

Biofilms: When the Bugs Get Clingy
Dr. David Hammer, Canterbury Health Laboratories, Christchurch
A Webber Training Teleclass

BIOFILMS
When the bugs get clingy

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Hosted by Jane Barnett
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- “I only know that I know nothing.”
– Socrates

- “If only I knew what little they know, then I’d know a little...”
– The BBC, The Goonshow

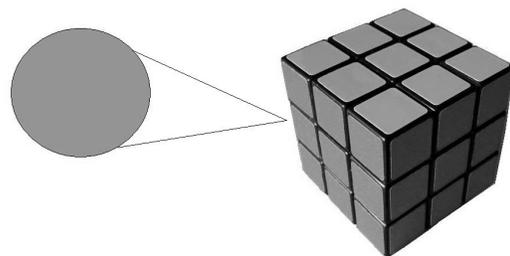
>99% microbes live in a biofilm

- Whereas conventional microbiology has concentrated on planktonic organisms
- So what?

You can’t solve a puzzle ...



by looking at only a part of it.



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What is a Biofilm?

- Structured, co-operative microbial community embedded in an extracellular matrix, usually attached to a surface
- Free-floating (planktonic) cells attach to become sessile
- Biofilm organisms usually express a different phenotype

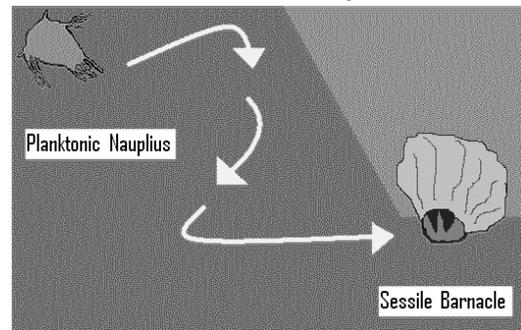
Planktonic vs Sessile Bugs

- Planktonic
 - From Greek 'wandering'
 - Free floating form
- Sessile
 - From Latin 'sitting'
 - Fixed to a site (usually an organic/ inorganic surface)

Consider barnacles.



Barnacle lifecycle



The Usual Suspects

- Gram positives
 - Staphylococcus aureus
 - Coagulase negative Staphs
 - Enterococci
- Gram negatives
 - Pseudomonas
 - Proteus
- Candida

Small Colony Variants

- Phenotype switching
- Grow much slower, if at all
- More adherent
- Less immunogenic
- Approx 10 x smaller than normal colonies
- Link with viable but non-culturable state?

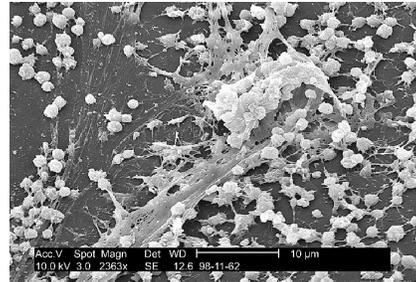
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Single or multiple species?

- Biofilms may consist of a single species or a complex community of organisms, the workings of which we are only beginning to fathom
- Different species may be competing or co-operating

Microscopic biofilms



Biofilm on needleless connector

Image courtesy of CDC

Macroscopic biofilms



Plaque and tooth decay

Image courtesy of COHB

Obvious biofilms



Biofilm on a kitchen plug

Really HUGE biofilms



Great Barrier Reef

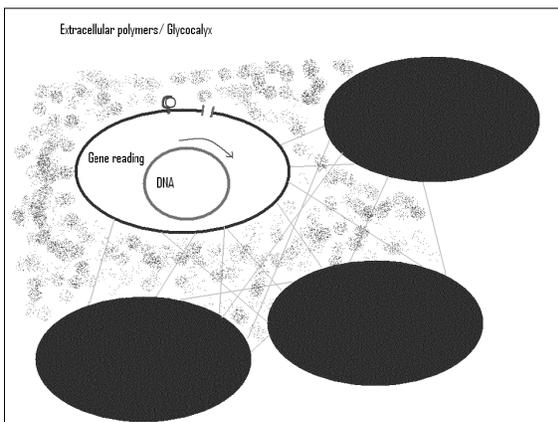
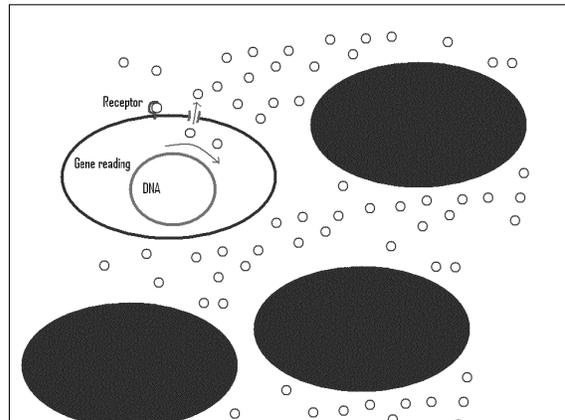
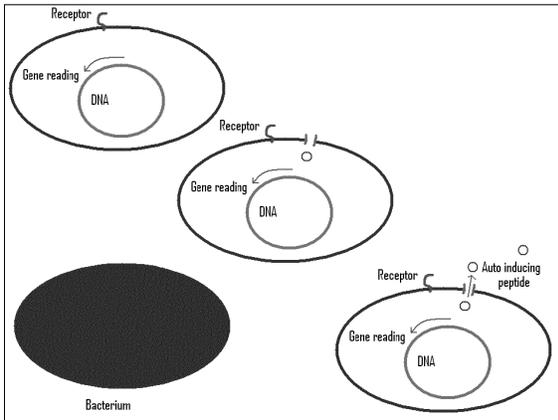
Quorum sensing and biofilms

- How do microbes know that there are other microbes around them?

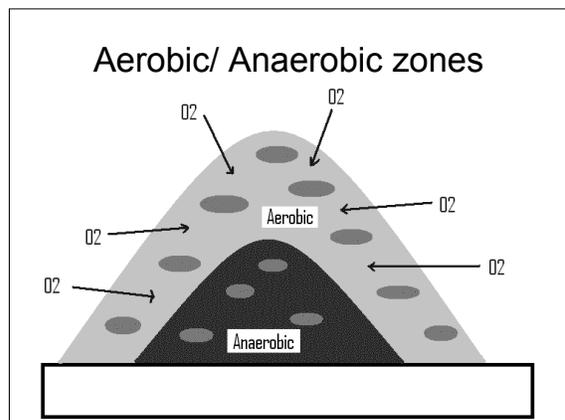
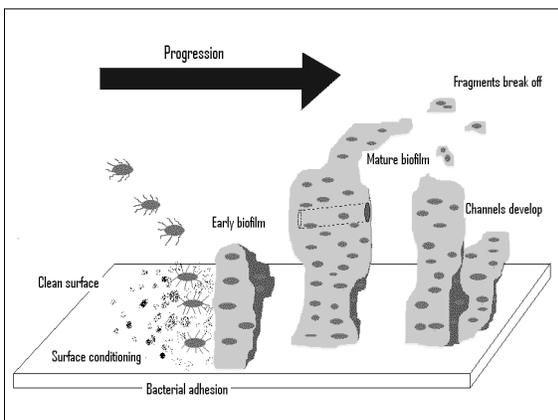
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- ### Biofilm development
- Surface conditioning with organic and inorganic materials
 - Colonising microbes become irreversibly adherent
 - Extra-cellular matrix produced
 - Biofilm develops often with subspecialisation of cells
 - Mature biofilm with channels for nutrient/ waste exchange



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Advantages to bacteria

- Increased environmental survival
- Resist being swept away
- Toxin production
- Resist phagocytosis
- Antibiotic resistance

Advantages to bacteria

- Increased environmental survival
 - Increased protection against heat, cold, UV

Advantages to bacteria

- Resist being swept away
 - Adherent colonies increase resistance to shear forces
 - Allow nutrients to flow to the colony and become trapped in the extra-cellular 'net'
 - Parts of mature biofilm that do shear off form excellent seeds for further colonies (preformed infectious dose)

Advantages to bacteria

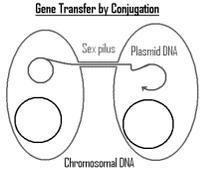
- Toxin production
 - Synchronised toxin production vastly increases amounts of toxin produced

Advantages to bacteria

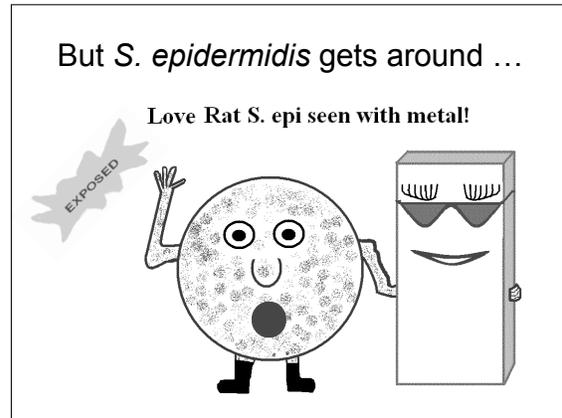
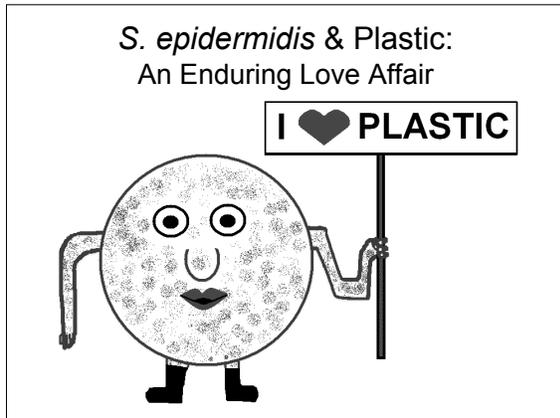
- Resist phagocytosis
 - Difficult for predatory amoebae or WBCs to engulf biofilm bacteria
 - Synchronised toxin production also reduces phagocyte numbers

Advantages to bacteria

- Antibiotic resistance
- 10 – 1000 times more resistant to Abx.
 - Decreased penetration of antibiotic?
 - Altered metabolism?
 - Sharing of resistance plasmids through close



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Advantages to humans

- Not all biofilms are bad news
- Commensal bacteria in the mouth, gastro-intestinal tract and vagina interfere with pathogen colonisation

Pathogenic biofilm examples

- Foreign bodies / Medical devices
 - Catheters
 - Lines
 - Prosthetic joints
 - Prosthetic heart valves
- Disease states
 - Otitis media
 - CF
 - Dental caries
 - *H. pylori*
- Environmental
 - Legionella in water supply pipes
 - Cholera in the Bay of Bengal

Diagnostic conundra

- Is the disease causing agent
 - the planktonic organism we detect or
 - is it hiding in a biofilm?
- Is the biofilm agent we detect
 - causing disease or
 - is it just colonising a site?

Infection Control & Biofilms

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Management in disease states

- Antibiotic use may have an influence
 - Carbapenems may increase alginate production by *Pseudomonas* in CF
 - Macrolides may inhibit *Pseudomonas* quorum sensing in CF

Environmental Management

- Water treatment before it enters hospital pipeline
 - UV, Heat, Chlorination
- Can't do much about cholera in Bengal
 - Just don't drink the water!

Prevention in devices What doesn't work?

- Bladder irrigation
- Chronic systemic antibiotic prophylaxis

Prevention in devices 1

- Biofilms form within minutes to hours of foreign body insertion – mature biofilms develop within 18 – 24 hours!
- Development depends on:
 - Number of microbial cells already present
 - Flow rate
 - Available nutrients
 - Antimicrobials
 - Ambient temperature

Prevention in devices 2

- Does the patient **really** need a catheter/ IV line/ etc?
 - Approx 50% of urinary catheters are not necessary.
- Can't do much about environmental factors but can reduce viable microbes by:
 - Good hand hygiene
 - Good skin prep
 - Appropriate prophylactic antibiotics

Prevention in devices 3

- Reduce opportunities for introduction of organisms
 - Optimising sites (tunnelled lines, suprapubic catheters, etc)
 - Proper disinfection before IV line use
 - Closed drainage of urine

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Treatment of infected devices
What works?

- Removal of the device
 - Is the only sure way to remove a biofilm

- Antibiotic therapy may or may not work
 - Depending on how well you can
 - get antibiotics to the site and
 - penetrate the biofilm and
 - eradicate the persisters

This is all just basic Infection
Control ...

- Surely science will save us?

Can we rely on technology?

- Antibiotic coated lines
- Silver coated lines
- New 'non-stick' materials
- Mixed evidence for above – may work for a limited time but at what cost:
 - Allergy?
 - Drug resistance?
 - Rough surfaces assist biofilm formation but no known material prevents it.

Experimental measures

- Electricity + Antibiotics
- Quorum sensing interference
 - Furanones from red seaweed (*Delisea pulchra*) interfere with QS but
 - toxicity issues limit use thus far
- Ethanol locks
- Iron scavenging materials reduce growth
- Bacterial interference

Treatment Summary

- Prevention is the best treatment
- Accept that biofilms will eventually form on most catheters
- Usually need to remove foreign body to remove biofilm
- New technologies will become available but will NOT replace basic infection control

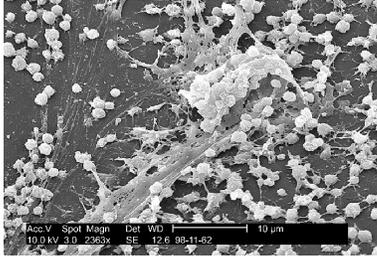
Treatment 2

- Basic Infection Control is the science that will save us

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The relative test:



If this was happening to your relative, how would you like them treated?

References

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