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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“I only know that I know nothing.”
– Socrates

>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

Macroscopic biofilms

Obvious biofilms

Really HUGE biofilms

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

Aerobic/Anaerobic zones

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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 contact

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S. epidermidis & Plastic: An Enduring Love Affair

But S. *epidermidis* gets around …

Advantages to humans

- Not all biofilms are bad news
- Commensal bacteria in the mouth, gastrointestinal 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?

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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?

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