



No Drugs for Bad Bugs



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What You Will Take Home

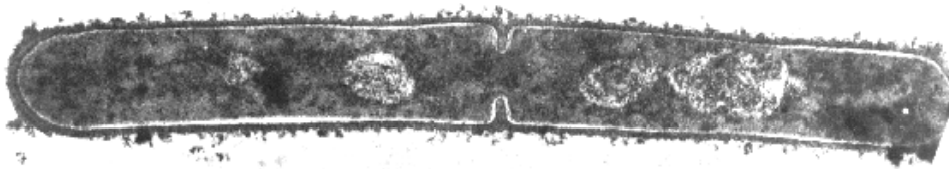
- > What are bacteria?
- > Where are they?
- > How many are there?
- > Are bacteria all bad?
- > Do they exchange bodily fluids?
- > Are superbugs **really** that super?
- > Are we really going back to the pre-antibiotic era?
- > What can we do about it?
- > What is UTS doing about it?



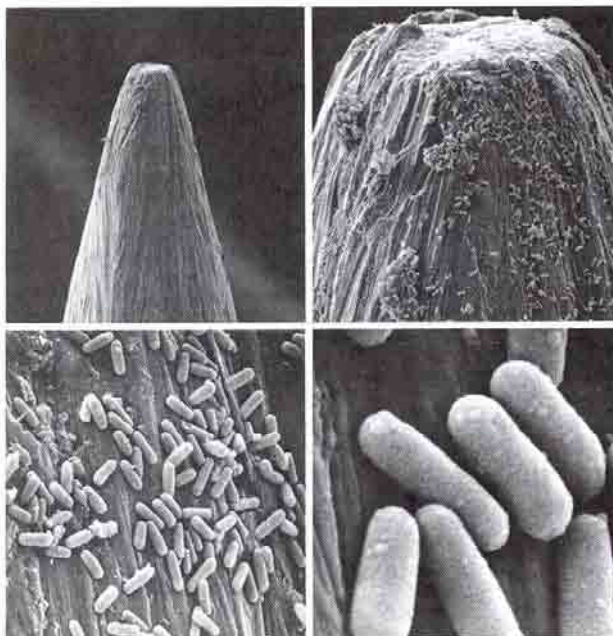
Janice Carr [Public Health Image Library \(PHI\)](#)



What Are Bacteria?



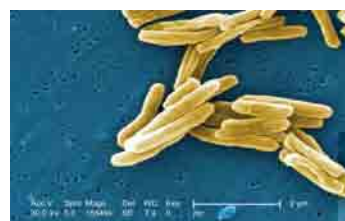
Bacteria are VERY Small!!



And diverse.....



20,000X



15,000X





Other Bacterial Facts



- > Been here longer than any other living thing
- > They are a few billion years old
- > Humans are only a few million years old
- > They live everywhere
- > There are more bacteria on a person's hand than there are people on the entire planet!
- > They live on and in humans
- > Bacterial cells produce 100x more protein in our body than we do!



Are All Bacteria Bad?

- > Without bacteria we would die
- > Pollution busters
- > Oil Eaters
- > Biological Factories
- > Biofuels
- > Digestion in our gut
- > Probiotics
- > Predict climate change



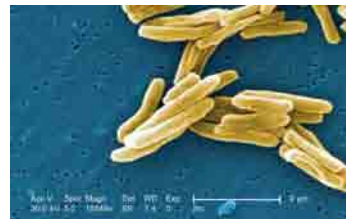


The Bad Bacteria Cause Disease and Death

- > From the air: tuberculosis and meningitis
- > From insects: Lyme Disease
- > From direct contact: anthrax, leprosy
- > From food and water: Cholera and Typhoid
- > From our skin: infected wounds



Photo Credit: Major Kirk Waibel, MD



TB



Acc.V Spot Magn Det WD |-----| 1µm
30.0 kV 2.0 -20000x SE 8.1 staph97-11-52

Staphylococcus



What Causes Infectious Disease?

Louis Pasteur

- > Attachment to host and colonization
- > Enters host cells or tissues and can end up in the circulatory system
- > Growth and multiplication occur, causing infection
- > They can produce toxins that alter host cell function
- > They can evade the host defenses and spread around the body

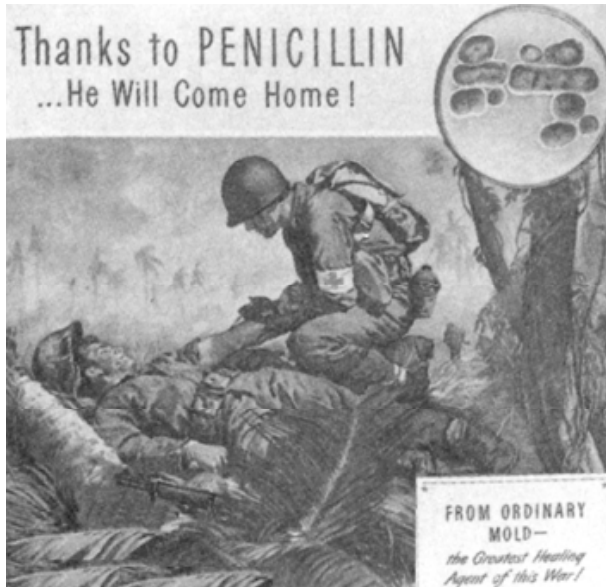


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The Miracle of Antibiotics



World War II

Before penicillin.....
death from bacterial infection was
assumed

1928 - first discovered by Alexander
Fleming ACCIDENTALLY!!

1939 -antibacterial properties
demonstrated by Howard Florey

1943 - mass production of penicillin

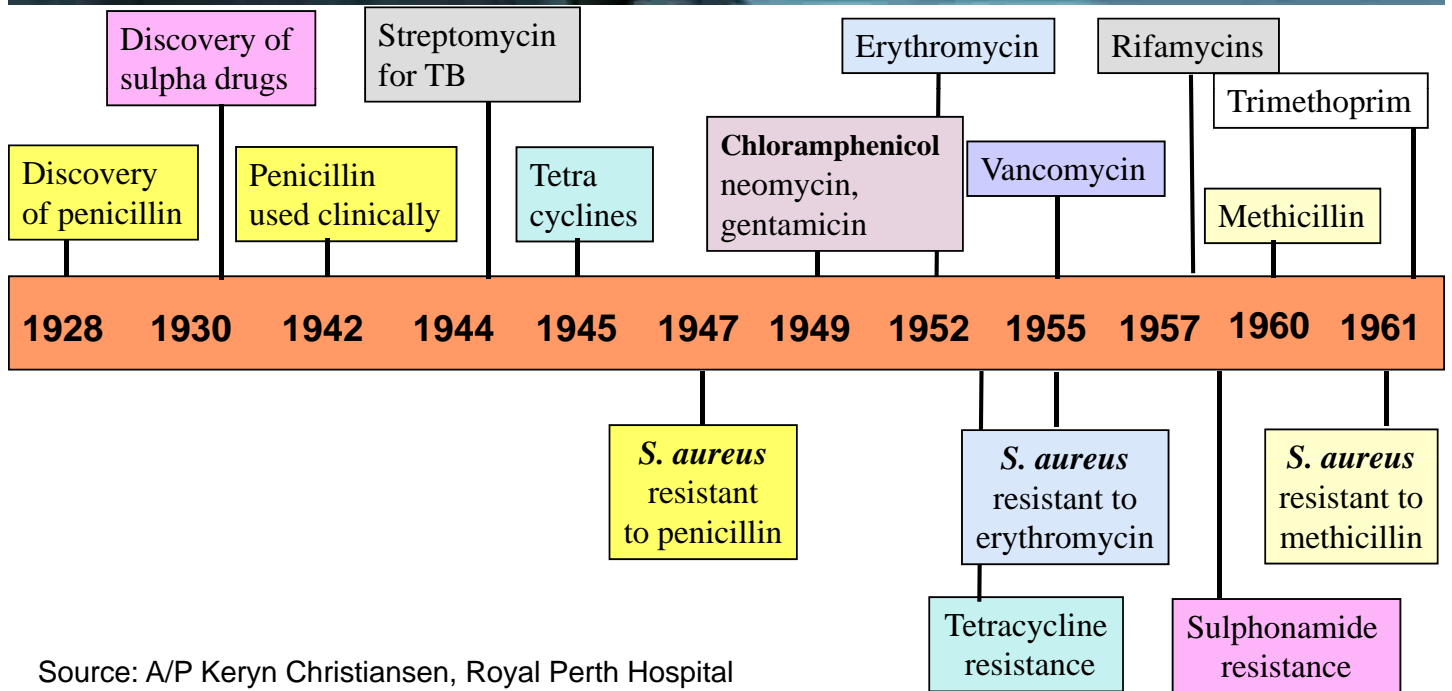
1945- Fleming, Florey and Chain won
Nobel Prize



What is an Antibiotic?

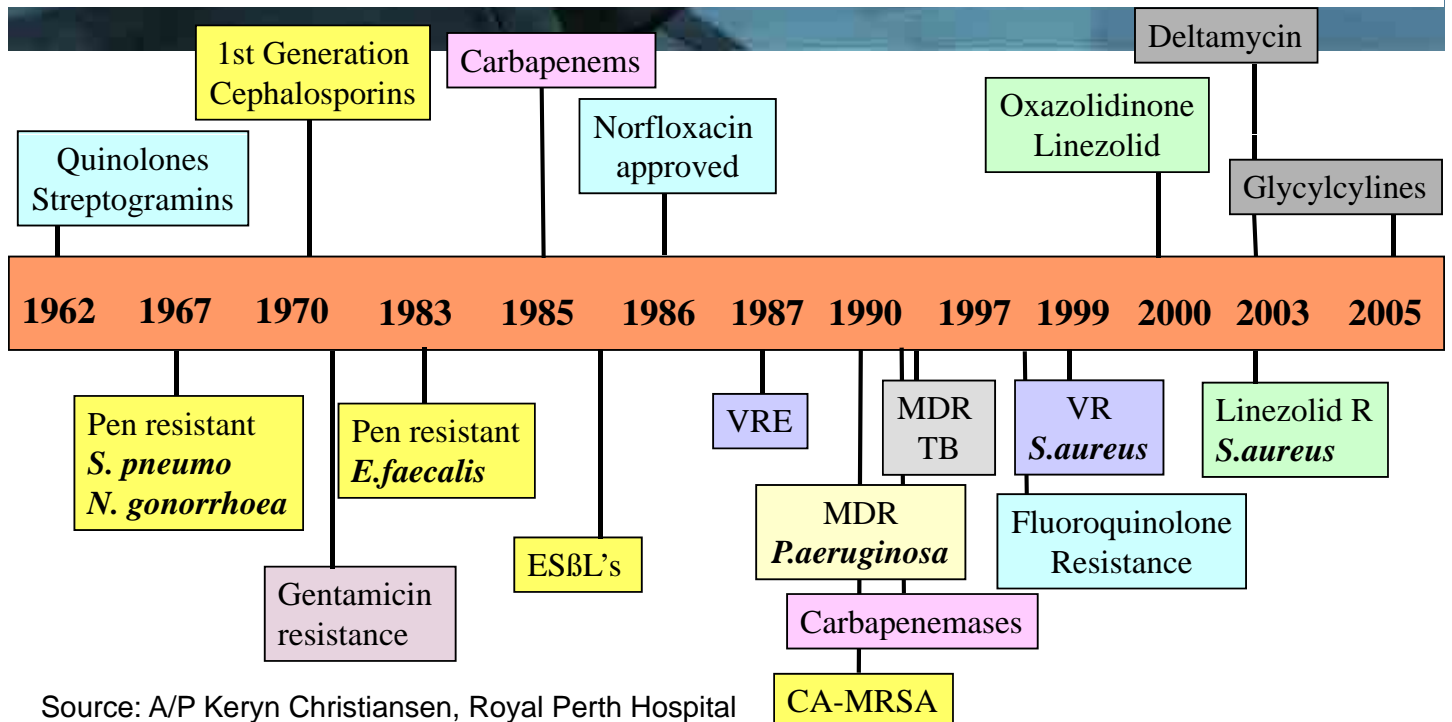
- > "antibiotic" (from the Greek *αντί* – *anti*, "against" + *βιοτικός* – *biotikos*, "fit for life")
- > coined by Selman Waksman in 1942 to describe any substance produced by a micro-organism that is antagonistic to the growth of other micro-organisms in high dilution.
- > Small molecules that target larger molecules essential for bacterial survival
- > Specific for bacteria

Emergence of Antibiotic Resistance



Source: A/P Keryn Christiansen, Royal Perth Hospital

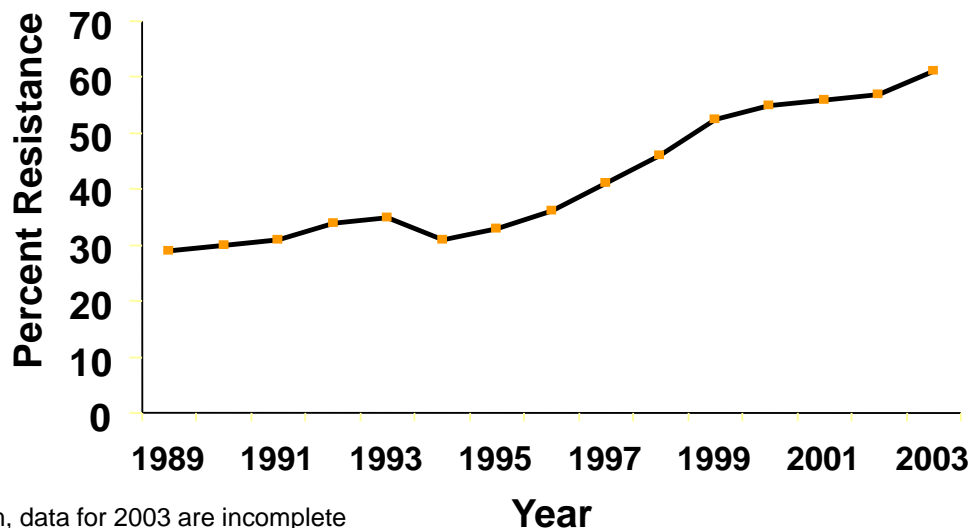
And counting.....



Source: A/P Keryn Christiansen, Royal Perth Hospital

A Common Trend

Proportion of *S. aureus* Nosocomial Infections Resistant to Oxacillin (MRSA) Among Intensive Care Unit Patients, 1989-2003*



*Source: NNIS System, data for 2003 are incomplete

Antibiotic Resistance: A Real Problem

“Large numbers of people are dying from resistant organisms, but I’m starting to wonder if you have to line body bags up in front of Parliament House to get any action”,

“For some organisms, we have absolutely nothing in the antibiotic pipeline. We’re not facilitating the development of any new antibiotics for these, so the drying up of the antibiotic pipeline is a major concern”

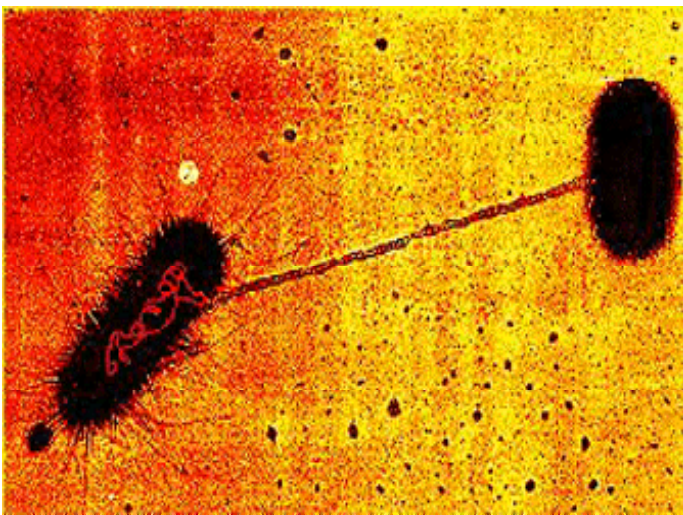
The Australian Microbiology Society President, Keryn Christiansen
The Age, July 7, 2008

Mechanisms of Resistance

- Make an enzyme that inactivates the antibiotic
- Change the target so that it is no longer recognized by the antibiotic
- Change cell permeability (don't let antibiotic in)
- Efflux pumps (pump antibiotic out)
- Bypass the function targeted by the antibiotic (esp for antibiotics that target metabolic pathways)

How does this come about?

Resistance Genes are Mobile

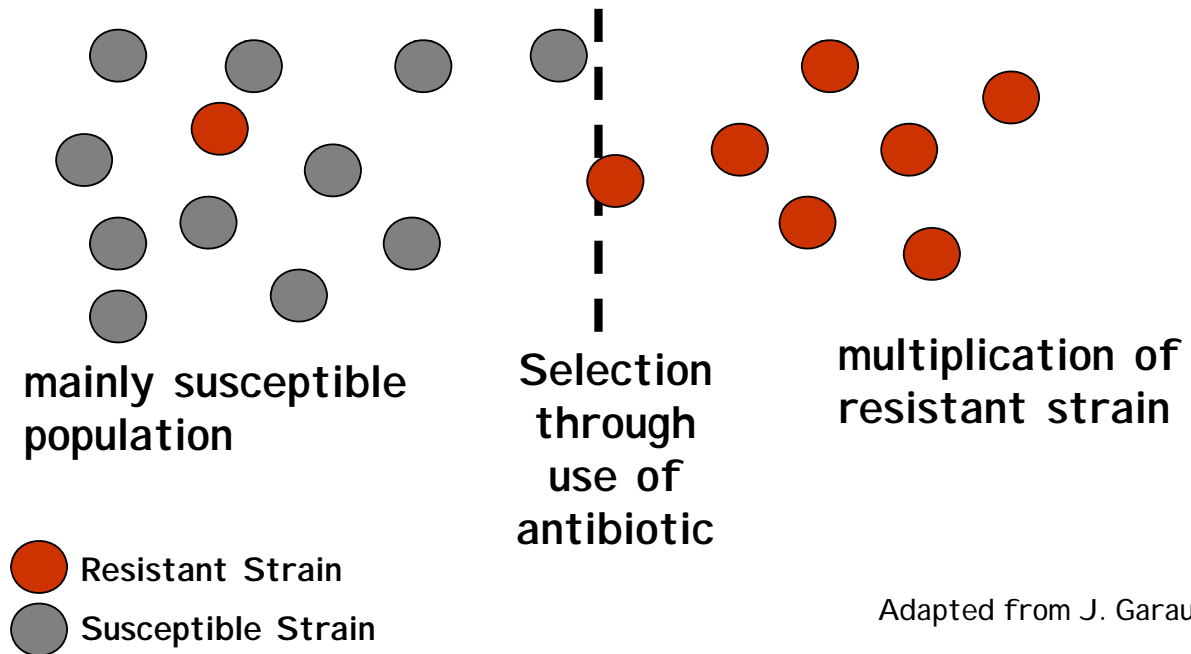


**Horizontal gene transfer:
one bacterium gives genes
to a second bacterium who
can then also pass them on**

**Professor Hatch Stokes
IBID, UTS**

**Professor Ruth Hall
University of Sydney**

Resistant Strains Have Always Been Present

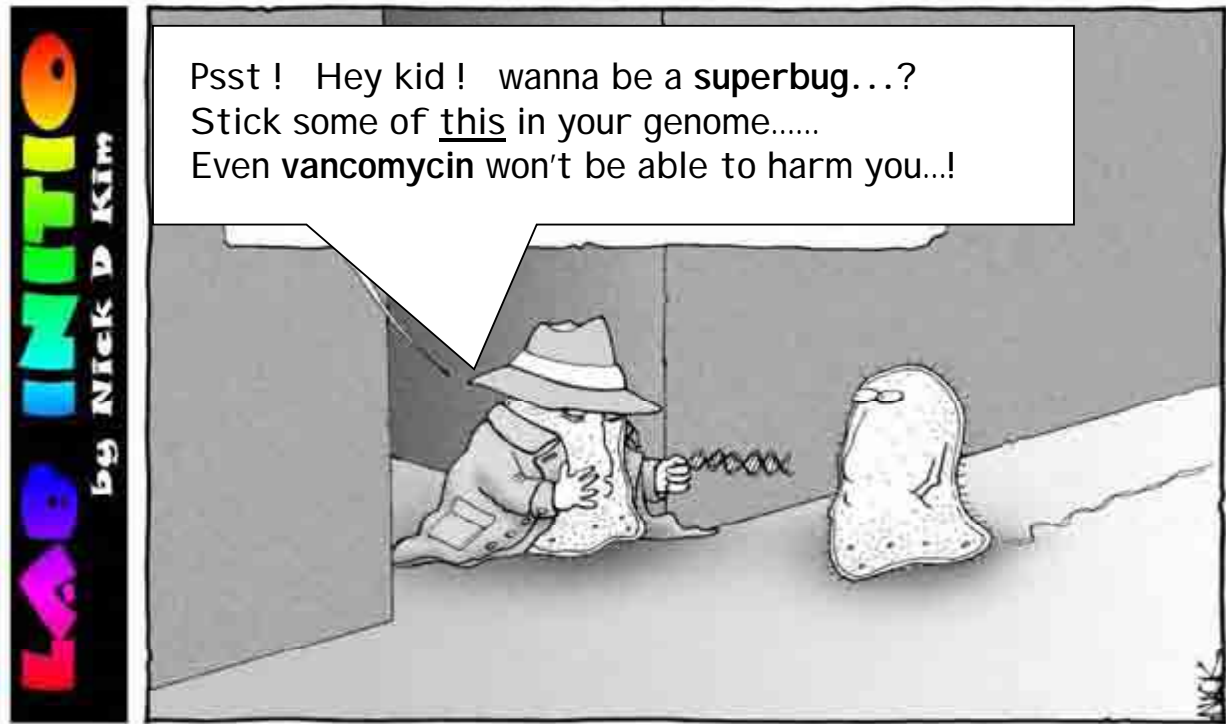


Adapted from J. Garau, 2006.

Magnifying the Problem

- > Not just one antibiotic resistance gene
- > Not just one species of bacteria





It was on a short cut through the intensive care unit that Albert was first approached by a member of the Antibiotic Resistance

What is a Superbug?

- > Multi-resistant Staphylococcus aureus (MRSA and VRSA)
- > Multidrug resistant TB (AIDS)
- > In hospitals and community
- > Acquisition of 'resistance' genes
- > Increased mortality, morbidity, prevalence/incidence of disease
- > **Potential for untreatable infection**



Question

- > How many of us are reservoirs of antibiotic resistant genes?

100%



What can we do about it?

1930



2008



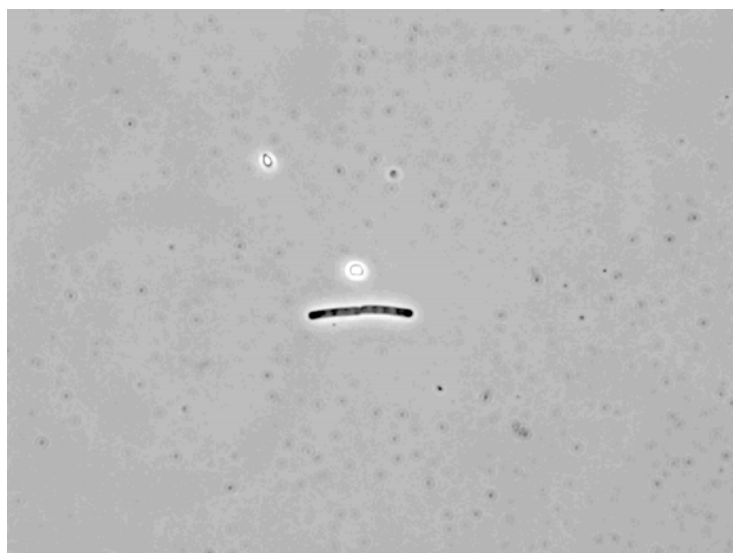


What can we do about it?

- > Nationwide surveillance of resistant strains
- > Isolation rooms in hospitals
- > When infection is not bacterial, don't use antibiotics
- > An antibiotic is not always the answer
- > Use less antibiotics in humans and agriculture
- > Be informed- Resources: Centre for Disease Control (USA)
- > Recognize the advertising hype: remember most bacteria are good
- > Identify new preventions and treatments by research
- > Antibiotics only target a few essential processes

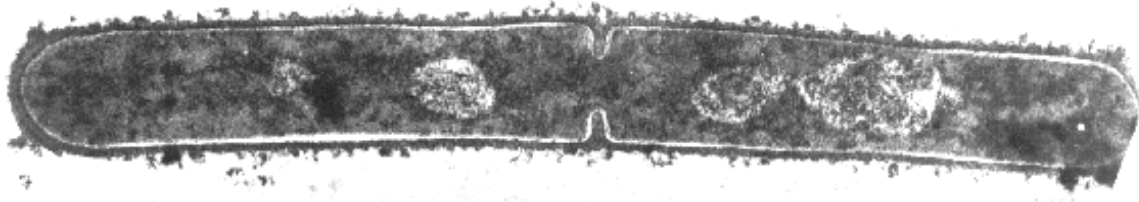


New Antibiotics





Targeting Cell Division



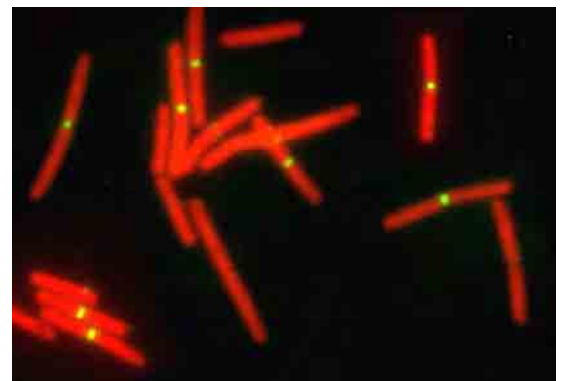
Identified new candidate drug targets

Lock and Harry (2008) Nature Reviews Drug Discovery

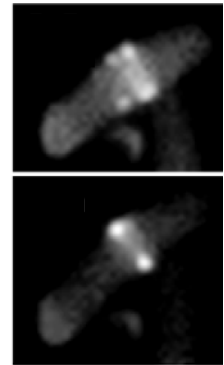
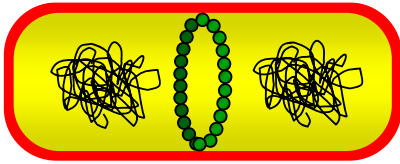


Targeting Superbugs

- > **Essential processes :**
DNA replication, protein synthesis
and cell division
- > **Fast-track approach:**
identify protein-protein interactions
- > **Identify inhibitors of interactions**
- > **Initial stage of antibiotic discovery**



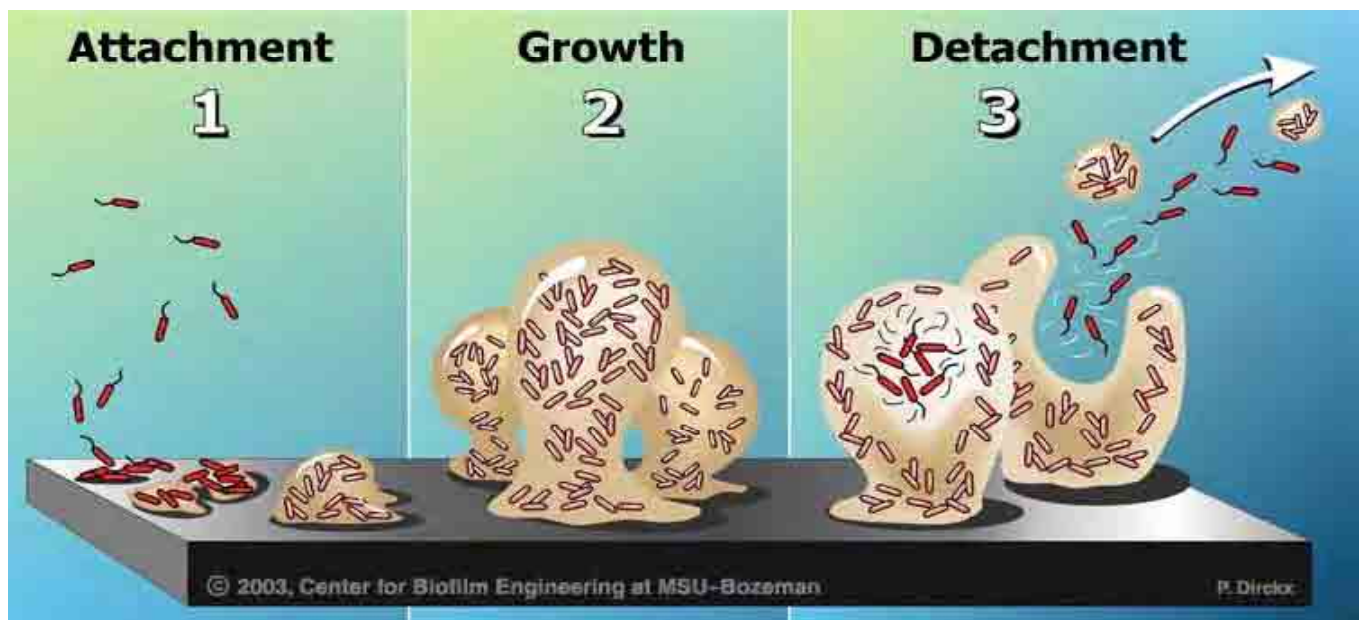
The Master of Cell Division: FtsZ



Molecular Microbiology (2007) 64, 487-499.



Bacteria Live in Communities: Biofilms



Legionnaire's Disease

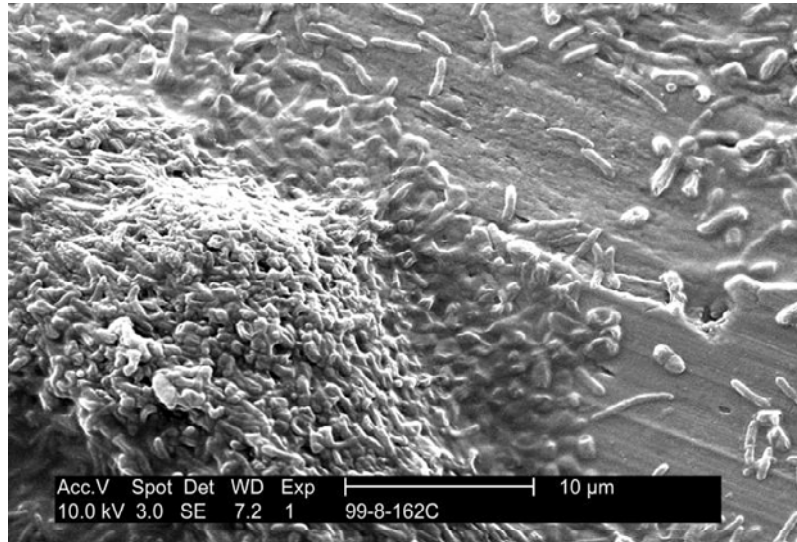
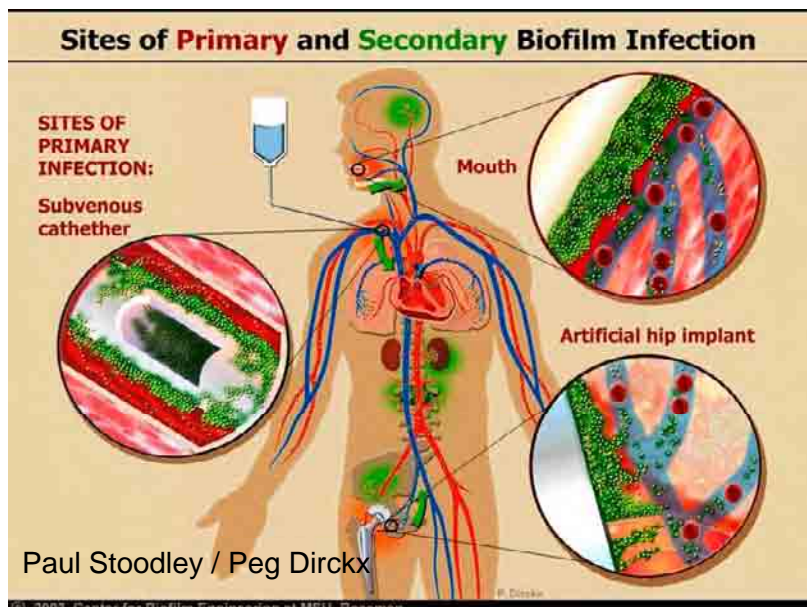


Photo: Janice Carr

Biofilm Infections



- > 80% of infections
- > Implants, medical devices
- > Recalcitrant to antibiotics
- > Big problem
- > Chronic wounds

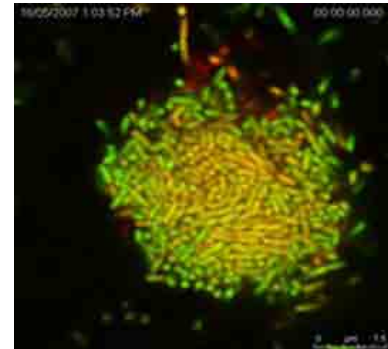
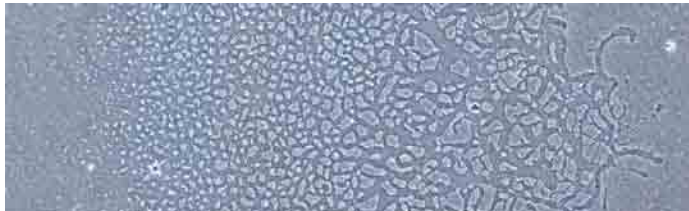


Biofilms in Infectious Disease

UTS: A/P Cynthia Whitchurch and Dr Lynne Turnbull

Biofilm development by bacterial pathogens

Pseudomonas aeruginosa -cystic fibrosis



A Sweet Ancient Remedy: Honey

- > Since dawn of time
- > Kills bacteria
- > Not just any honey works (Manuka, Medihoney)
- > Honey destroys biofilms of *S. aureus* and *P. aeruginosa*
- > Antibiotic resistance to honey could not be generated
- > Honey wound dressings-ideal properties





Chronic Wounds and Honey

- > Chronic wounds –global health problem
- > What is in honey that can kill biofilms?
- > How does it do it?
- > What if it can do this with chronic wounds?



Liz Harry, Cynthia Whitchurch, Lynne Turnbull (IBID, UTS)

Dee Carter, Shona Blair (University of Sydney)

Ralf Schlothauer Comvita Pty Ltd (Manuka UMF®, Medihoney)



SO.....

- > Bacteria are good for you
- > Very few are bad
- > Superbugs are REALLY smart
- > Antibiotic resistance is an urgent issue
- > Yes, bacteria do exchange bodily fluids
- > There are lots of resources
- > Prevention is better than cure

Australian Society for Microbiology
Center for Disease Control (CDC) USA



THANKS

- > TO YOU
- > Associate Professor Jon Iredell, Westmead
- > Associate Professor Keryn Christiansen, Royal Perth Hospital
- > Professor Hatch Stokes, UTS
- > Associate Professor Cynthia Mitchell
- > Associate Professor Dee Carter
- > Dr Shona 'Honey' Blair
- > Associate Professor Jock Harkness
- > Australian Society for Microbiology
- > Bruce Milthorpe, Dean of Science, UTS
- > Robert Button, Media Office, UTS



My Research Team!