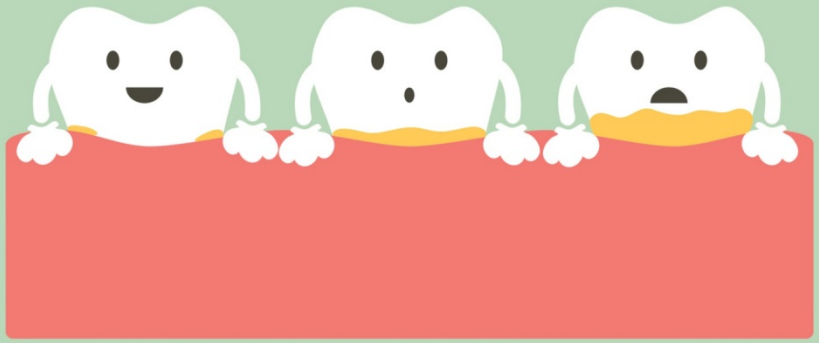
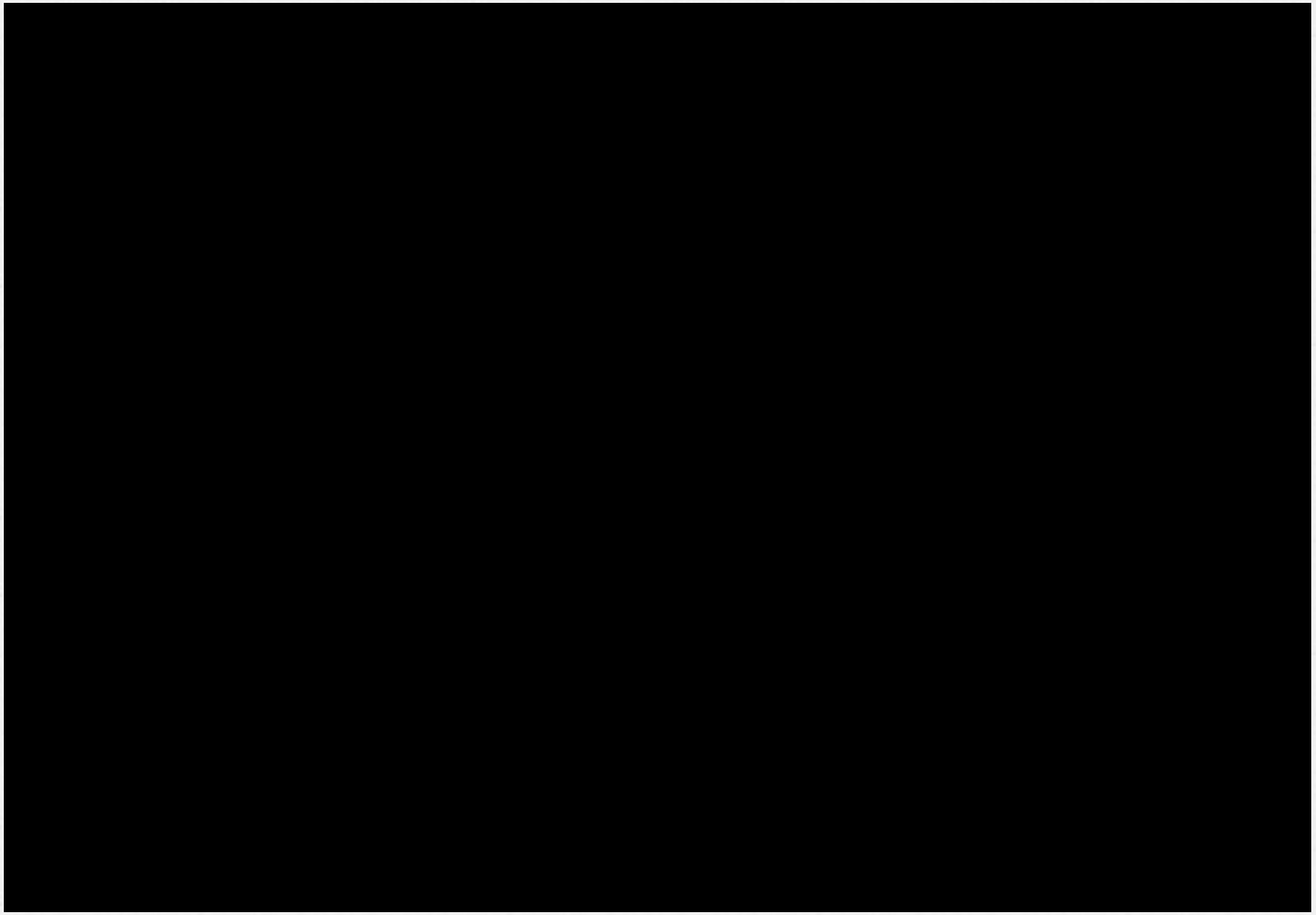
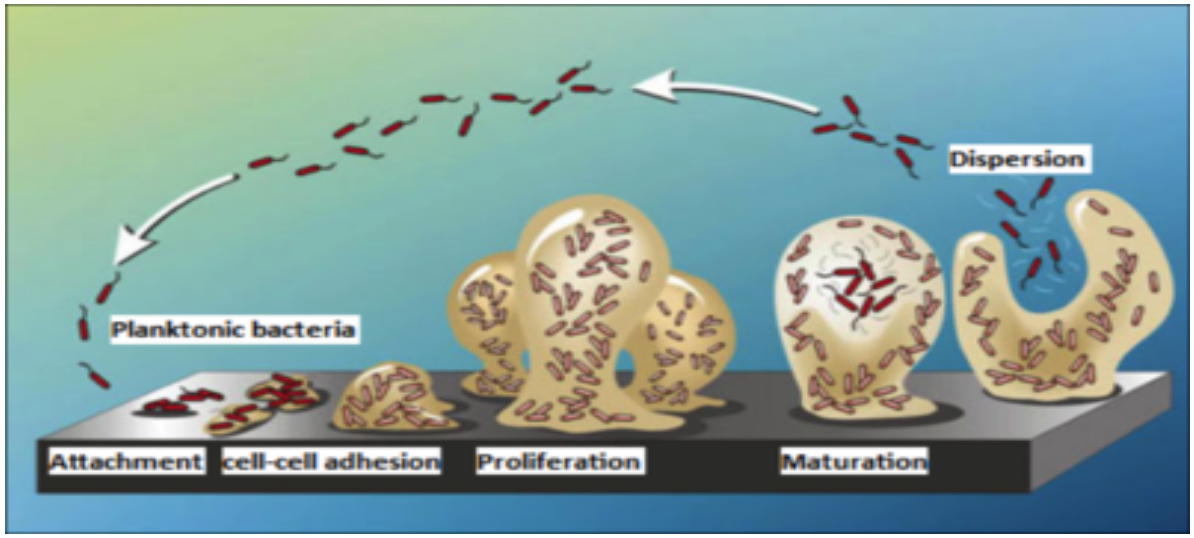
HOW WE CAN DEAL WITH ORAL BIOFILM (DENTAL PLAQUE)



By Shelly L. Fritz, DDS—*NMDA Journal Editor*

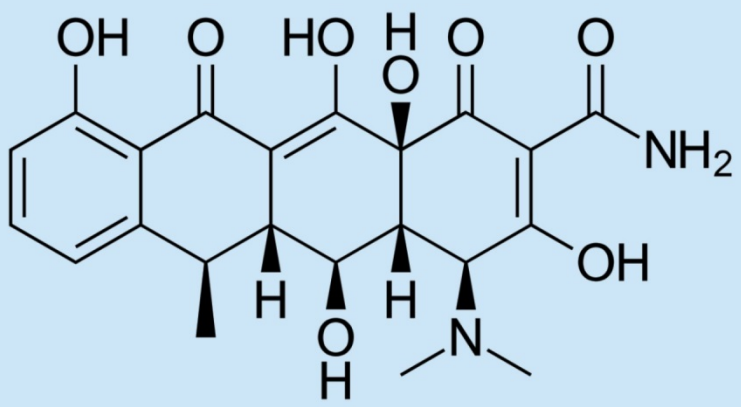


We know that we can get rid of the biofilm matrix but it quickly re-forms often in minutes on any moist surface. We also know that even young polymicrobial colony loads in dental plaque can cause an inflammatory response. Our progressing knowledge of the relationship between the host and biofilms determines the onset and progression of periodontal disease and dental caries giving us clues on how to contain the process of growth and virulence.



The easiest way to control colonies is to **mechanically remove them**. Daily oral hygiene, prophylaxis, scaling, and root planning, progressing to surgery for deep pockets and furcations and tissue regeneration are proven deterrents in population propagation and growth.

Systemic antimicrobials such as **penicillin, tetracycline and metronidazole** for moderate to severe chronic periodontitis are used adjunctively. These therapies do benefit patients but antimicrobial resistance due to gene changes in the bacteria, the formation of resister and persister bacteria and a matrix that inhibits access to the bacteria make this strategy ineffective to destroy biofilms. Systemic antimicrobials work best on planktonic forms.



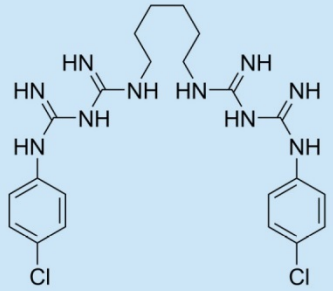
Orally administered **doxycycline** (20mg bid) used for 3 to 9 months does not promote microbial resistance and does improve host response, hence a positive outcome with sub-antimicrobial dosed (SD) doxycycline reduces inflammation via anti-collagenolytic, anti-matrix-degrading metalloproteinase, and cytokine down-regulating properties as well as increasing gingival crevicular fluid levels. SD doxycycline (Periostat 20 mg) has clinical utility in periodontitis. It was first used in the treatment of moderate facial acne and in the treatment of rosacea. Acne lesions are full of biofilms.

Arestin (minocycline microspheres) and **Atridox** (doxycycline hyclate) are locally applied antimicrobials. They are placed in the affected pocket—Arestin for 14-21 days and Atridox for 7 days with retreatment at 12 months. These antibiotics are sustained released keeping the antimicrobial load above the minimum inhibitory concentration and maintaining systemically low levels of the antibiotic. Because the antibiotic is contiguous to the biofilm over a long period of time, the planktonic bacteria are destroyed and the matrix is penetrated to kill the sessile bacteria. Antibiotics kill bacteria as they are growing. Sessile bacteria are slow-growing or can become dormant in the presence of an antibiotic. Therefore, this method of having an antibiotic present for days at the site of the biofilm is more effective than systemic antibiotics.

Polyols starve bacteria, in particular **xylitol**. This is ingested by the strep bacteria in biofilm preferring this sugar over sucrose. In the absence of Strep. mutans, sucrose is not fermented to acid. The strep bacteria starve as they receive no nutritional value from xylitol. Xylitol also inhibits Candida albicans from attaching to a surface like dentures. It also inhibits the attachment of Lactobacillus species as this species causes root decay. FDA considers xylitol a food like salt and pepper. Optimal dosage is 6 to 10 servings a day in lozenges, gum, and naturally occurring fruits, vegetables, tea, coffee (plants). However, too much ingested xylitol causes diarrhea.

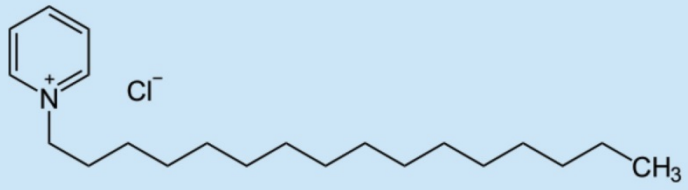
GUM PerioBalance is a **probiotic** in a lozenge form. The theory is that the biofilm colony will accept/recruit these bacteria instead of more lethal ones. However, quorum sensing molecules change the behavior and structures of bacteria. I did not find any research that elucidates that the probiotic bacteria remain probiotic in the colony.

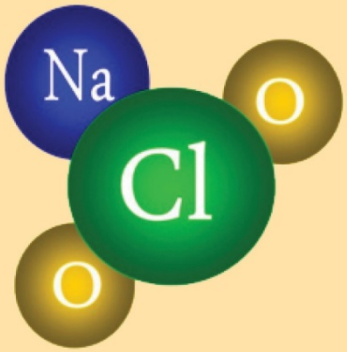
Essential oils, (**eucalyptol, menthol, methyl salicylate and thymol**) in numerous private label brands and Listerine, interact with alcohol in solution and drill through the biofilm matrix and lyse the bacteria and fungi within. Even though the oils destroy all the organisms they reach, they don't reach very deep.



Chlorhexidine (CHX), (3M Peridex, Colgate Perioguard, and alcohol free G*U*M Chlorhexidine Gluconate, bind salivary mucins reducing pellicle formation which inhibits bacterial colonization. It binds the bacteria so they can't attach to the tooth's surface. CHX is substantive, meaning it sticks to the surface of the biofilm. In this way it can inhibit bacterial colonization for about three weeks. It can also penetrate the biofilm to midlevel. CHX is cationic, interacting with the negatively charged bacterial cell surface and translocating to the cytoplasmic membrane, rupturing it. Penetration in the biofilm matrix is key: the younger the colony (the colony is in a steady state at three weeks), the CHX is more effective. The longer the CHX treatment, the longer it takes for repopulation. The susceptible and persistent cells recover and the susceptible cells change to persister cells. The biofilm is back to its normal self in about two months. Because CHX penetrates deeper (midlevel) and kills all microbes in the biofilm it can reach, it is the gold standard of all the mouthwashes.

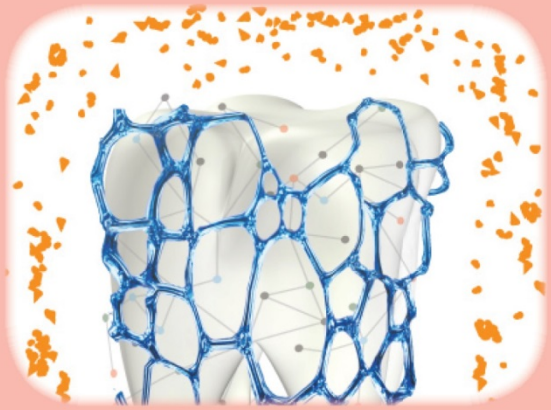
Cetylpyridinium chloride (CPC) also ruptures cell membranes and inhibits cell attachment or biofilm maturation, but it does not penetrate as deep as CHX.



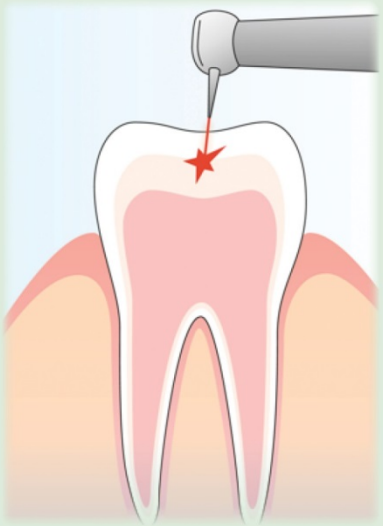


Stabilized chlorine dioxide (CloSYS, Oxifresh, MATATACORO) is formulated to prevent gingivitis. It works very well in the prevention and eradication of biofilms in industrial cooling systems and water distribution systems. Like ozone and chlorine, chlorine dioxide is an oxidizing biocide and not a metabolic toxin. This means that chlorine dioxide kills microorganisms by disruption of the transport of nutrients across the cell wall, not by disruption of a metabolic process. Stabilized chlorine dioxide is ClO2 buffered in an aqueous solution. Adding an acid to the required concentration activates the disinfectant. It has removed biofilm from water systems and prevents it from forming, when dosed at a continuous low level. Hypochlorite, on the other hand, has been proven to have little effect on biofilms. Even though it has been used for 200 years, I could find only one paper which claimed it inhibits proteases that originate from oral bacteria. It was no more effective than CHX.

Delmopinol hydrochloride (G*U*M PerioShield) interferes with the bacterial adherence to biofilm. It doesn't kill bacteria—it prevents them from sticking to the teeth by coating the teeth and gums thus blocking adhesion.



It is approved by the FDA as a Class II medical device that affects the structure of the body with no intended purpose through chemical action within or on the body, dependent on metabolization to achieve its primary intended purpose.



Lasers disrupt biofilm in seconds. A miniature Q-switched Nd:YAG laser with thin fibers and special probes generated plasma formation and a resulting shock wave effect sufficient to disrupt biofilm without harming the underlying host structure (various indwelling prosthetics). A Super-Pulsed CO2 laser was used on dental implants to remove biofilm. The HA coated surface (Steri-Oss) melted but the phosphate-enriched titanium oxide surface (NobelReplace) and the hydrophilic sandblasted and acid-etched surface (Straumann SLActive) were fine. Because of its water absorption, the Erbium YAG laser is the best choice to remove periodontal biofilm. Of course, biofilms regrow immediately, so adjunctive care is required.

Sonic waves used in sonic toothbrushes do not remove biofilms, but the **bubbles** generated by the sonic waves do. The collision of the bubbles at any angle between 5 and 45 degrees removes the biofilm.

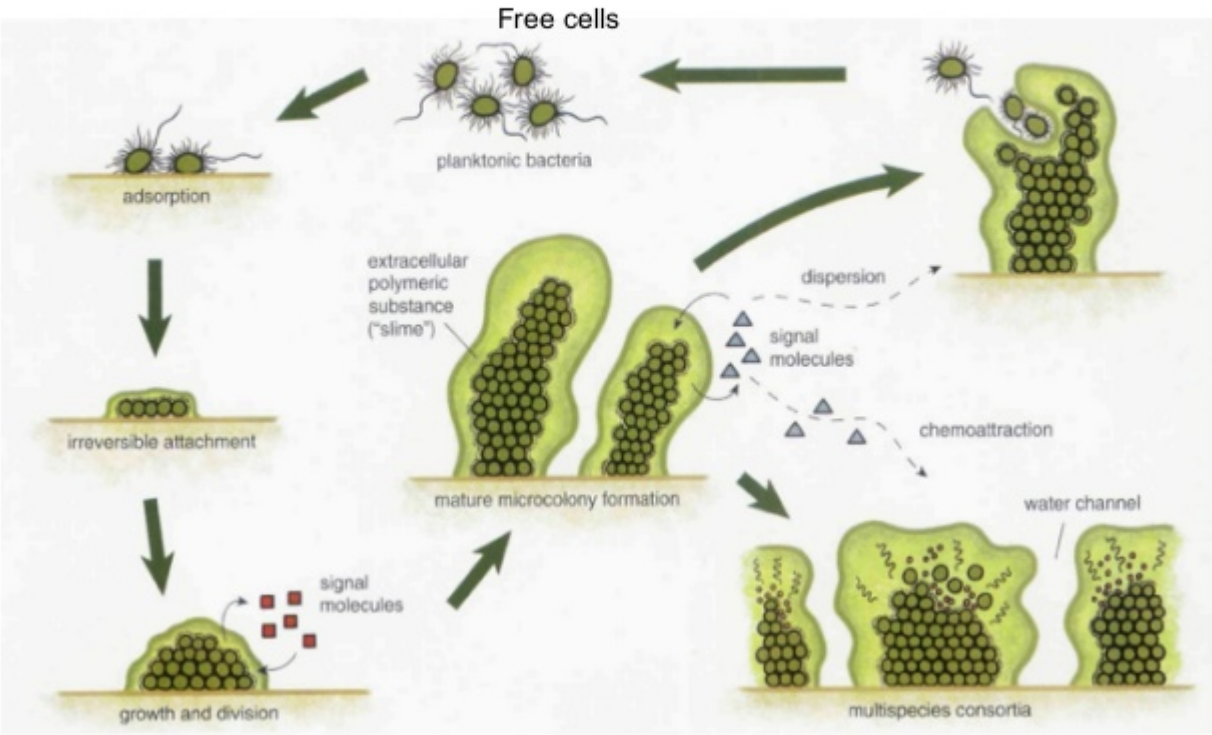
Homeostasis

Dr. David J. Shuch in a letter to JADA in December 2009 congratulates Dr. Christoph Schaudinn and his colleagues in the August 2009 JADA , "Periodontitis: An archetypical Biofilm Disease", "*Should we be concerned with killing all the pathogens, or is it more important to modify the environment so that the bacteria associated most closely with pathogenicity are replaced by bacteria that are tolerated better by healthy tissue?*"

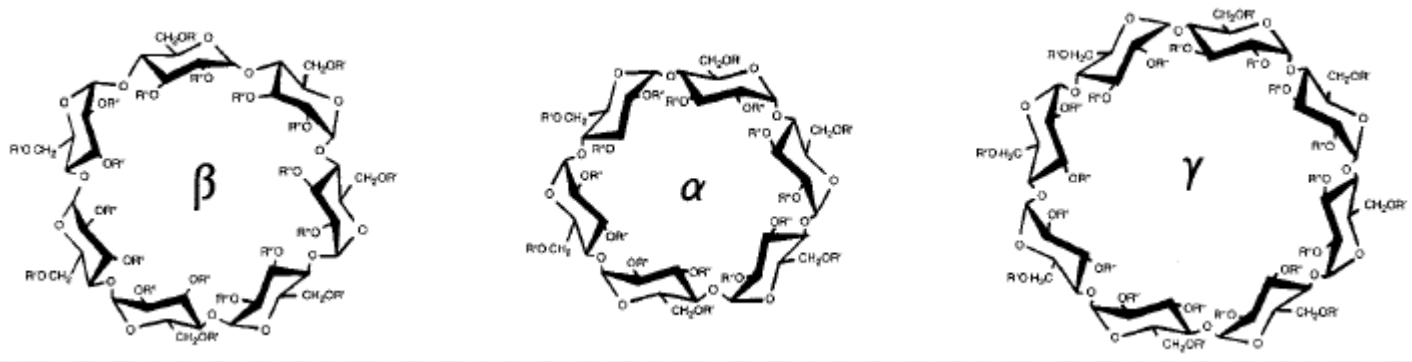
Dr. Shuch says that he and his fellow researchers know that there are two main axes that determine a homeostatic oral plaque biofilm: "**Thickness**-too thin or atrophic, and root surface sensitivity, oral ulcerations or both become more common, too thick and anaerobic respiration results, with low pH concentrations at the biofilm-host interface, oxidative stress of the soft tissue membrane or both. **Predominate chemical reactions**-acid-base, resulting in loss of hard tissue structure, or oxidation-reduction, resulting in soft tissue inflammatory conditions. By working to bring both of these axes close to their zero point by the application of appropriate therapeutic agents, we build up the "soil" and oral health improves."

Novel Strategies for Eradication

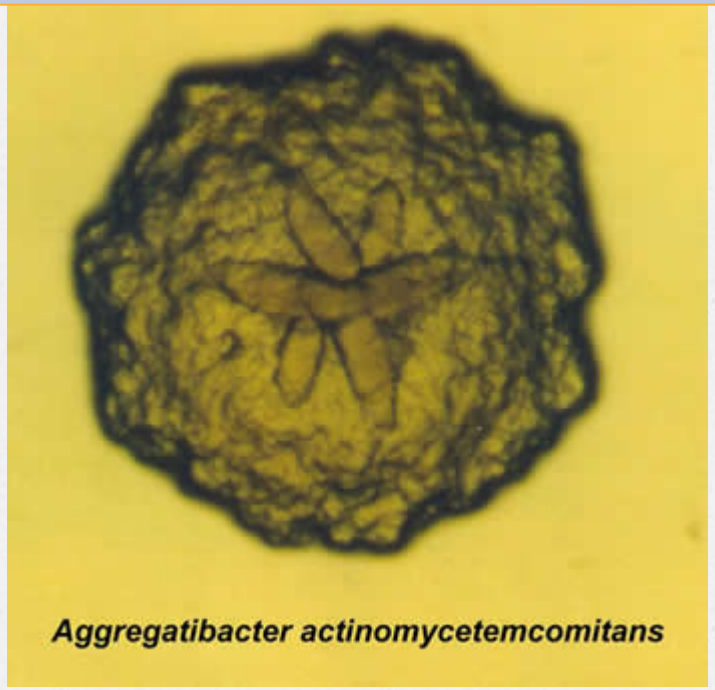
Understanding biofilm formation offers novel strategies for eradicating them. Microbial adhesion to a macro-rough or smooth surface makes no difference in the ability to affect the surface of the biofilm. Immune responses can only affect the outer surfaces where the antigens adhere. There are host/guest strategies to increase the efficacy of antimicrobials.



Inclusion compounds like cyclodextrin create a hydrophobic cavity that surrounds the drug. The inclusion complex protects and gives the drug a path through the matrix to the microbes.

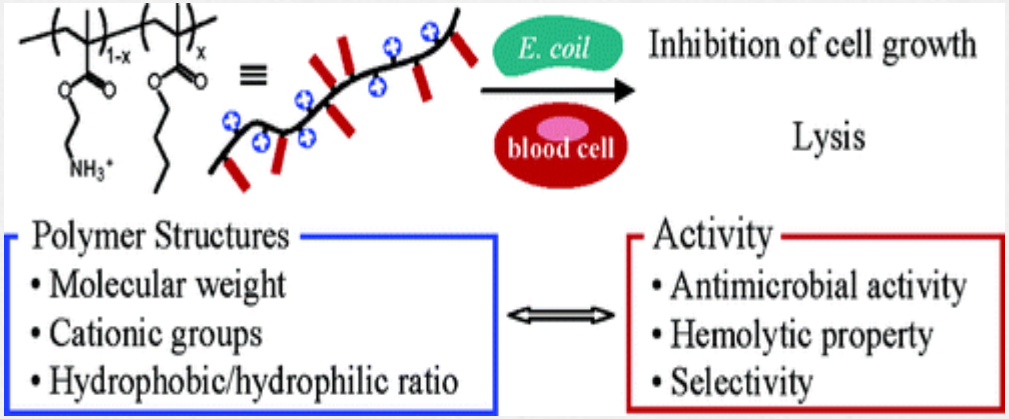


Microbe switching such as the use of a mutant of Aggregatibacter actinomycetemcomitans form tightly-adhered colonies but are unable to release planktonic cells to the surface and environment. Using a bred (cultivated) phenotype to replace a wild type produces less growth.

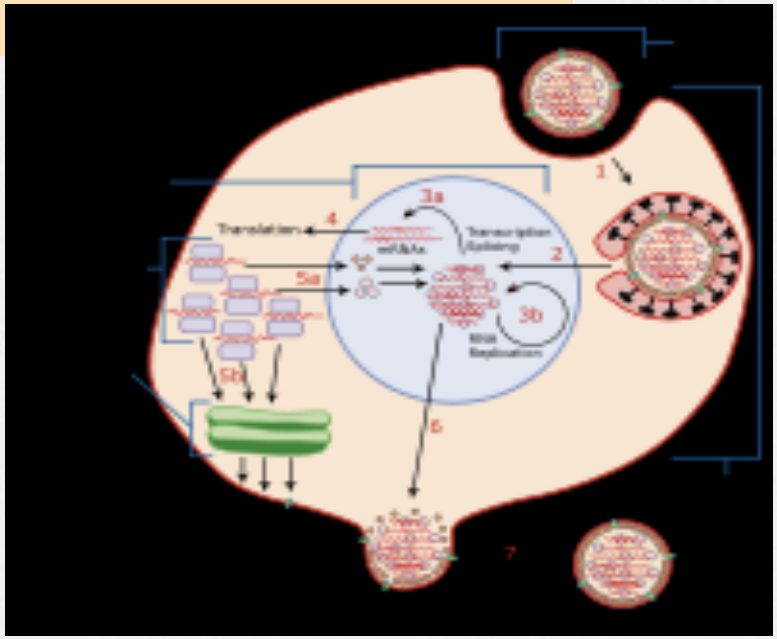


Aggregatibacter actinomycetemcomitans

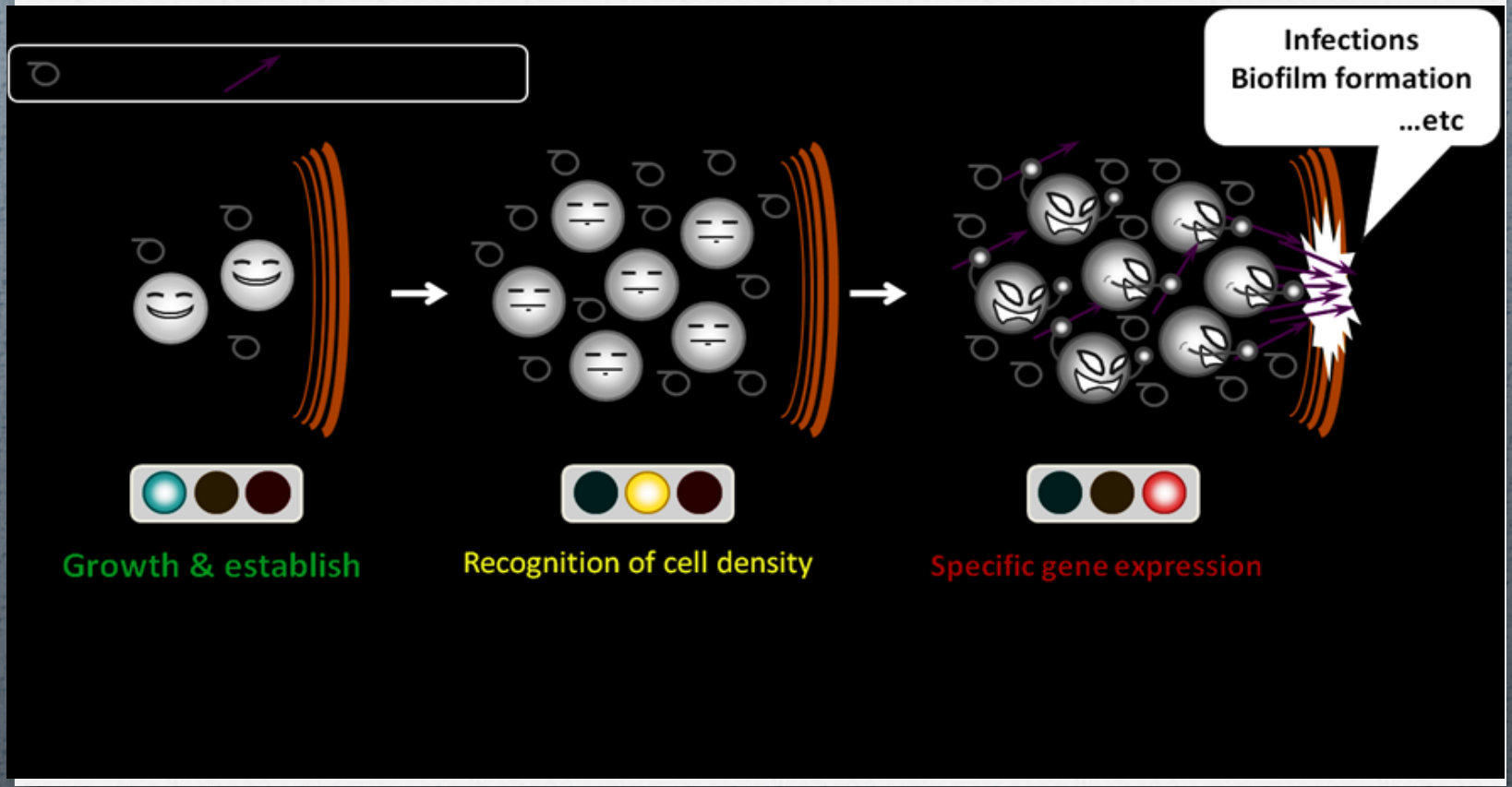
The surface is the most important prerequisite for biofilm formation, so physical and chemical surface modification is another strategy by which eradication might occur. However, microbes want to form on a hydrophobic surface that is rough on a nano- and microscale. Conditioning layers or coatings that are antimicrobial or non-biofouling include polymethacrylate derivatives with cationic side chains that pacify the exposed surface chemistry that provides a site of attachment for the bacteria. After one hour of exposure, the homesteaders are dead.

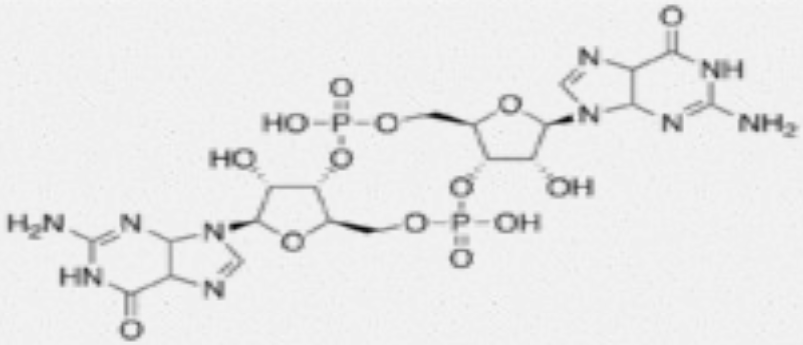


Viruses that infect bacteria, a bacteriophage, or phage enter a cell at a specific receptor. They randomly float around until they find a loving and compatible receptor, enter the cell and change its DNA or RNA to produce more viruses and ultimately kill the cell. Phage therapy was dropped when antibiotics came of age. With the advent of antimicrobial resistance, lytic bacteriophages are back in favor for further research. They must find a way to not attack good bacteria.

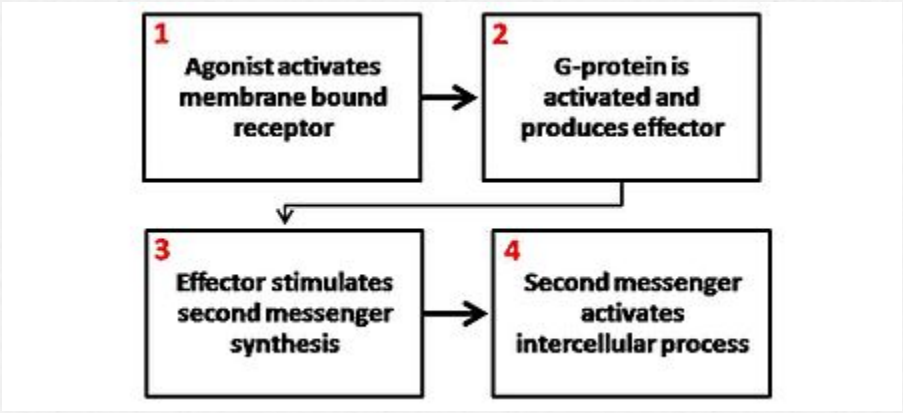


Quorum-sensing inhibitors and anti-QS peptides – such as furanones, ginseng, garlic and azithromycin – increase the susceptibilities of both Gram- negative and positive bacterial biofilms to antibiotics

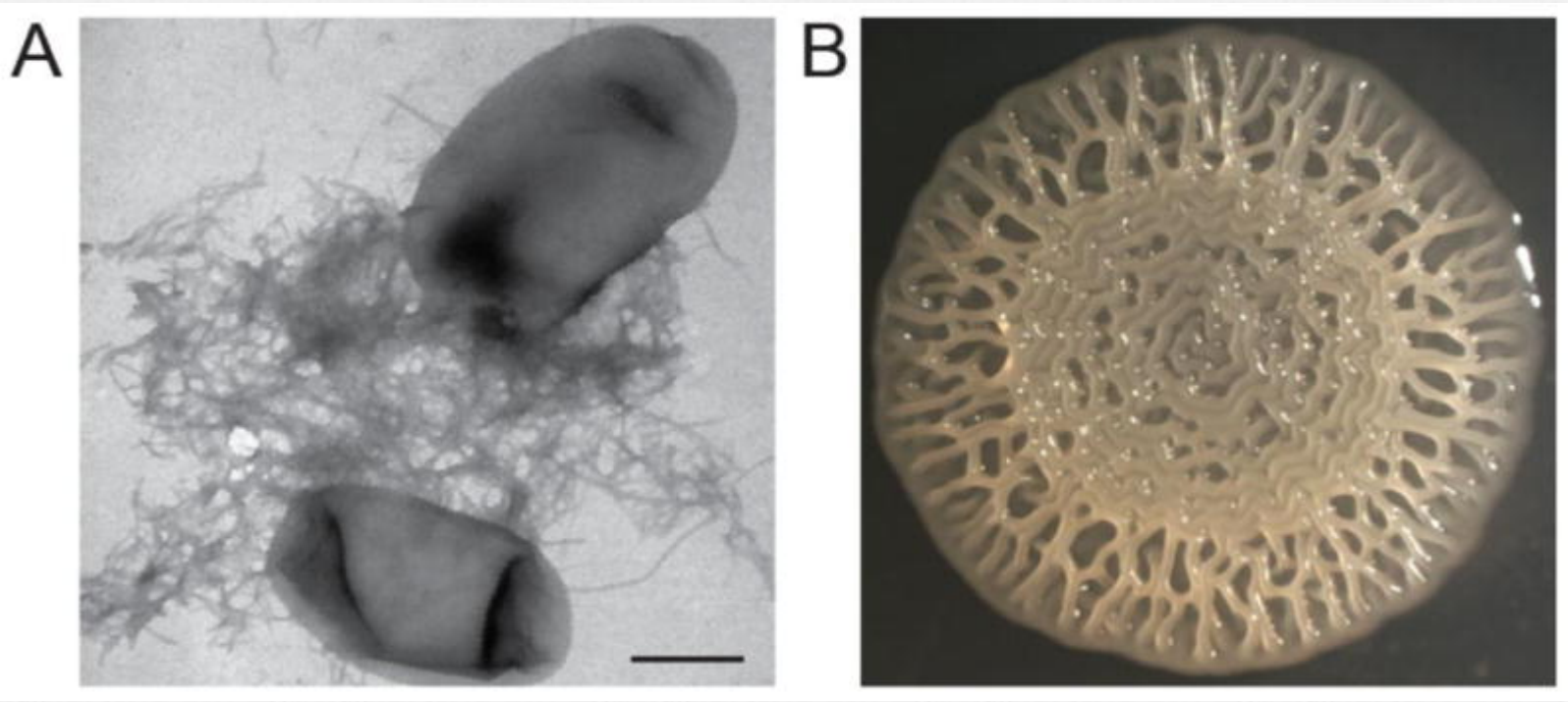




Second messengers cause life style changes such as converting motile bacteria to sessile ones changing the virulent state of an acute infection to the less virulent state in a chronic biofilm infection. Modulating the c-di-GMP signaling pathways is another way to manage the biofilm life cycle.



Amyloid fibers called curli that function on the cell surface of bacteria develop biofilm and other community behaviors. The **peptidomimetics** that target protein to protein interactions can inhibit curli biogenesis. Parthenolide disrupts pre-established biofilms secreting amyloid proteins.



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