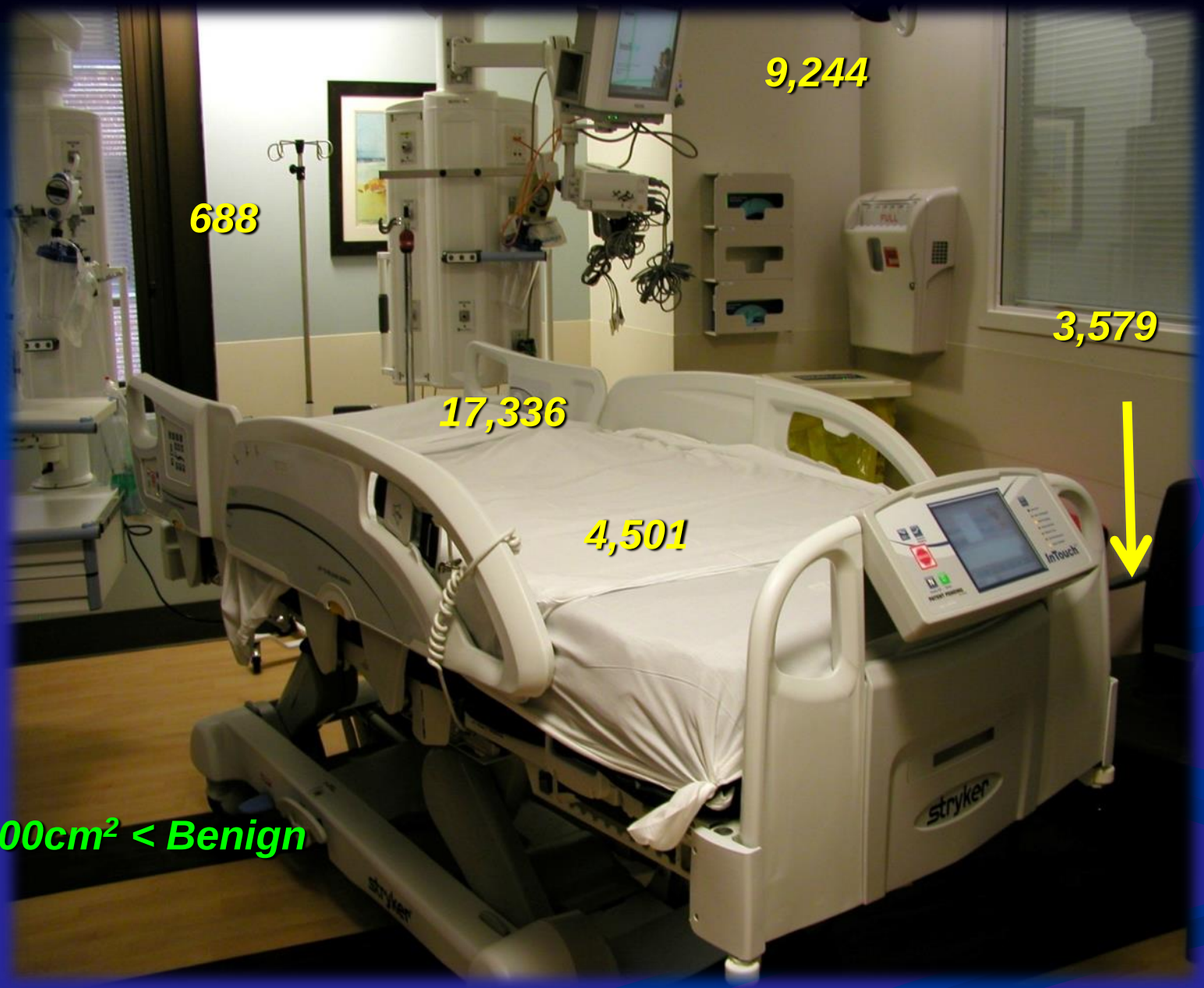
Cu overwhelms the cell



$$Cu\ (I) + H_2O_2 \rightarrow Cu\ (II) + O_2 + OH^- + OH\cdot$$

Rapid 200,000x uptake of Cu(I) in seconds and attack cell

Generation and attack by Reactive Oxygen Species



When we look, the risk is omnipresent!

M. Schmidt

INTERVENTION WITH COPPER







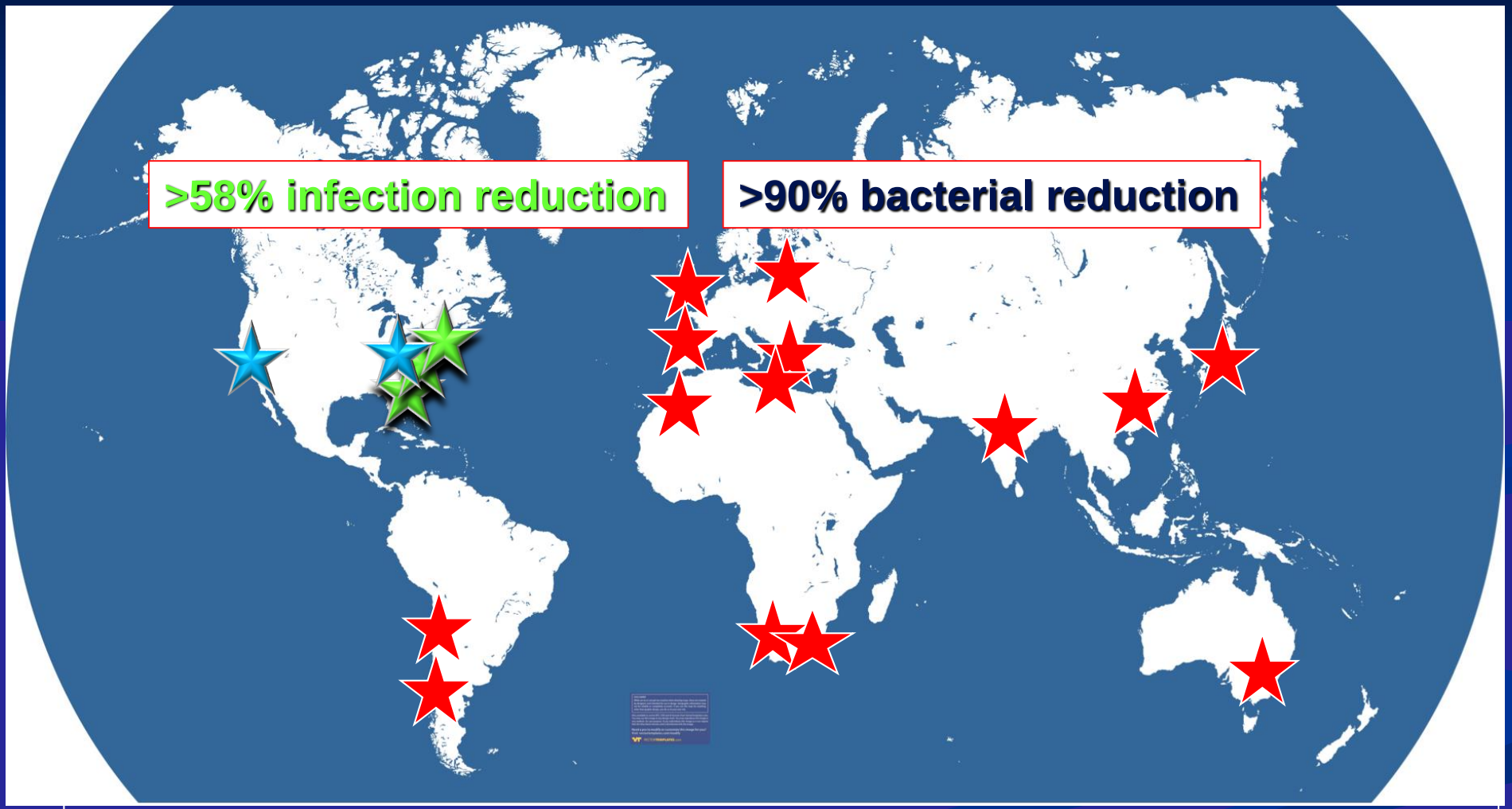

Schmidt *et al.*, JCM 50, 2217-2223 (2012)

Risk was Significantly Lower with Copper

16 rooms sampled weekly for a period of 21 months, n=1012

Schmidt *et al.*, JCM 50, 2217-2223 (2012)

Ward Trials Worldwide



HCAIs: 8.43% **58.1% reduction** HCAIs: 3.4%

(p= 0.013)

Norfolk, VA Paediatric Unit Trial Cu composites/linens >**68%** MDRO, *C. difficile*

Copper alloy touch surfaces are an *additional* infection prevention measure

Works 24/7

+

+ Cu+ ™

Copper reduces bioburden and infection
Saves lives, saves £££

>400 Cu alloys now registered with US EPA with an antimicrobial claim – being deployed in healthcare, public buildings, public transportation etc

New build hospital, payback in 3 months

Acknowledgements

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Emma Roe et al.

Copper Alliance

Harold Michels

Cu Copper Alliance