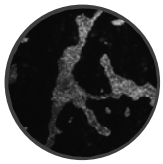
Biofilms in Human Disease

Dr. Ryan Jordan, Cytergy

A Webber Training Teleclass



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BIOFILMS AND THEIR ROLE IN HUMAN HEALTH
2004 Short Course Series: Biofilms

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Presenter's Bio: Dr. Ryan Jordan

Mt. Rainier October 2002

- Senior Research Engineer, Center for Biofilm Engineering at Montana State University (1995-2003)
- Co-Founder and Chief Operating Officer, the Biofilm Institute, 1999-2003
- Editor-in-Chief, Biofilms Online (1999-2003)
- Senior Partner, Cytergy (www.Cytergy.com) 2003-Present

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- Biofilm Research & Consulting Services
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Outline

1. Biofilm Fundamentals
2. Survey of Biofilms in Human Health
3. Therapeutic Strategies for Biofilm Control
4. Biofilms and Antimicrobial Resistance
5. Anti-Biofilm Medical Devices
6. New Frontiers: Intercellular Chemical Signaling

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What is a Biofilm?

- A community of microorganisms attached to a surface
- Contrast to "planktonic" cells:
  - Individual cells suspended in a fluid medium

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What Makes up a Biofilm?

- Living microorganisms
  - Bacteria, yeast, algae, protozoa
- Dissolved & solid organic byproducts
  - Polysaccharides, lipids, proteins
- Solid inorganic detritus
  - Minerals, soil
- Dissolved inorganics
  - Metal salts, cellular metabolism byproducts

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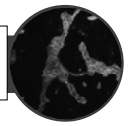
What are Key Features of Biofilm?



- Multicellular
- Multispecies
- Extracellular polysaccharide (EPS) matrix
- Three dimensional structure

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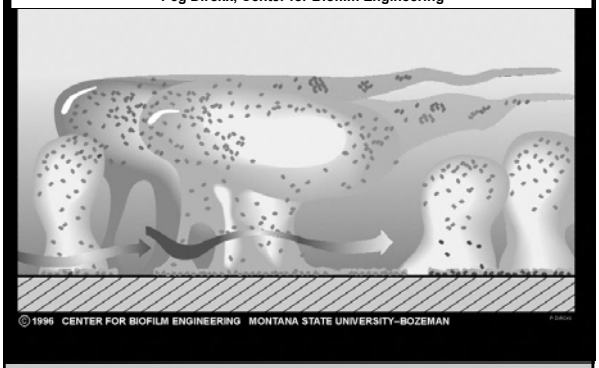
Schematic of Biofilm Structure

Peg Dirckx, Center for Biofilm Engineering



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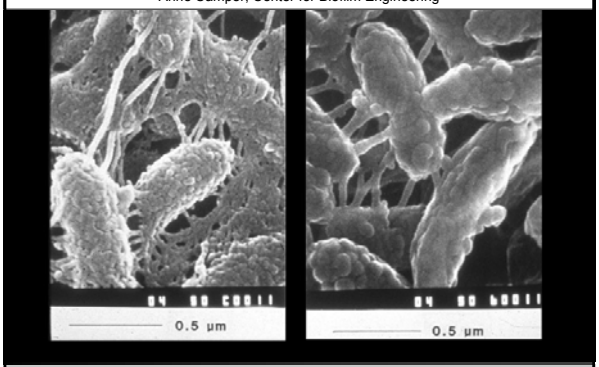
Bacterial Biofilm Encased in EPS Matrix

Anne Camper, Center for Biofilm Engineering



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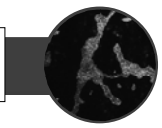
How Does Biofilm Form?



- Three Key Processes:
  - Attachment
    - Adsorption / adhesion of a microbial cell to a solid surface
  - Colonization
    - Establishment of a microbial community at the site of attachment
  - Growth
    - Maturation of a three-dimensional biofilm community

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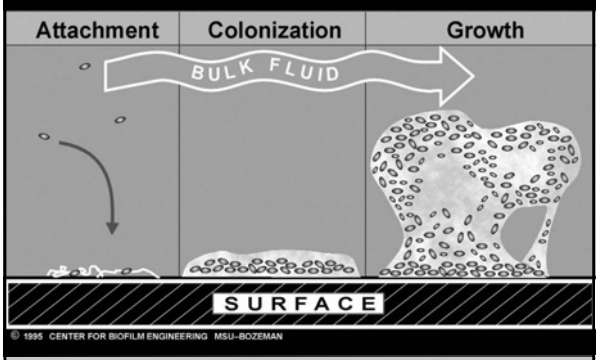
Biofilm formation:



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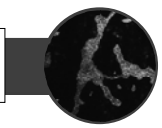
Where are Biofilms Found?



- Natural environment
  - e.g., streambed
- Industrial systems
  - e.g., water distribution pipes
- Human body
  - e.g., mouth, stomach lining, skin
- Criteria for biofilm growth:
  - Any confluence of a water-based fluid, a surface, and microorganism

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What Makes Biofilm Ubiquitous?

- Microorganisms are ubiquitous
- Biofilm is the preferred mode of growth
  - Individual & community efficiency
  - Survival mechanism
- Resistance to extreme conditions
  - Heat & cold
  - Starvation
  - Dessication
  - Resistance to toxic substances

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2. Biofilms in Human Health

- Waterborne Illnesses
- Airborne Illnesses
- Foodborne Illnesses
- Household Biofilms
- **Medical Devices & Implants**
- **Infectious Diseases**
- **Dental Health**

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Medical Devices and Implants

- Catheterization
- Prosthesis
- Superficial Reconstruction
- Organ Transplant & Repair
- Wound Healing

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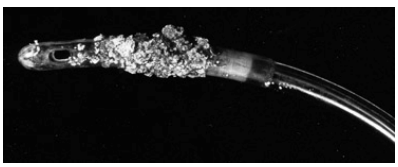
Catheterization

- Catheters and other invasive devices are the #1 exogenous cause of hospital-acquired infections
- Central venous catheters
- Foley (urinary) catheters



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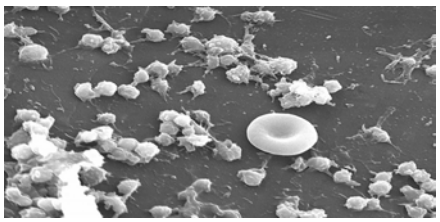
Biofilm on Intravenous Catheter Connecter 24 hours after Insertion



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Prostheses

- Artificial limbs
- Prosthetic eyes
- Dentures

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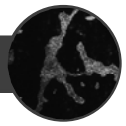
Superficial Reconstruction



- Epi/dermal infection
- Subcutaneous infection

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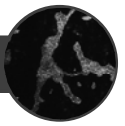
Organ Transplant & Repair



- Kidneys
  - transplant, dialysis*
- Heart
  - transplant, artificial organ, valve repair or replacement
- Contamination during organ transfer

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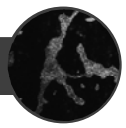
Wound Healing



- Contamination from outside environment
- Proliferation of infection in the wound
- Proliferation of infection in the wound dressing

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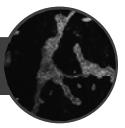
Infectious Diseases



- The role of biofilms in originating, mediating, and proliferating infectious diseases is becoming more important (better understood) with an increasing number and variety of infections.

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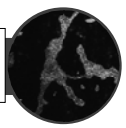
Biofilms are Indigenous to the Body



- Healthy microflora exists in:
  - Ear, nose, mouth, and throat
  - Gastrointestinal tract
  - Skin
  - Vagina
  - Bowels, colon
  - Etc.

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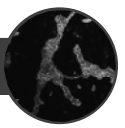
Biofilm Mediated Infectious Diseases



- Eyes
- Ear, Nose, and Throat
- Heart & Lungs
- Gastrointestinal Tract
- Urinary & Sexual Function
- Skin

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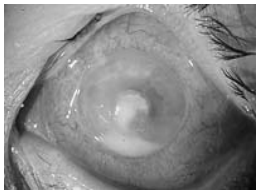
Infectious Diseases of the Eye



- Conjunctivitis
- Dacryocystitis (infection of the lacrimal sac)
- Bacterial corneal ulcer (photo)

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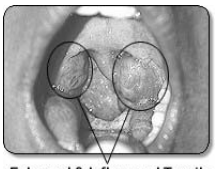
Infectious Diseases of the Ear, Nose, and Throat



- Tonsillitis & pharyngitis
- Sinusitis
- External otitis
- Bronchiolitis
- Diptheria

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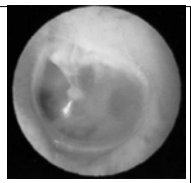
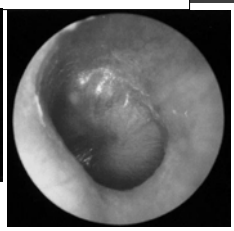
Otitis media


Normal Eardrum


Infected with acute *Otitis media*

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Heart and Lungs

- Tuberculosis
- Whooping cough
- Myocarditis, pericarditis (e.g., meningococcal meningitis)
- Endocarditis

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Pneumonia

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Cystic Fibrosis

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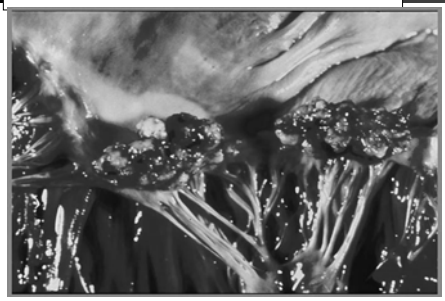
Endocarditis



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Other Biofilm Mediated Diseases

- GI Tract Infections
- Urinary Tract Infections
- Skin Infections

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Dental Health

- Dental Caries
- Periodontal Disease
- Halitosis
- Dental Unit Waterlines

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Dental Caries

- Description
  - Enamel-bound biofilm (plaque) metabolism of carbohydrates (sugars and starches), producing acids that dissolve tooth enamel
- Control
  - Plaque removal is extremely difficult after it has formed highly calcified deposits on the enamel surface
  - Physical removal of the biofilm (flossing, brushing, professional cleaning)
- Prevention
  - Antimicrobial rinses
  - Fluoride
  - Dental sealants

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Periodontal Disease

- Definition
  - Infection of tissues surrounding and supporting the teeth; key cause of tooth loss in older adults
- Stages
  - Gingivitis (early)
  - Periodontitis (late)
- Role of biofilm
  - Biofilm colony infestation into the gum tissue
  - Remote location makes it extremely resistant to antimicrobial therapies
  - Emphasizes the need for debridement as the primary treatment
- Prevention
  - Development of rinse treatments that prevent biofilm colonization of gum tissues

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Halitosis

- Cause
  - Metabolic activity of oral bacterial biofilm feeding on post nasal drip (back of tongue)
  - Protein metabolizers (in contrast to sugar metabolizers)
- Compounds produced
  - Hydrogen sulfide (rotten eggs)
  - Methyl mercaptan & skatole (feces)
  - Cadaverine (corpses)
  - Putrescine (decaying meat)
  - Isovaleric acid (feet)

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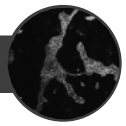
Dental Unit Waterlines



- Problem Scope
  - Biofilm growth in dental unit waterlines poses potential risk of pathogen exposure to patients
  - Exposure risk is highest to immuno-compromised individuals

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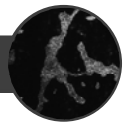
Dental Unit Waterlines



- Why are DUW's are so susceptible to biofilm formation?
  - Flow is low volume, slow, and laminar
  - Small tube diameter, high SA/V ratio
  - Long tubing lengths
  - Room temperature or warmer
  - Plastic tubing

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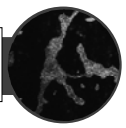
DUW Biofilm Control Strategies



- Cleaner source water (e.g., independent reservoir systems)
- Point of use microorganism filtration (e.g., reverse osmosis)
- Point of use disinfection (e.g., UV irradiation)
- Regular DUW maintenance
  - Chemical cleaning
  - Physical cleaning
  - DUW replacement

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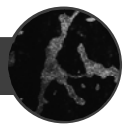
3. Therapeutic Strategies



- Disruption of biofilm cell function
- Disruption of biofilm structure
- Inhibition of biofilm growth

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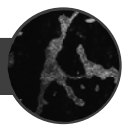
Disruption of Biofilm Cell Function



- Traditionally accepted method for antibiotic-based infection control
- Objective
  - Kill individual cells by targeting specific cell function
- Problem
  - Biofilms are notorious for their ability to "protect" individual cells in their community

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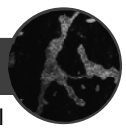
Disruption of Biofilm Structure



- Traditional method in cleaning industrial manufacturing equipment
  - Soaps, detergents, surfactants, physical removal
- Problematic in-vivo due to potential for negative host response (side effects)

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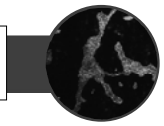
Disruption of Biofilm Structure



- Objectives
  - BIOFILM → PLANKTONIC
  - Disrupt the EPS matrix that binds cells together
  - Promote cell detachment from the surface
- Much room for R&D
  - Biofilm disrupting chemicals
  - Methods of implementing / delivery

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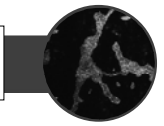
Inhibition of Biofilm Growth



- Create either
  - An anti-biofilm surface
  - An anti-biofilm forming cell
- Antimicrobial coatings
  - Devices & implants
- In-vivo strategies for tissue infection prevention?

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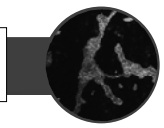
4. Antimicrobial Resistance



- Nosocomial infections
- Antibiotic resistant bacteria
- Mechanisms of antimicrobial resistance by biofilms

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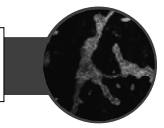
Nosocomial Infections



- Antibiotic resistant bacteria
- Hospital air & water systems
- Hospital staff sanitation
- Reusable device / instrument contamination
- Surgical procedures

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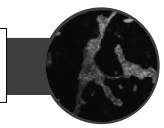
The Nosocomal *Troika*



- *Staphylococci*
- *Pseudomonads*
- *E. coli*
- Note: These families of organisms are known to produce healthy, antimicrobial-resistant biofilms

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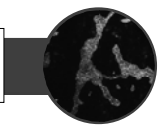
Common Nosocomial Infections



- Nosocomial pneumonia
- Surgical wound infections
- Vascular access-related bacteremia

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Nosocomial Bacteria: The Problem

- Acquired antibiotic resistance
- Organism of greatest concern:
  - Vancomycin-resistant Staphylococcus aureus (VRSA)

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Antibiotic Resistant Bacteria

- Hospitals, and especially, intensive care units (ICU's), are a breeding ground for ARB's
- The risk of leaving a hospital with an ARB infection is real
- More info:
  - http://www.cdc.gov/drugresistance/
  - http://www.cdc.gov/ncidod/hip/aresist/visa.htm

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Biofilms and Nosocomial Infections

- Biofilms are playing an increasingly important role in the spread of nosocomial infections because:
  - Renovation of aging hospitals increases risk of airborne fungal and bacterial pathogens present as biofilm in the infrastructure (molds, Legionella)
  - Increasingly aggressive medical and surgical interventions (implants, organ transplants, device use) places patients at a higher risk

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Mechanisms of Antimicrobial Resistance by Biofilms

- Slow penetration
  - Failure of antimicrobial to penetrate biofilm structure
- Stress response
  - Failure of antimicrobial efficacy against a stressed microorganism
- Altered microenvironment
  - Reduced efficacy of antimicrobial agent in different parts of the biofilm
- Persisters
  - Survival of residual population following antimicrobial treatment

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Slow Penetration

- Resistance results from the inability of the antimicrobial agent to reach all cells in a biofilm
  - Agent reacts with other components of the biofilm matrix
  - Concentration of agent is too low and remains diffusion-limited

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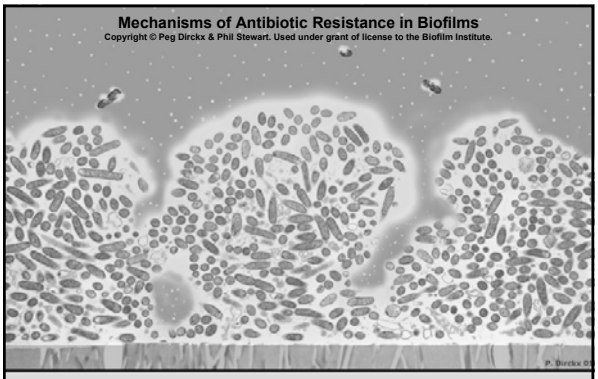

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Stress Response

- Some cells in a biofilm may be exposed to environmental stress (toxicity, lack of nutrients) and elicit a "stress response" that makes them less prone to attack by an antimicrobial agent

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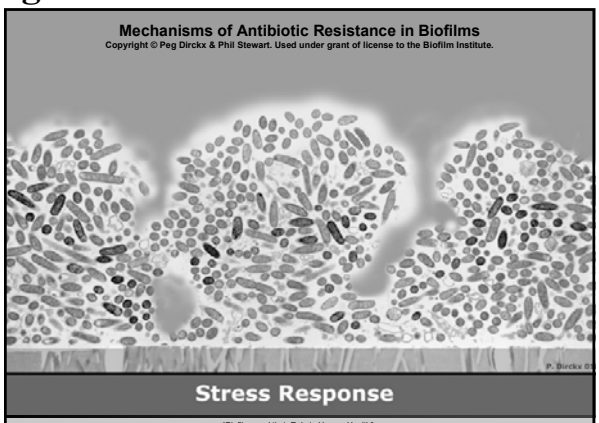

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Altered Microenvironment

- Localized microniches within a biofilm may harbor a microenvironment that may render an antimicrobial agent ineffective
  - Changes in solution chemistry
  - Exudation of components that could neutralize the antimicrobial

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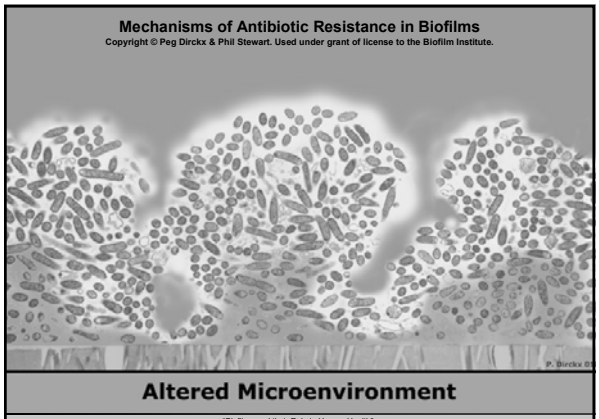

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Persisters

- Some of those little suckers just won't go away.
  - e.g., antibiotic resistant strains

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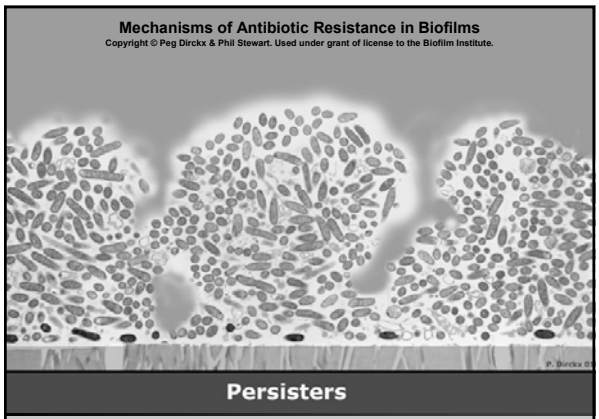

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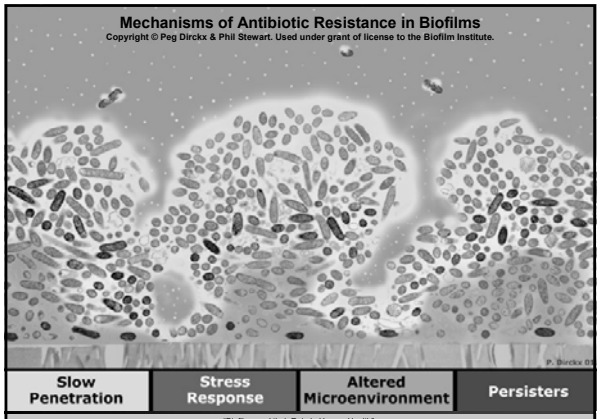

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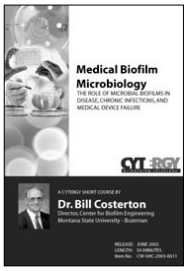
Additional Resources (CD Courses)

http://www.Cytergy.com/

- "Biofilms"
  - An Introduction to Microbial Biofilm Science and Engineering Concepts, by Paul Stoodley
- "Medical Biofilm Microbiology"
  - The Role of Microbial Biofilms in Disease, Chronic Infections, and Medical Device Failure, by Bill Costerton
- "Battling Chronic Infections"
  - A State of the Science Review of Antimicrobial Resistance in Biofilms, by Phil Stewart



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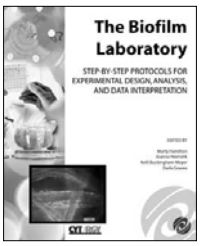
Additional Resources (Books)

http://www.Cytergy.com/

- "Advances in Biofilm Science and Engineering"
  - R. Jordan, Ed., with A. Camper, H. Ceri, H.C. Flemming, P. Gilbert, R. Kolter, and A. C. L. Wong
- "The Biofilm Laboratory"
  - Step-by-Step Protocols for Experimental Design, Analysis, and Data Interpretation, Ed. by M. Hamilton



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