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Biofilms: a sticky situation

Antibiotic stewardship

- New national condition of participation
- The bugs are winning
- Previous hazards of wound care
- Biofilms are the poster child of the problem

What is biofilm?

- Symbiotic collection of micro organisms protected and held together by self generated polymers(matrix).
- Bacteria primarily exist by attaching to the surface of living and inanimate objects.
- Think coral reef

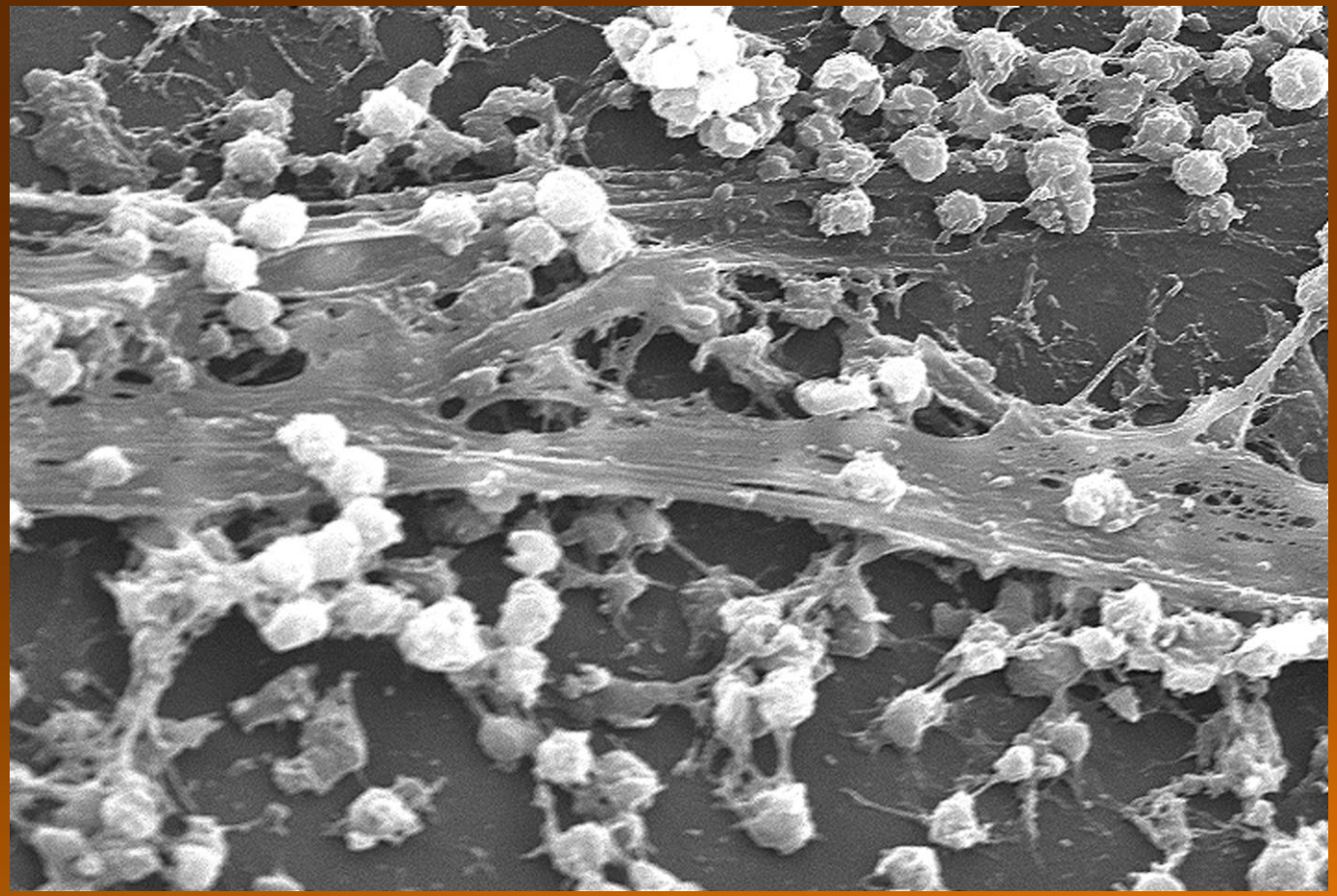
How do biofilms form?

- Extracellular appendages- flagella or cilia attach to a surface and temporarily prevent removal.
- Irreversibly attach using extracellular polymers- polysaccharides- which become the matrix.
- Organisms reproduce forming colonies protected by matrix
- Develops water channels to deliver nutrients and oxygen to growing cells

Where does a biofilm form?

- On almost any living or inanimate object in nature.
- Clinically relevant biofilms form on indwelling medical devices, living tissues, heart valves, lungs, the middle ear, and many more.
- Rougher and more hydrophobic like plastic develop films easier than smooth, hydrophilic surfaces- glass.

Real life biofilm-



Medical devices prone to biofilm

- Central venous catheters
- Contact lenses
- Mechanical heart valves
- Pacemakers
- Peritoneal dialysis catheters
- Prosthetic joints
- Urinary catheters

Most common micro organisms in biofilm

- Type of bacteria is largely dependent on the location within the body.
- Central venous catheters- Staph, Enterococcus, followed by a few gram negative bugs and candida.
- Prosthetic heart valve- Streptococcus, Staph, Enterococcus
- Urinary catheter- Staph Epi, E Coli, Klebsiella, Enterococcus, Proteus
- Artificial joint- Staph, Strep, anaerobes-Bacterioides, E Coli, Pseudomonas

Clinical significance *****

- Exceptionally harder to treat than normal infection.
- Antibiotics must diffuse through the polysaccharide matrix
- Dramatically decreased susceptibility to antibiotics
- Biofilm E Coli requires 1,500 times the MIC of ampicillin.
- Staph Aureus requires 110 times the MIC of vancomycin

Difficulty in treatment ***

- Closer proximity allows easier plasmid transmission of resistance mechanisms
- Growth rates slows- most antibiotics act on growing cells
- Older is worse. Higher resistance percentages and greater resistance.

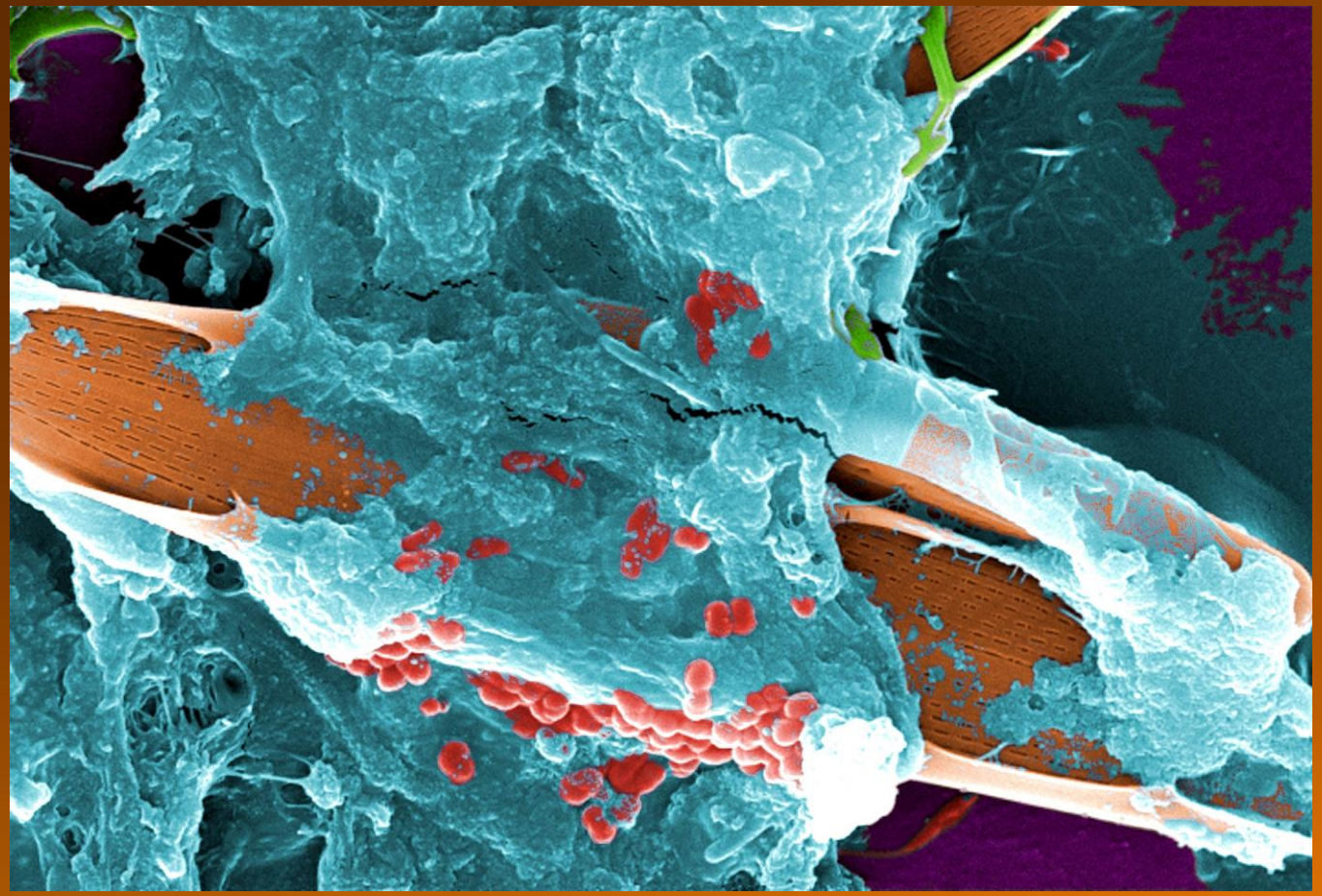
Difficulty in treatment ***

- Septic emboli
- REMOVE THE BIOFILM CONTAMINATED DEVICE!!

- Standard MIC testing is not applicable

Clinical conundrum- C&S interpretation

- Basically two potential colonies of bacteria in same person- which is the true susceptibility?
- Did biofilm contaminate the systemic infection?
- When is it truly cured?
- Free floating bacteria are killed but bacteria in the film are still alive
- Signs- recurrent infections/fevers with identical bacteria



Coag Negative Staphylococci

- Commonly found on skin
- Blood cultures commonly thought of as contaminate
- However most commonly found on medical devices
- Repeat the blood cultures, especially in patients with devices

Pseudomonas lung biofilm

- Cystic Fibrosis
- Pseudomonas makes a biofilm on the lung
- Low dose antibiotics actually cause bacteria to excrete glycogen matrix as a defense mechanism

Ears and feet

- Chronic diabetic foot infections are thought of as biofilms as are chronic ear infections

Treatment

- 1- Prevent the contamination- aseptic technique and minimize duration of placement
- 2-minimize microbial attachment via engineering controls
  - Impregnate devices with silver nanoparticles to prevent biofilm attachment

Treatment

- 3- High dose antimicrobials to penetrate biofilm or ethanol in catheter lock solution
  - Combination of antibiotics and COMBINATION of routes can be more effective- topical and IV
  - Beta-lactams may be worst choice for biofilms- size, ph, etc

- Agents that have shown to penetrate biofilms effectively:
  - Rifampin has been shown to improve efficacy of vancomycin or linezolid against MRSA
  - Gentamicin is synergistic with ampicillin. Vancomycin and linezolid for Enterococcus.
  - Daptomycin, minocycline, tigecycline can be more effective than vancomycin or linezolid for MRSA infections
  - Fluoroquinolones
    - Levofloxacin, ciprofloxacin, moxifloxacin

Treatment

- Catheter lock solution composed of minocycline, EDTA, and 25% ethanol has shown to eradicate MRSA biofilm after 15 min of exposure.
- Remove the infected device.
- Time of removal matters- Antibiotics need to be given for 48hr to kill free floating bacteria- so the new catheter is not immediately recolonized

Newest ideas in biofilm prevention

- Quorum sensing inhibitors
- Quorum sensing- how bacteria communicate to each other
- The bacteria use chemicals to send out messages, quorum sensing is the next bacteria hearing and acting on that chemical signal.
- It allows multiple bacteria to act in the same manner- such as building a biofilm.

Newest ideas in biofilm prevention

- 2nd messengers, amyloid arms, bacteriophages, other bacteria, microbubble ultrasonics.
- 2-A – small molecule for inhibiting biofilms- sponge derived.
- Even antigens from the biofilm are being looked at as targets for vaccination.

Potential benefits outside of medicine

- Biofilms cost billions in the industrial, sewer, etc industries
- Research is being done on how we purposely use them to prevent water contamination
- That bacteria and biofilms are used in industry to remediate contaminated areas

Questions?