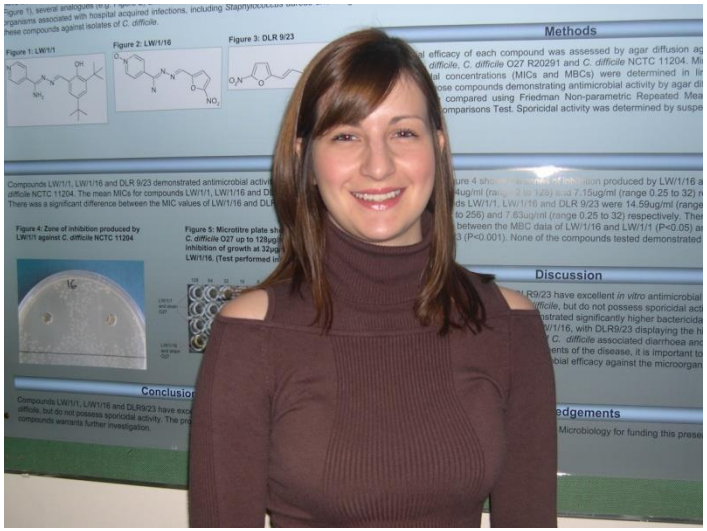
Aston University
Life & Health Sciences

Dealing with C. diff spores: “germinate, exterminate”

Peter Lambert

School of Life and Health Sciences, Aston University



Dr Laura Wheeldon
KTP Associate

Professor Peter Lambert
Antimicrobial Agents

Dr Tony Worthington
Clinical Microbiology

Knowledge Transfer Partnerships

INSIGHT HEALTH LIMITED

DH Department of Health

EPSRC
Engineering and Physical Sciences Research Council

Clostridium difficile

Antibiotic associated diarrhoea

leading cause of hospital acquired infection in UK

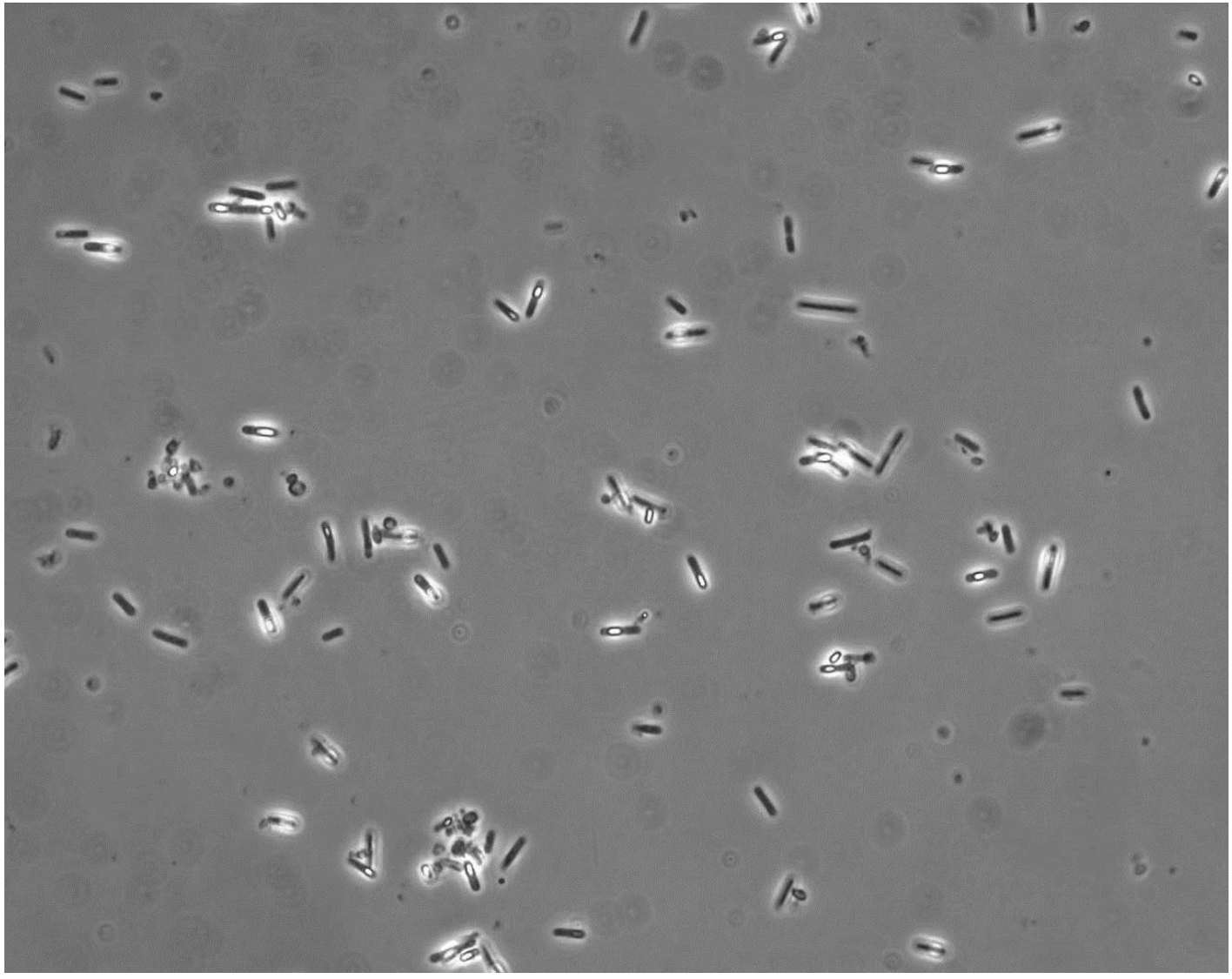
~15,000 cases and ~2,000 deaths pa

Major Outbreaks

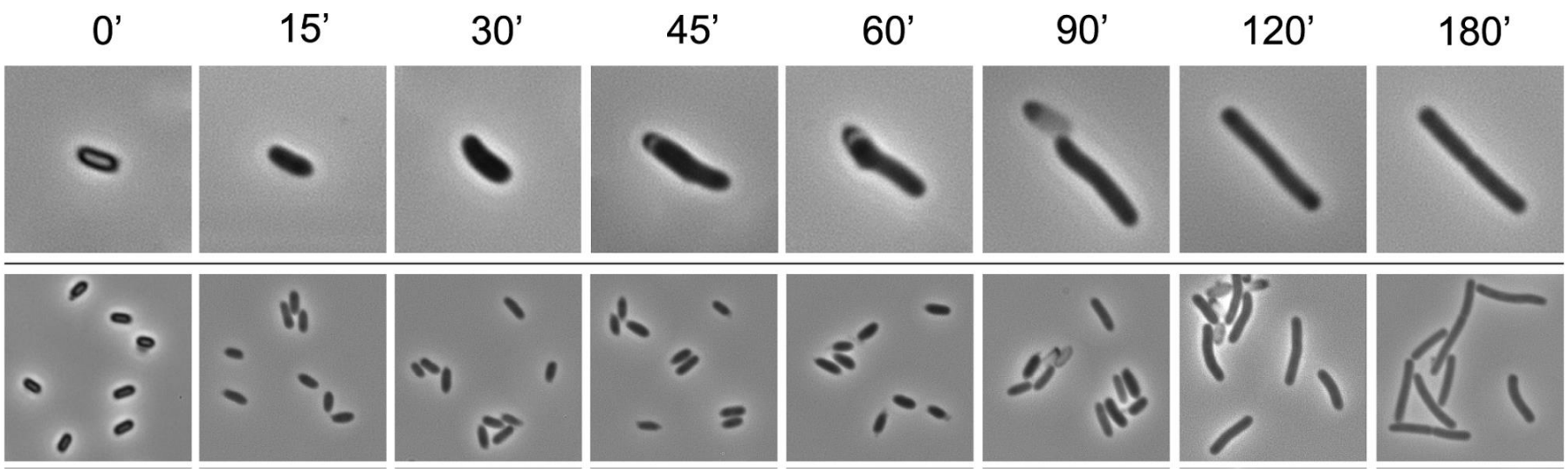
(2006) Maidstone and Tunbridge Wells

1170 infections, 90 deaths

C. diff produces spores



Ingested spores germinate in gut



Growing cells produce toxins which cause diarrhoea

Dembek et al Plos ONE (2013) 8 e64011

Why do we see so many cases?

Patients receiving antibiotics are vulnerable

C diff spores are:

- Persistent (survive months/years)
- Transmissible (hands, healthcare equipment)
- Resistant (to common disinfectants)

Infection Control Strategies
Breaking the Chain of *C. difficile*

Controlling antibiotic use

prompt detection and isolation of patients

effective hand hygiene

environmental cleaning and disinfection

Disinfection of C. diff spores

Need sporicidal agents:
bleach or peracetic acid

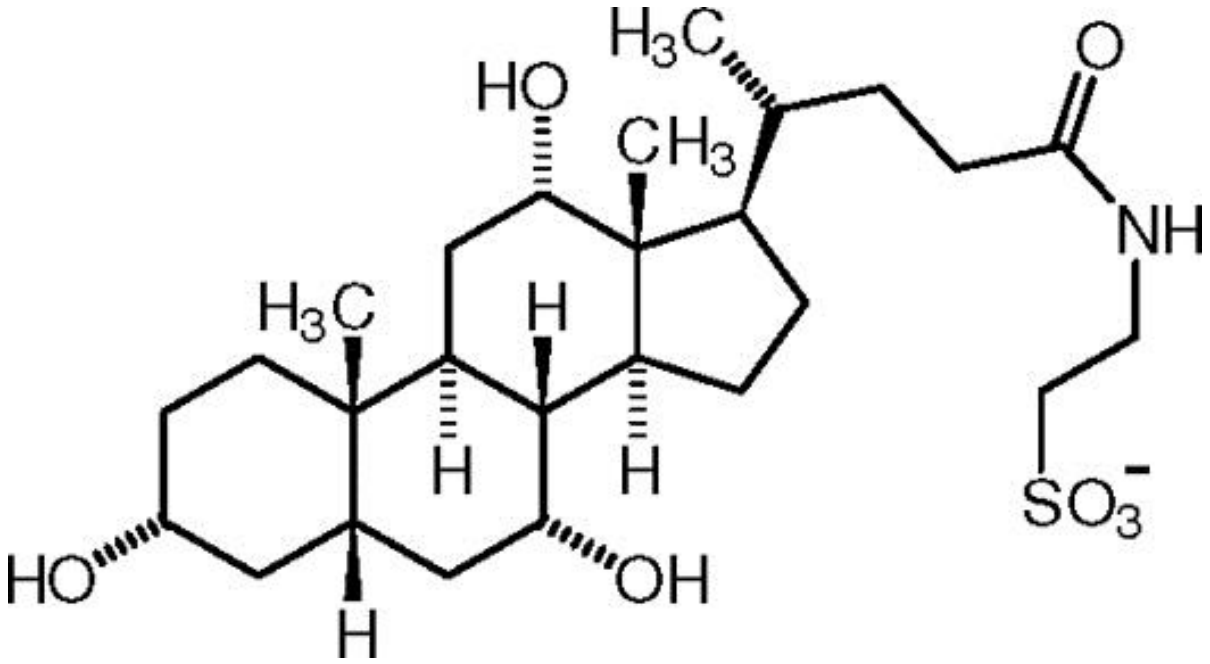
hazardous and corrosive

Alternative strategy to kill C. diff spores

Trigger spores to germinate, then kill with common disinfectants

“germinate exterminate”

Spore germination is triggered in the gut by bile salts and amino acids



Taurocholate

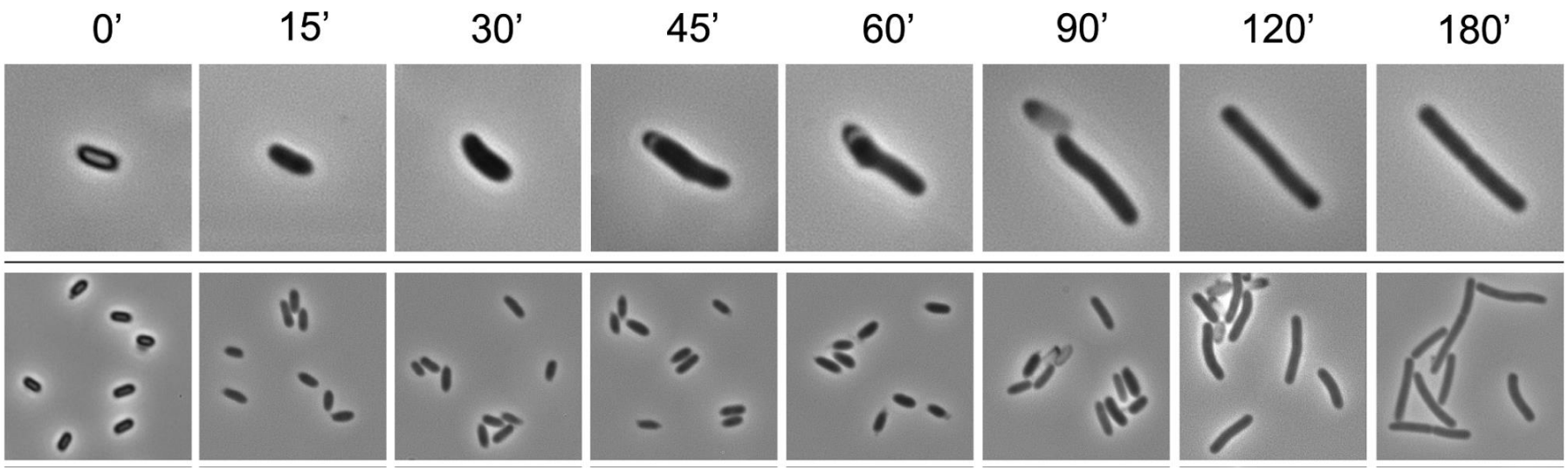
Optimised spore germination solution

Taurocholate plus glycine and histidine as co-germinants, pH 6.8

Germination triggered by short term exposure (<5 min)

Germinating spores are immediately sensitive to heat and common disinfectants (no out-growth needed)

Spores become sensitive upon exposure to germinant

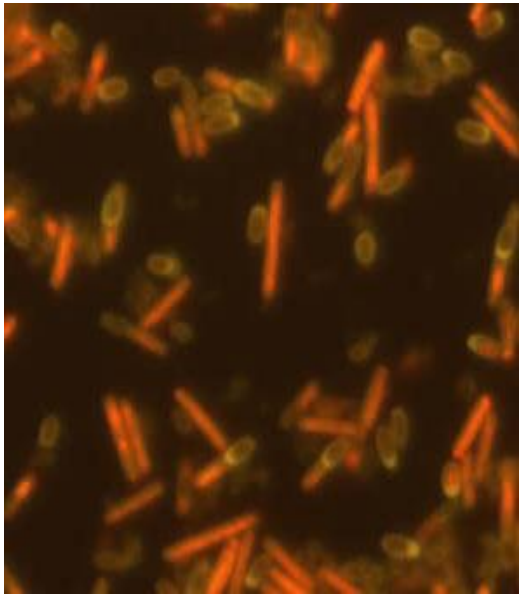


Germinating spores are sensitive to common disinfectants

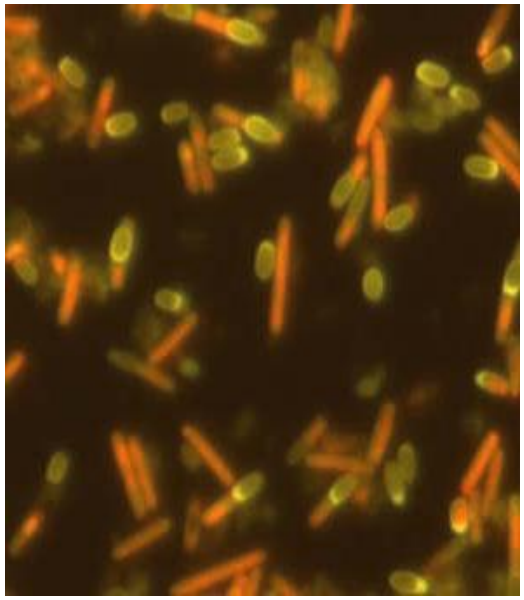
Exposure to germinant

Visualisation of *C. difficile* spore germination (aerobic conditions / room temperature)

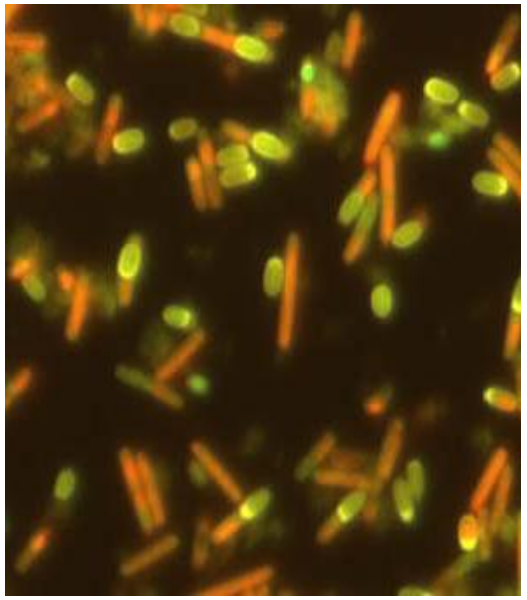
0 min



5 min



10 min



C.difficile spores exposed to germination solution

Green = metabolically active and sensitive

Can we germinate and exterminate at the same time?

Addition of mild disinfectants to the germinant

- Benzalkonium chloride (0.03% w/v)
- Benzyl Alcohol (1% v/v)

Germinates and kills spores of *C. difficile*

99% kill of spores in 30 minutes in one application

Kills other clinically relevant microorganisms

99.999% kill of *E. coli, P. aeruginosa, E. hirae, S. aureus* in 5 minutes

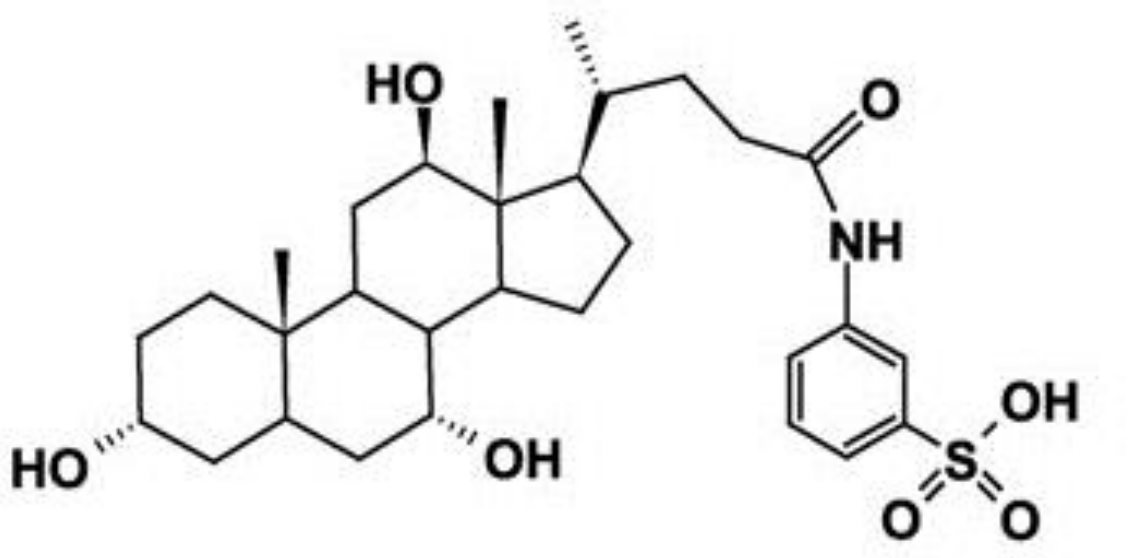
Use as spray or wipe to kill C. diff spores

Hospitals

Care homes

Domestic

Opposite strategy is being developed for treatment of infection (anti-germination)



CamSA

Howerton A et al. J Inf Dis (2013) 207 1498-1504

Further information

Wheeldon L J et al.
J Antimicrob Chemother (2008) 62 522-5
J Appl Microbiol (2008) 105 2223-30
J Appl Microbiol (2011) 110 987-994
PCT/GB2011/050278