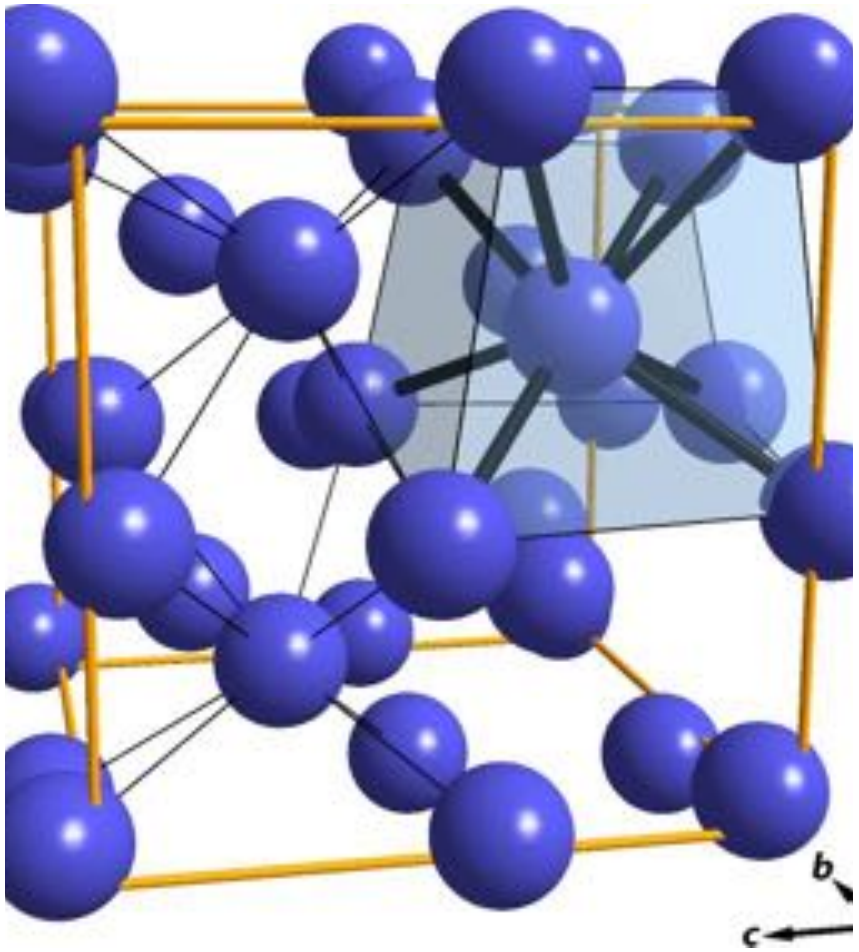
Beginning of Microbes

- Bacteria first appeared on earth about 3.6 billion years ago, long before the appearance of *Homo sapiens* around 100,000 years ago.. ***Van Leeuwenhoek*** was the first person to visualize, graphically illustrate, and label "animalcules" (bacteria) that he found in ***plaque*** scraped from his own teeth.

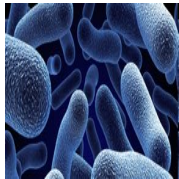
Biofilm is a complex substance.

- A biofilm is a complex aggregation of microorganisms growing on a solid substrate. Biofilms are characterized by structural heterogeneity, genetic diversity, complex community interactions, and an extracellular matrix of polymeric substances.

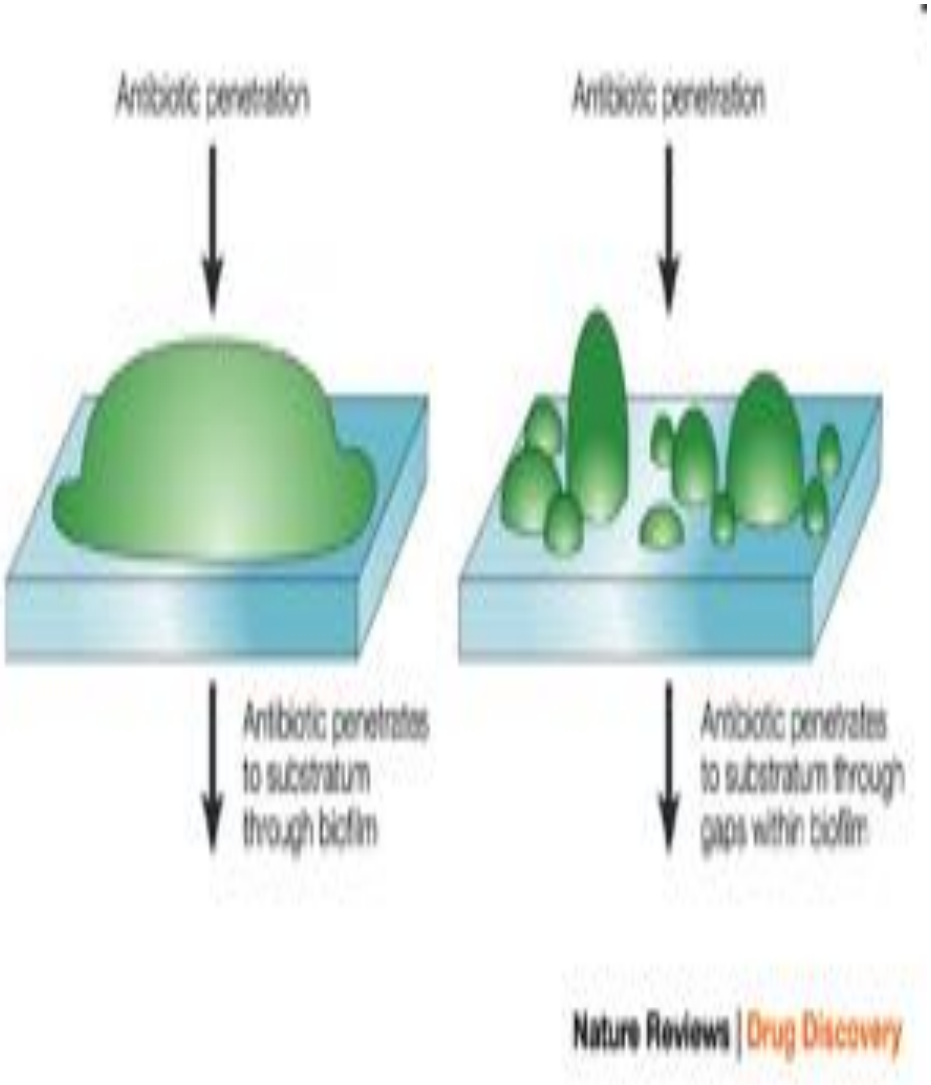


Biofilm supports the Bacterial growth

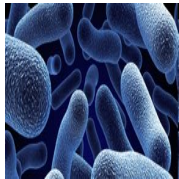
- Biofilm are a common mode of bacterial growth in nature and their presence has an enormous impact on many aspects of our lives, such as sewage treatment, corrosion of materials, food contamination during processing, pipe collapse, plant-microorganisms interaction in the biosphere, the formation of dental plaque, the development of chronic infections in live tissue (mastitis, Otitis, pneumonia, urinary infections, osteomyelitis) or problems related to medical implants.



Biofilms increases Antibiotic resitance

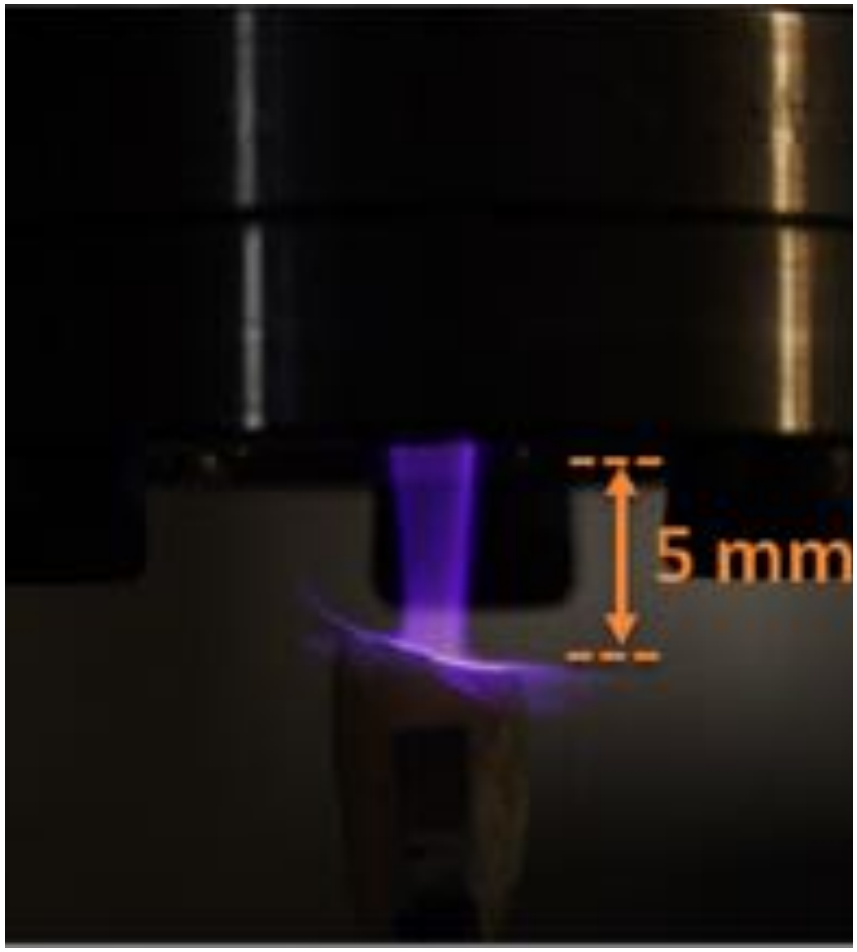


With microorganisms are highly resistant to antimicrobial treatment and are tenaciously bound to the surface

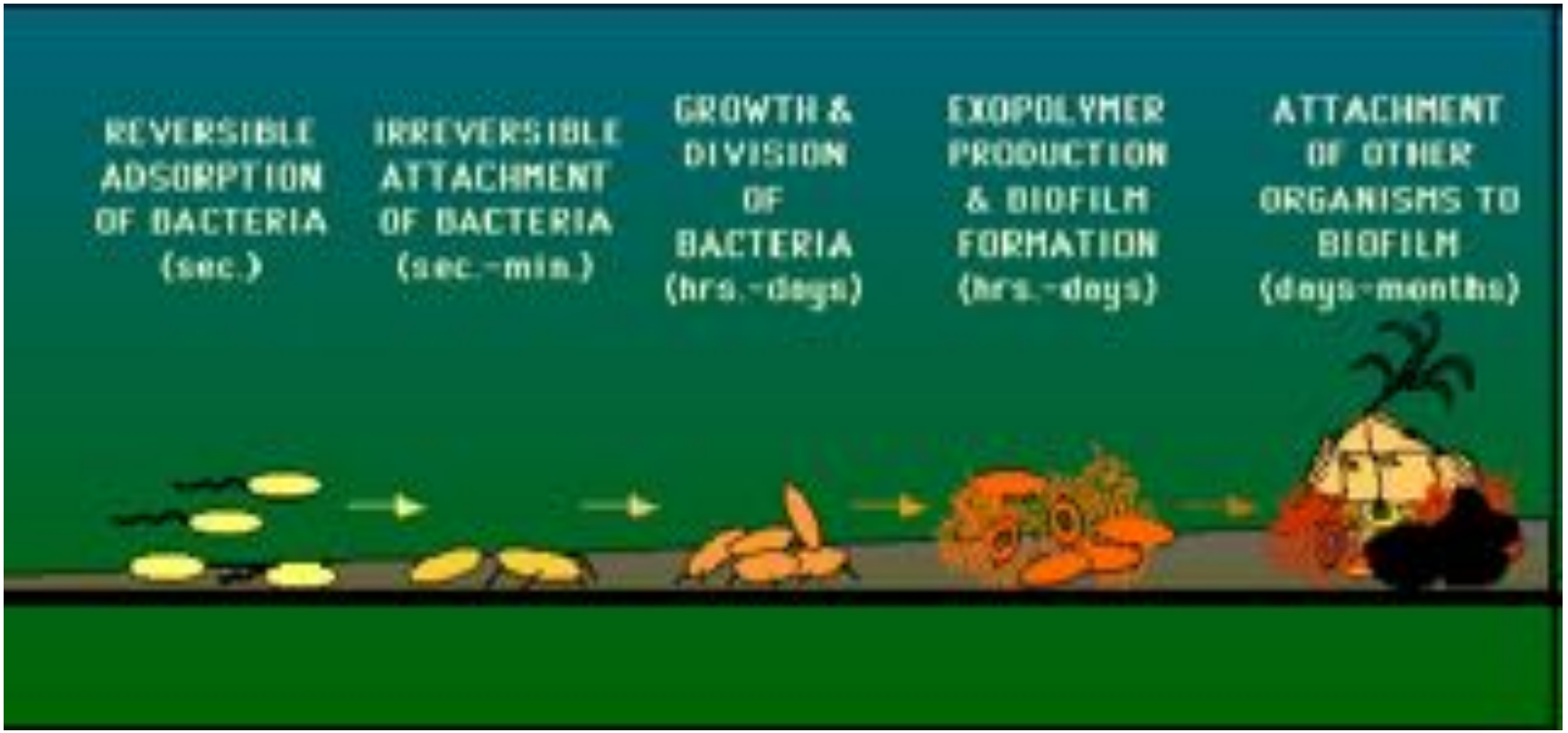


Technology understands Biofilms better…

- Technological progress in microscopy, molecular genetics and genome analysis has significantly advanced our understanding of the structural and molecular aspects of biofilms, especially of extensively studied model organisms such as ***Pseudomonas aeruginosa***.

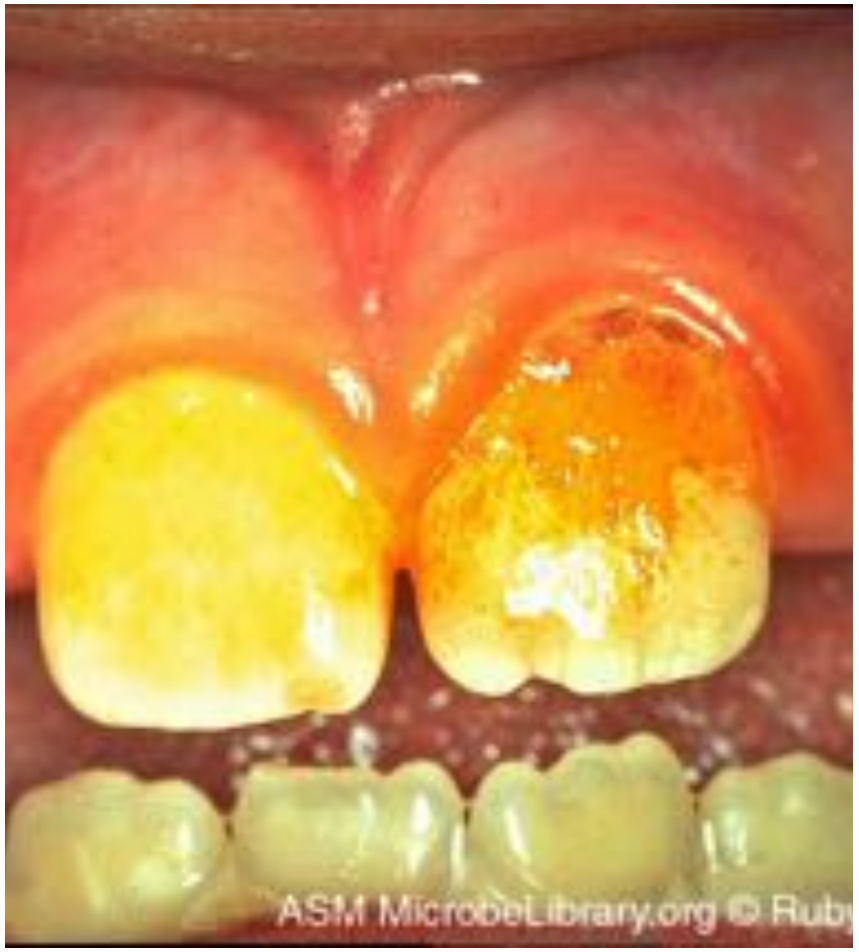


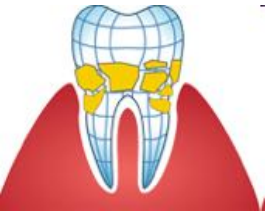
Steps in Biofilm formation



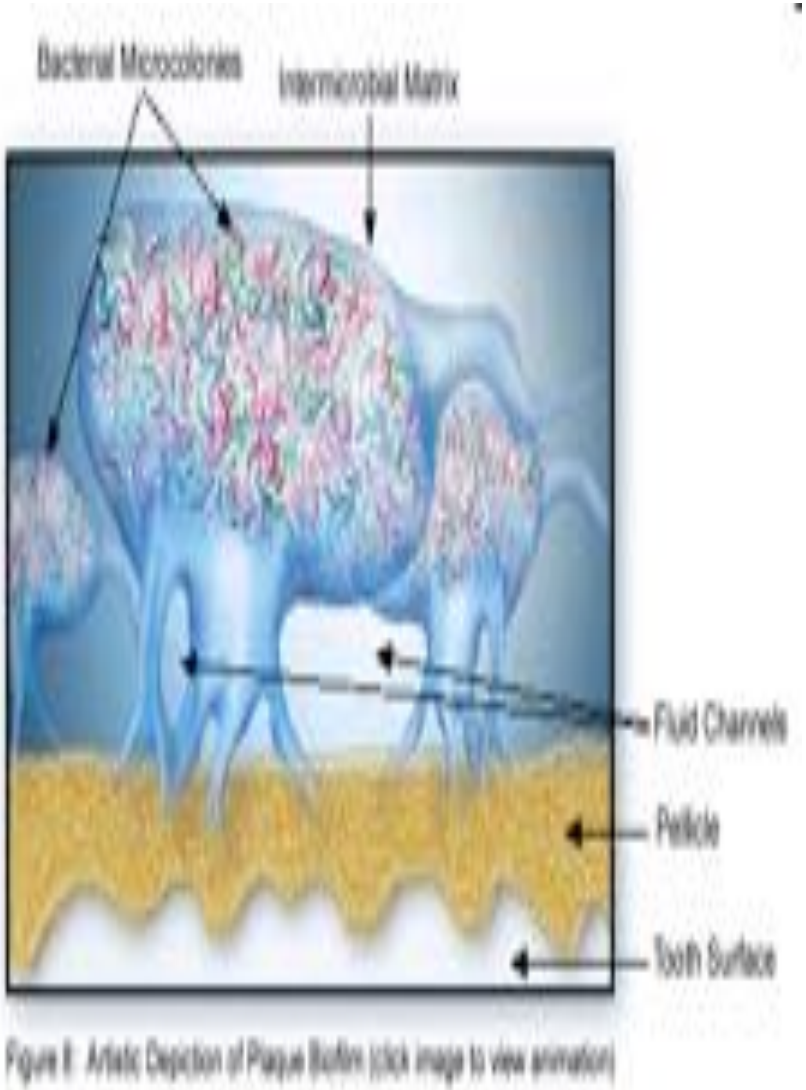
Dental plaque

- Dental plaque is a yellowish biofilm that build up on the teeth. If not removed regularly, it can lead to dental caries.

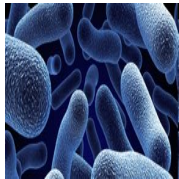


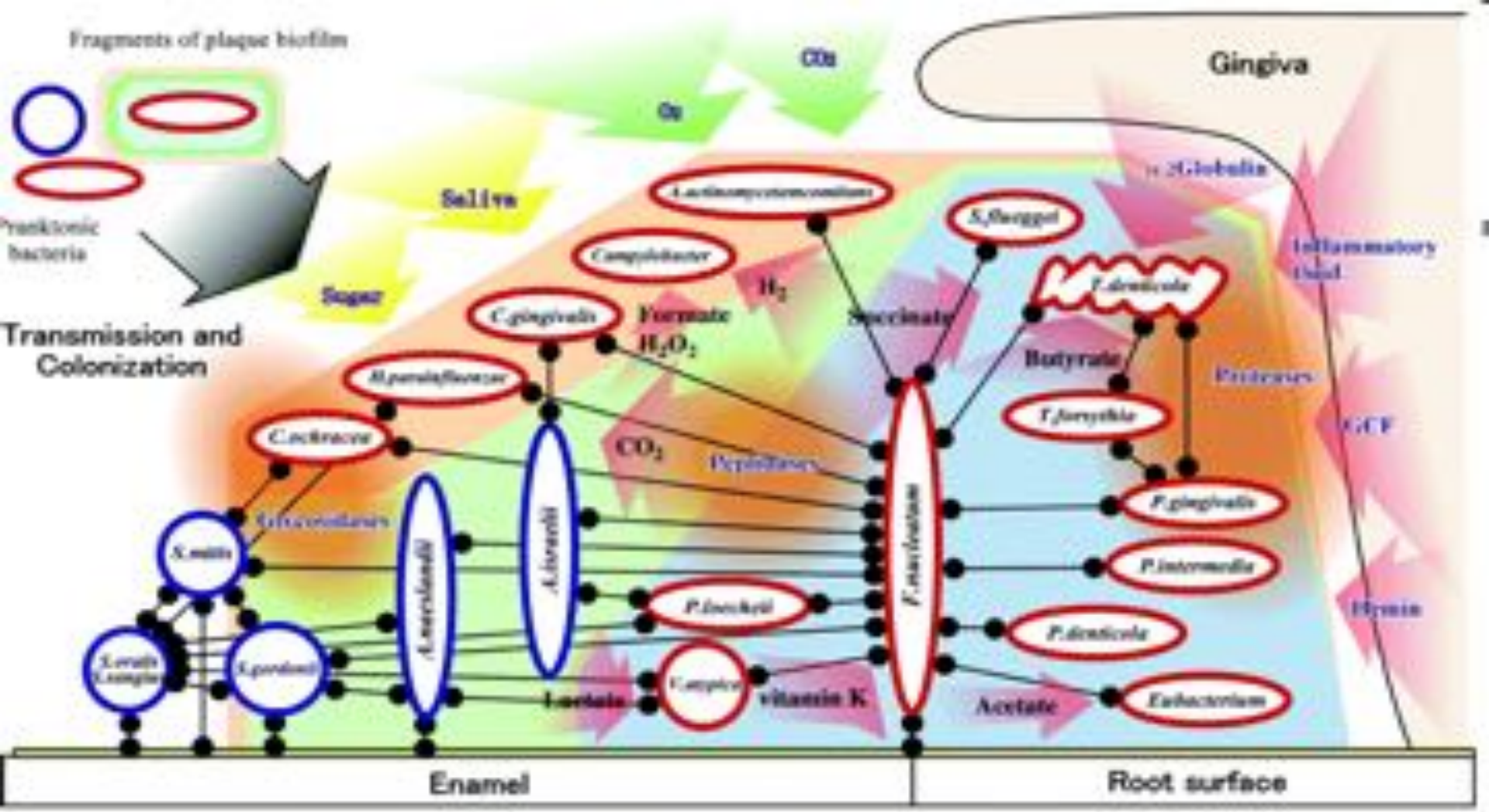


Formation of Dental Biofilms



- Through the growth process of the plaque bio film, the microbial composition changes from one that is primarily gram-positive and streptococcus-rich to a structure filled with gram-negative anaerobes in its more mature state.





Early colonizer ⇨ Secondary colonizer ⇨ Late colonizer : **Microbial succession**

(Gram ⊕ cocci) (Gram ⊕ ⊖ rod) (Gram ⊖ rod/ motile) **(Dominant microorganisms)**

Aerobic ⇨ Capnophilic / Facultative anaerobic ⇨ Anaerobic : **Environment modification**

Saliva (saccharolytic) ⇨ GCF (proteolytic) : **Nutrition supply**

CDC – on Biofilms

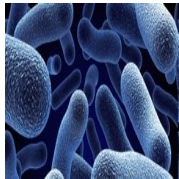
- Biofilms form on the surface of catheter lines and contact lenses. They grow on pacemakers, heart valve replacements, artificial joints and other surgical implants. The ***CDC*** (*Centers for Disease Control*) estimate that over 65% of Nosocomial (hospital-acquired) infections are caused by biofilms.

Biofilms interfere in Antibiotic Therapy

- Bacteria growing in a biofilm are highly resistant to antibiotics, up to 1,000 times more resistant than the same bacteria not growing in a biofilm. Standard ***antibiotic therapy*** is often useless and the only recourse may be to remove the contaminated implant.

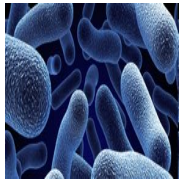
Bacteria associated with Biofilms differ

- Bacteria living in a biofilm can have significantly different properties from free-floating bacteria, as the dense and protected environment of the film allows them to cooperate and interact in various ways. One benefit of this environment is increased resistance to detergents and antibiotics, as the dense extracellular matrix and the outer layer of cells protect the interior of the community.



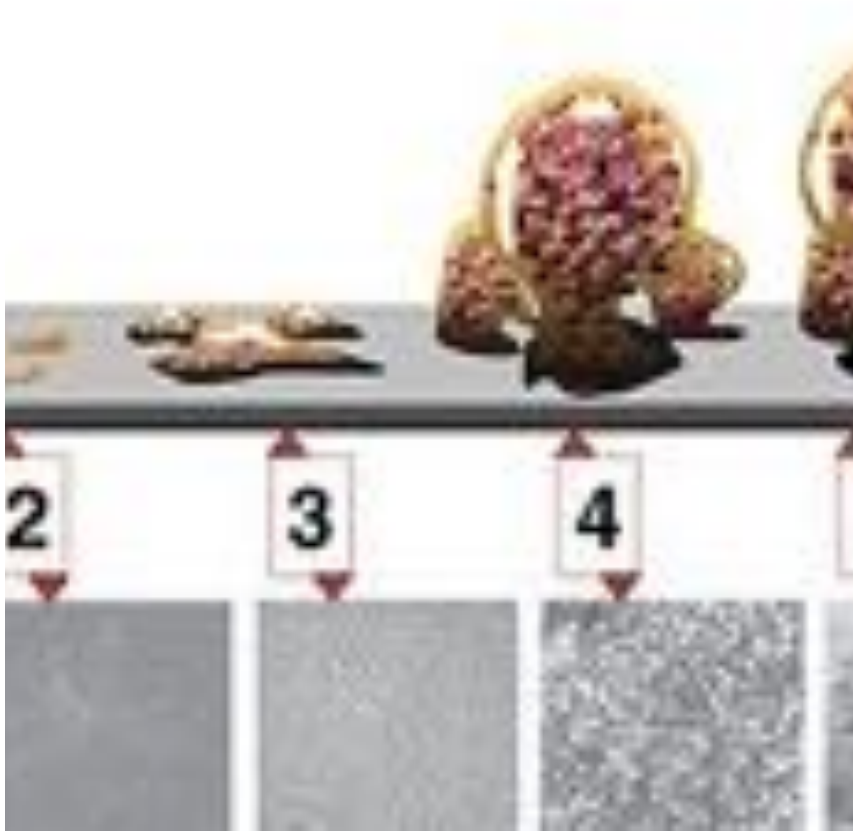
Biofilms a Great threat to Implants

- A significant number of people are affected by biofilm infections which develop on medical devices implanted in the body such as catheters (tubes used to conduct fluids in or out of the body), artificial joints, and mechanical heart valves. When implanted material becomes colonized by microorganisms, a slow developing but persistent infection results.

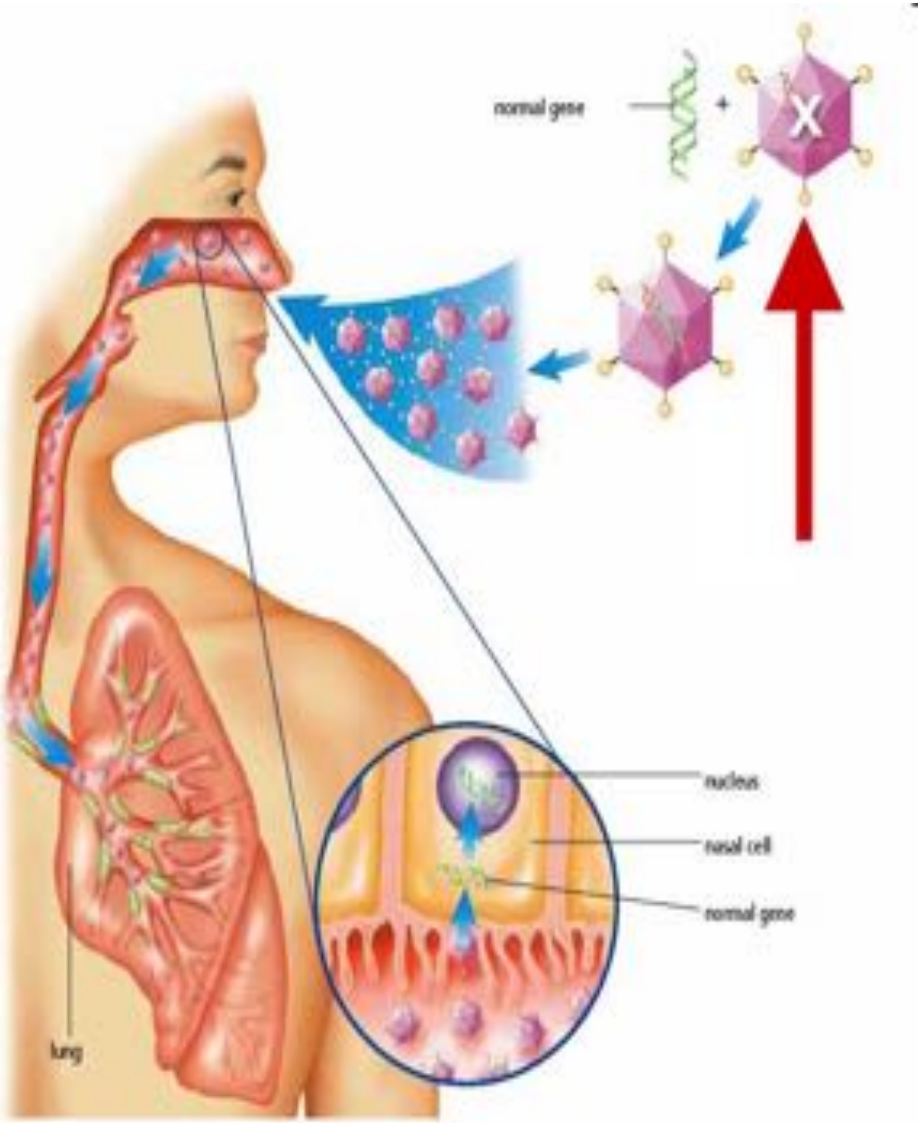


Biofilm and Antibiotic resistance

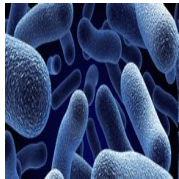
- A key property of bio films is that individual microorganisms are bound together by a polymeric substance This protective encapsulation is believed to play a role in some antibiotic-resistant infection.



Biofilms in Cystic fibrosis

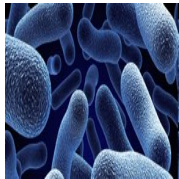


- Biofilms are involved in numerous diseases. In cystic fibrosis patients have Pseudomonas infections that often result in antibiotic resistant biofilms.



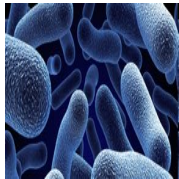
Endocarditis and Biofilms

- Microorganisms may attach and develop biofilms on components of mechanical heart valves and surrounding tissues of the heart, leading to a condition known as prosthetic valve endocarditis. The primary organisms responsible for this condition are *S. epidermidis, S. aureus, Streptococcus* spp., gram-negative bacilli, diphtheroids, enterococci, and *Candida* spp. These organisms may originate from the skin, other indwelling devices such as central venous catheters, or dental work.



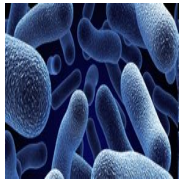
Biofilms and Contact lenses

- Bacterial biofilm formation on contact lenses and contact lens storage cases may be a risk factor in contact lens-associated corneal infections. Studies have shown that contamination of lens cases by bacteria, fungi, and amoebae is common with 20% to 80% of lens wearers having a contaminated lens case.



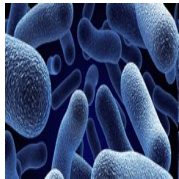
Urinary catheters and Biofilms

- Urinary catheters are tubular latex or silicone devices, which when inserted may readily acquire biofilms on the inner or outer surfaces. The organisms commonly contaminating these devices and developing biofilms are ***S. epidermidis, Enterococcus faecalis, E. coli, Proteus mirabilis, P. aeruginosa, K. pneumoniae,*** and other gram-negative organisms. The longer the urinary catheter remains in place, the greater the tendency of these organisms to develop biofilms and result in urinary tract infections.



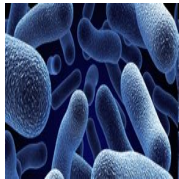
Biofilms and indwelling medical devices

- Biofilms on indwelling medical devices may be composed of gram-positive or gram-negative bacteria or yeasts. Bacteria commonly isolated from these devices include the gram-positive *Enterococcus faecalis, Staphylococcus aureus, Staphylococcus epidermidis*, and *Streptococcus* viridians; and the gram-negative *Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis,* and *Pseudomonas aeruginosa*.



*Indwelling catheters and Biofilms**

- Central venous catheters, the reference method for quantification of biofilms on catheter tips is the roll-plate technique, in which the tip of the catheter is removed and rolled over the surface of a nonselective medium. Quantification of the biofilm depends on the number of organisms recovered by contact with the agar surface. Biofilm-associated cells on the inner lumen of the device are not detected with this method, which has low diagnostic sensitivity and low predictive value for catheter-related bacteraemia.

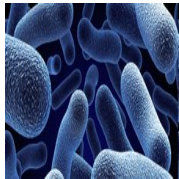


Indwelling catheters and Biofilms*

- In addition, this method cannot detect more than 1,000 colony-forming units (CFU) per tip. A method that used sonication plus vortexing as a means of quantifying biofilms on catheter tips showed that a level of 104 CFU per tip is predictive of catheter-related septicaemia

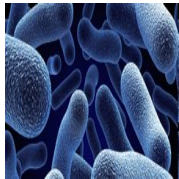
* **Biofilms and Device-Associated Infections**

Rodney M. Donlan Centers for Disease Control and Prevention Atlanta, Georgia, USA



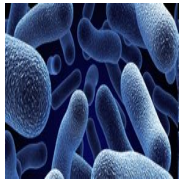
Antibiotic therapy alone may not cure ?

- Antimicrobial agents are administered during valve replacement and whenever the patient has dental work to prevent initial attachment by killing all microorganisms introduced into the bloodstream. **As with biofilms on other indwelling devices, relatively few patients can be cured of a biofilm infection by antibiotic therapy alone**



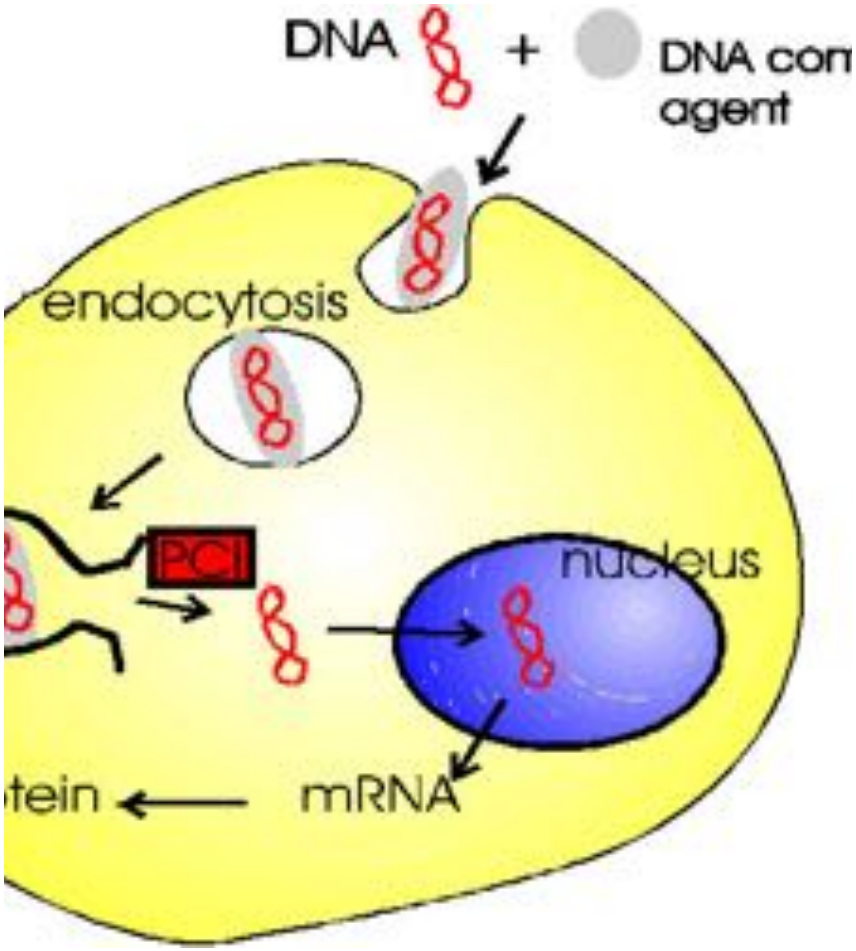
Biofilms need higher concentration of Antibiotics

- Biofilms are remarkably difficult to treat with antimicrobials. Antimicrobials may be readily inactivated or fail to penetrate into the biofilm. In addition, bacteria within biofilms have increased (up to 1000-fold higher) resistance to antimicrobial compounds, even though these same bacteria are sensitive to these agents if grown under plank tonic conditions.



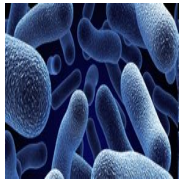
Biofilms help Gene transfer

- Biofilms increase the opportunity for gene transfer between/ among bacteria.. Gene transfer can convert a previous a virulent commensals organism into a highly virulent pathogen.



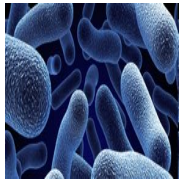
Biofilms contribute for new phenotypes

- Bacteria express new, and sometimes more virulent phenotypes when growing within a biofilm. Such phenotypes may not have been detected in the past because the organisms were grown on rich nutrient media under plank tonic conditions. The growth conditions are quite different particularly in the depths of biofilms,



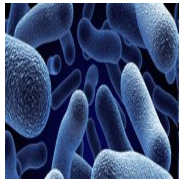
Biofilms – Protects from Phagocytosis

- Phagocytes are unable to effectively engulf a bacterium growing within a complex polysaccharide matrix attached to a solid surface. This causes the phagocyte to release large amounts of pro-inflammatory enzymes and cytokines, leading to inflammation and destruction of nearby tissues.



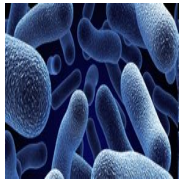
Current objectives on Biofilm research

- o Development of improved imaging of biofilms in situ;
  oDevelopment of improved clinically relevant in vitro and in vivo models of biofilms under specific in vivo conditions such as flow rate, nutrient content, and temperature;
- o Development of better probes (genetic, metabolic, and immunological) for real- time analysis;
  o Studies of quorum sensing/signaling molecules;



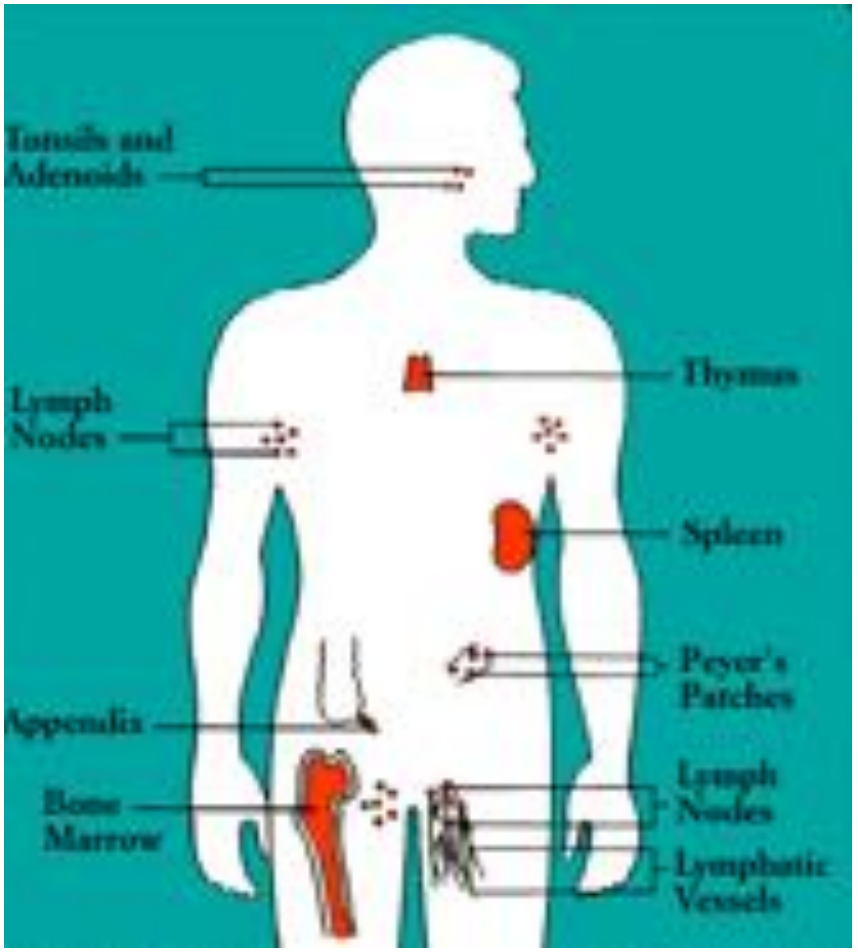
Current objectives on Biofilm research

- o Further characterization of biofilm-specific gene expression;
- o Studies of the exchange of genetic material within biofilms;
- o Studies of organic contaminants on substrata, and their influence on biofilm structure;
  o Development of novel approaches to control pathogenic bacteria by, for example, devising strategies to favour growth of non-pathogenic microorganisms in biofilm communities;



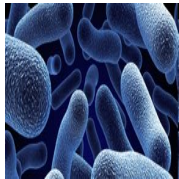
Current objectives on Biofilm research

- o Studies of pathogenic mechanisms of microbes growing in biofilms;
  o Elucidation of mechanisms of resistance of biofilms to antimicrobial agents; o
  Studies of host immune responses, both innate and adaptive to biofilms;



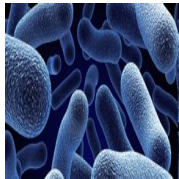
Current objectives on Biofilm research

- In studies of infectious lung disease in cystic fibrosis;
  - Studies on the potential of diagnostic procedures such as Bronchoalveloar lavage (Irrigation) and bronchoscopy to disturb local biofilm flora and inoculate distant locations;
- Development of mathematical models and computer simulations of biofilms;
  - Development of the methodology for the prevention and control of biofilms from catheters, water unit lines, and other clinically important solid surfaces;.



Searching for alternatives – Tissue engineering

- Role of biofilms in multiple pathologies and the difficulty in resolving these pathologies speaks to the importance of developing means of replacing or enhancing the therapies already in use. The use of synthetic materials in the body ranges from catheters to mesh to stents to heart valves and beyond. Until the development of viable and practical tissue engineering, then number and types of applications in which synthetic materials are used will continue to increase.



Emerging Methods

- Several researchers are finding solutions for the cure of Biofilms , yet it is experimental, with advances in molecular biology better model treatments can be identified to reduce the problem of Biofilm interference in Antibiotic therapy.