

**The Bugs:  
Microbial Considerations in Rendering Periodontal Treatment**

Presented by:  
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**Agenda:**

- Titillating Tidbits
- Landmarks in Dental Therapy
- Relationship Between Oral and Systemic Conditions (Inflammation)
- Microbial Challenges
- Oral Cancer
- Therapy Considerations and Challenges

At about 5 MILLION TRILLION TRILLION (that's not a double-word typo...), bacteria and archaea vastly outnumber ALL other life-forms on earth

A word or two about what a TRILLION represents: 1,000,000,000,000

- One trillion miles is roughly the distance of 350 trips from Earth to Pluto
- A MILLION seconds ago was twelve days ago
- A BILLION seconds ago was 1959
- A TRILLION seconds ago—that's 31,688 years— Neanderthals stalked the plains of Europe

Microbes have been recovered—ALIVE!—from the petrified gut of a 40 million year old bee!

An average adult inhales 14 pints of air and about 8 microbes every minute—approximately 10,000 critters daily!

EVERY human cell has microbial components—vestiges of bacteria  
Scientists have trained E. coli bugs to assemble into glowing bull's eye shapes on command

Bacteria have been around for at least 3.5 BILLION years—making them the oldest known life-form on earth

Your body has 10 TIMES more bacterial cells than human cells

Women harbor a greater variety of bacteria on their hands than men

E. coli travel 25 times their own length in 1 second—equivalent to a horse running 135 miles per hour

Mitochondria—the cell's 'powerhouse'—are the descendants of bacteria that were engulfed by larger microorganisms BILLIONS of years ago

In 2006, a probe at a South African gold mine turned up bacteria living nearly TWO MILES underground—living on the energy given off by radioactive rocks

Another species (Deinococcus radiodurans) can survive almost 10,000 times the dose of radiation lethal to humans—making it an ideal candidate for the cleanup of nuclear waste

Australian scientists found that a bacterium called Ralstonia metallicurans that can turn dissolved gold into solid nuggets

Scientists from Imperial College London and the University of Edinburgh have found that tiny crystals found inside bacteria provide a magnetic compass to help them navigate through sediment to find the best food  
Floating bacteria are extremely effective at spurring condensation leading to snow and rain—spraying bacteria into clouds could potentially lead to new rain dances

*Pseudomonas natriegens* (an ocean-dwelling bacterium) can go from birth to reproduction in 10 minutes—in 5 hours a single cell could give rise to 1 BILLION+ offspring

Most bacteria have yet to be discovered—in 2003, one research team found more than a MILLION never-before-seen bacterial genes in ONE sea trolling excursion

Wearing headphones for just one hour will multiply the number of bacteria in the ear 700 times

### **Headliners: Microbes Survive Space**

*Streptococcus mitis* lived three years on the moon after surviving a space launch, the vacuum of space, continual radiation exposure, temperatures of only 20 degrees above absolute zero, and a lack water, food or energy source

‘I always thought the most significant thing we ever found on the whole...moon was that little bacteria who came back and lived.’--

Commander Pete Conrad; Apollo 12; 1991

### **Headliners: Germs Taken Into Space Come Back Deadlier; Schmid, R; The Associated Press; Idaho Statesman; 9/25/07**

It sounds like the plot for a scary B-movie: Germs go into space on a rocket and come back stronger than ever

Except...IT REALLY HAPPENED!!!

The germ: *Salmonella* (yep, the same guy that causes food poisoning)

The trip: Space Shuttle STS-115 (September 2006)

The reason: Scientists wanted to see how space travel affects bacteria

The result: Mice fed the *Salmonella* from space were THREE times more likely to get sick and died quicker than mice fed the earthbound variety

‘Wherever humans go, microbes go, you can’t sterilize humans.

Wherever we go, under the oceans or orbiting the earth, the microbes go with us, and it’s important that we understand...how they’re going to change.’--Cheryl Nickerson; associate professor; Center for Infectious Diseases and Vaccinology; Arizona State University

Although researchers were able to identify 167 genes that had been altered in the *salmonella* that went into space, they do not know for certain what caused the changes

A likely explanation: Researchers believe it is related to FLUID SHEAR—microgravity environments diminish the force of liquid passing over the bacterial cells

It is thought that the cells are responding not to microgravity but indirectly to microgravity in the low fluid shear effects

**Headliners: Scientists Make Bacteria That Do Basic Logic Steps;  
Smolke C and Win MN; California Institute of Technology; Science;  
10/17/08**

Scientists report success in engineering microbes with an internal ‘decision tree’ logic that controls their behavior

The bacteria can perform four basic operations of logic—AND, OR, NAND, and NOR

The technique—relying on the the insertion of custom-designed snippets of DNA into bacteria or yeast—could give scientists a whole new level of control when designing microbes for a variety of uses

**Headliners: From Scum, Perhaps the Tiniest Form of Life; Jillian Banfield, University of California (Berkley) et al; as reported by William Broad; reporter; New York Times; 12/23/06**

Scientists found archaea living in a remarkably inhospitable environment—drainage water as caustic as battery acid from a mine in Northern California

The microbes are about 200 nanometers wide—the size of large viruses (bacteria average about 5 TIMES that size)

Scientists say the discovery could bear on estimates of the pervasiveness of exotic microbial life—which some experts suspect forms a hidden biosphere extending down MILES whose total mass may exceed that of all surface life

## **Landmarks in Dental Therapy**

### **1940’s**

National Institute of Dental Research (NIDR) established in 1948 with the broad mandate ‘to improve the dental health of the people of the United States’

### **1950’s**

Important experiments demonstrating the crucial role of bacteria in periodontal disease

Discovery that bactericidal agents (such as antibiotics) were effective in reducing periodontal disease symptoms

### **1960’s**

Dogma was that all bacterial deposits had equal potential to induce disease—accumulation was key

Tissue damage occurred when plaque accumulation overcame host’s ability to defend

### **1970’s**

Periodontal disease and dental caries resulted as an ‘opportunistic’ bacterial infection—selective increase in one or more bacteria as a result of ‘environmental opportunities’

## 1980's

### Role of Immune Status

'Immunocompromised' refers to an individual with either a hypo- or hyperfunctioning immune system

Autoimmune disorders such as Sjögren's and SLE predominantly affect females

Immunocompromised patients are at higher risk for oral problems such as candidiasis

### **Headliners: Triggering Autoimmune Assaults: Mouth Bacteria Unleash Inflammation-Inducing Protein; Raloff J; as reported in ScienceNews; 5/10/08**

What triggers the development of autoimmune disorders—such as MS, rheumatoid arthritis, lupus, etc.—has perplexed experts for decades. Researchers from the University of Connecticut Health Center are reporting that certain oral microbes—notably *Porphyromonas gingivalis*—can inappropriately rev up the immune system which may ultimately lead to autoimmunity.

One 'trigger contender' is a fatty compound—phosphoethanolamine dihydroceramide ('PEDHC')—a product of the common periopathogen. Once in the bloodstream, PEDHC encounters immune cells which misinterpret the product as actual bacteria and mount a full blown attack. The findings of this study are potentially VERY important: 'It presents a new area to look at in terms of possible therapeutic agents' to prevent autoimmune diseases or diminish their severity--Nicholas LaRocca; National Multiple Sclerosis Society (which funded the study)

Also weighing in: 'There is evidence to suggest that periodontitis could indeed be a causal factor in the initiation and maintenance of the autoimmune inflammatory response that occurs in [rheumatoid arthritis].

If proven, chronic periodontitis might represent an important modifiable risk factor for RA.'--Nature Reviews Rheumatology 5, 218-224 (April 2009); Paola de Pablo et al: Periodontitis in systemic rheumatic diseases

Any thoughts on what may limit *Porphyromonas gingivalis* infections????

## 1990's

### What We Have Learned:

- Ultrasonic instrumentation spares the tooth structure\*\*\*
- Minimizes operator time and fatigue
- Provides greater access to deep pockets and furcations

### **Headliners; Electrical Signals Help Direct Wound Healing; Bakalar N; As reported in Discover; 1/07**

Since the mid-1880's, biologists have wanted to understand electricity and how it fits into the myriad of chemical and physical responses involved in wound healing.

As #73 in the top 100 science stories for the 2007 year, it was reported that researchers from the University of Aberdeen in Scotland found that an electrical current can direct epithelial cells both to and from wounded

tissue AND that the speed of the migration is in direct proportion to the amount of voltage applied

Many manufacturers claim to use these same principles to drastically improve healing of persistent and difficult to resolve lesions

One example: The LifeWave BST is a handheld device that stimulates the tissues surrounding ulcers and other difficult-to-treat wounds to build up a safe level of electrical activity that kick starts the natural healing process (clinical trials are under way in Austria, Belgium, Italy, Sweden, and the U.S.)

What's New: InSIGHT Ultrasonic Inserts

For More Info:

Discus Dental

(800) 422-9448

[www.insightultrasonics.com](http://www.insightultrasonics.com)

Shift towards educating the patient to be co-clinician

**Risk factors for periodontal diseases were recognized**

They included:

- Diabetes mellitus
- Pregnancy
- HIV infection
- Smoking and substance abuse

Effects of medications on periodontal health were identified

Gingival overgrowth as a result of:

- Anticonvulsants (phenytoin)
- Calcium channel blockers (nifedipine)
- Immunosuppressants (cyclosporine)

Americans take more medicine per person than ANY other country

**Headliners: United States is #1 in prescription meds!; As reported on Sunday Morning; 10/22/06**

The United States comprises about 5% of the world's population—yet consumes 42% of the world's prescription medications

Annually, we spend \$251 billion per year on 3.5 billion prescription medications

In the 'That's-not-all' Category: According to a recent study sponsored by the Agency for Healthcare Research and Quality ('AHRQ'), 1 in 5 prescriptions that are written are for non-approved uses—and 73% of the time, there is little or no proof that the prescription drug will work!

**Headliners: Washington University and Pfizer Extend Research Collaboration Agreement; Caroline Arbanas; 1/28/09; accessed at: <http://mednews.wustl.edu/news/page/normal/10886.html> on 9/23/09**

Washington University in St. Louis and the pharmaceutical company Pfizer Inc. will collaborate more closely under a new biomedical research agreement that has the potential to move discoveries from the laboratory bench to patients' bedsides more quickly

The \$25 million, five-year agreement represents a new model of partnership between academia and industry by bringing together University and Pfizer scientists to jointly propose, design and carry out research projects as well as to develop talented biomedical researchers through a fellowship program

### **Challenges for the new MILLENIUM**

The current projection is that one out of every five Americans will be 65 y/o or older by 2010

About 30% of adults 65+ years old are edentulous compared to 46% twenty years ago

More people living longer than ever before also presents an increase in chronic and disabling diseases affecting the orofacial region

More than 400,000 cancer patients will develop oral complications as a result of treatment

At all ages, people at the lowest socioeconomic levels have more severe carious lesions and periodontal diseases

**Headliners: For want of a dentist: Maryland boy, 12, dies after bacteria from tooth spread to his brain; Mary Otto; The Washington Post accessed on MSNBC.com 2/28/07**

By the time 12-year-old Deamonte Driver's toothache got any attention, bacteria from an abscess had spread to his brain, doctors said

After two operations and more than six weeks of hospital care, the Prince George's County boy died

A routine, \$80 tooth extraction might have saved him—if his mother had been insured

In the past few years, a growing body of scientific evidence suggests an exquisite link between oral inflammation and systemic disorders such as:

- Cardiovascular disease
- Premature/Low birthweight deliveries
- Pulmonary diseases/disorders
- Stress

Having BOTH **inflammation** and high cholesterol together is especially ominous—resulting in a NINE-FOLD increase in cardiovascular risk

### **Inflammation in Review**

Lacking tools to describe interactions among cells and molecules, early doctors defining inflammation had to focus on what they could see and feel

Today we know that the outward signs of inflammation reflect a pitched struggle playing out on a microscopic battlefield

### **Macrophages**

These are the ‘garbage collectors’ of the cellular world

Ingested bacteria are killed within these vacuoles (usually through the generation of toxic inorganic radicals) and then are excreted—unless the macrophage becomes constipated

Macrophages also secrete MANY cytokines which are important in the inflammatory process

Among the few:

- Tumor Necrosis Factor (especially ‘TNF- $\alpha$ ’)
- Interleukin-1 (‘IL-1’)
- Interleukin-6 (‘IL-6’)

Chronic wounds fail to progress through the normal pattern of wound repair, but instead remain in a state of chronic inflammation predominantly characterized by abundant PMN and macrophage infiltration

Persisting inflammatory cells play a major role in the generation of proinflammatory cytokines (**IL-1, TNF- $\alpha$ , and IL-6**) and a protease rich and **pro-oxidant hostile microenvironment\*\*\*\***

All three cytokines (IL-1, IL-6, and TNF- $\alpha$ ) can be carried to distant sites via the blood and can induce an acute phase reaction

In an acute phase reaction, the body responds by increasing the hepatic synthesis of a number of plasma proteins

One of the most important of these hepatic plasma proteins is **C-Reactive Protein (‘CRP’)**

Found in trace amounts in healthy people, it is quickly becoming the leading marker for systemic inflammation

Levels of C-Reactive Protein

Normal CRP	<0.11 mg/dL
Moderate CRP	0.12-0.19 mg/dL*
High CRP	0.20-1.50 mg/dL*

\*Indicates cause for concern

However, CRP levels can go up to 400-500 mg/dL in seriously ill people  
Common conditions leading to marked changes in CRP include:

- Trauma
- Surgery
- Burns
- Advanced malignancy
- Alzheimer’s disease
- Heart disease
- Blood sugar disorders
- Smoking
- Obesity
- Dental disease\*\*\*

A chronic inflammatory state, as evidenced by elevated CRP, results in significant damage to the arterial system

The Women’s Health Initiative supports the CRP link to cardiovascular disease

Those women with the highest levels of CRP had 5 TIMES the risk of developing cardiovascular disease and 7 TIMES the risk of having a heart attack or stroke

CRP levels predicted risk of these events even in women who appeared to have no other pertinent risk factor

Now for the men: The Physicians' Health Study, which evaluated CRP levels and heart disease in 22,000 initially healthy men, also supports the relationship between inflammation and heart attack

Research on CRP indicates that cholesterol-filled plaques in blood vessels may not pose any real danger unless they are affected by inflammation

**Here's what's happening:**

Investigations that began over twenty years ago have now demonstrated that arteries bear little resemblance to the 'inanimate pipes' they were once considered to be

They contain living cells that communicate constantly with one another and their environment

These arterial cells participate in the development and growth of atherosclerotic deposits

**KEY CONCEPT: These deposits arise IN—not 'on'—vessel walls**

Relatively few of the deposits expand so much that they shrink the bloodstream to a pinpoint

A type of inflammatory response—the same one that causes gingival inflammation—underlies ALL phases of the disorder including the creation of plaques to their growth and rupture

The clearest picture of inflammation's role in the onset of atherosclerosis comes from investigations into low-density lipoprotein —a.k.a. 'bad cholesterol'

LDL particles transport cholesterol from their source in the liver and intestines to various tissues—which use it to repair membranes or produce steroids

High-density lipoproteins ('HDLs') haul cholesterol to the liver for excretion or recycling

HDL also combats atherosclerosis by interfering with the oxidation\*\*\* of LDL— HDL carries antioxidant enzymes able to break down oxidized lipids

Scientists have long known that, although the body needs LDL and cholesterol, excessive amounts promotes atherosclerosis

The mystery was how a LDL surplus lead to vascular plaque formation

Meanwhile, a 'healing' process also accompanies the more chronic, low-level kind of inflammation that operates in atherosclerosis

By carefully examining vessel walls of people who have died from heart attacks, pathologists have demonstrated that most attacks occur after a plaque's fibrous cap breaks open, prompting a blood clot to develop over the break

**Oral Inflammation and PTLBW Babies**

Some interesting research has demonstrated distinct hormonal influences on the immune systems of pregnant women—which may contribute significantly to the etiology of pregnancy gingivitis

Among the ‘immune tidbits’:

- Lymphocytes have a decreased antigenic response (P. intermedia)
- Migration of inflammatory cells and fibroblasts is hampered
- Prostaglandin E2 increases in response to progesterone (important in PTLBW link to oral inflammation\*\*\*)

During pregnancy, prostaglandin levels gradually increase—reaching their peak at the time of labor

A woman’s body reacts to the infections in her mouth by producing prostaglandins—very potent inflammatory mediators

If extra prostaglandins are being produced—such as those associated with gingivitis—a woman’s body may interpret this as a sign it is time to go into labor (even though the baby is not at full term)

Researchers at the University of Alabama found that women with severe periodontal disease in their second trimester of pregnancy tended to give birth anywhere from 3 to 8 weeks before their due date

The researchers advised expectant mothers to increase their level of oral hygiene and seek regular professional care during pregnancies

### **Periodontal Inflammation and COPD**

It is believed that the bacteria that cause periodontal diseases can travel into the lungs and cause inflammation and infection

Studies have shown that patients with periodontal diseases have one and a half times the risk for developing COPD than those without periodontal inflammation

### **Stress and Inflammation**

Studies are increasingly demonstrating a link between stress and periodontal diseases

Scientists have discovered that a period of stress will disrupt a wide variety of immune functions such as:

- Formation of new lymphocytes and their release into the circulation
- The time preexisting lymphocytes stay in the circulation
- The manufacture of antibodies in response to an infectious agent
- Communication among lymphocytes (“cytokines”)

The best-documented way in which such immune suppression occurs is via glucocorticoids (example: cortisol)

Glucocorticoids can cause shrinkage of the THYMUS GLAND

Most of the thymic tissue is made up of new lymphocytes that are ready to be secreted into the bloodstream

Additionally, glucocorticoids inhibit the release of certain cytokines (examples: INTERLEUKINS and INTERFERONS)

This inhibition of cytokines causes lymphocytes to be less responsive to an infectious challenge

High levels of financial stress and poor coping skills are likely to DOUBLE the chances of developing periodontal diseases

**Headliners: Take It Easy & Reduce Tooth Loss!; Jeffrey Gross, DDS; associate clinical professor; Case School of Dental Medicine; as reported in Woman's World; 6/23/08**

As many as 57% of recent studies link stress to periodontal diseases—the leading cause of tooth loss

‘A constant onslaught of cortisol depresses your body’s ability to kill off damaging bacteria in the mouth, plus it dampens your immune system’s ability to heal and repair tissue damage, allowing small gum problems to mushroom into bigger ones.’--Gross, J

Most experts believe that psychosocial factors--stress, moods, and anxiety--play an important role in the development of TMDs

While no strict “TMD personality” has been defined, persons suffering from TMDs report higher levels of stress, anxiety and depression than others

Efforts to control stress can have a positive impact on the development and duration of TMDs

**Headliners: An Investigation into the Effects of Gum Chewing on Mood and Cortisol Levels During Psychological Stress ; Andrew Scholey, Ph.D.; lead researcher; Professor of Behavioral and Brain Sciences; Swinburne University in Melbourne, Australia; presented at the 2008 10th International Congress of Behavioral Medicine; results reported by Rick Naurert, PhD; senior news editor; reviewed by John M. Grohol, Psy.D.; appearing in www.PsychCentral.com; 9/1/08**

The study examined whether chewing gum is capable of reducing induced anxiety and/or acute psychological stress while participants performed a battery of ‘multi-tasking’ activities

The findings??? The use of chewing gum was associated with higher alertness, reduced anxiety and stress, and improvement in overall performance on multi-tasking activities

Additional findings: Stress levels were lower in participants who chewed gum—levels of salivary cortisol in gum chewers were lower than those of non-gum chewers by 16% during mild stress and nearly 12% in moderate stress

**Headliners; Dentist Says Chest Massages Legitimate; Fresno Bee; 10/13/07**

A dentist accused of fondling the breasts of 27 female patients is trying to keep his dental license by arguing that chest massages are an appropriate procedure in certain cases

Dr. Mark Anderson says that dental journals discuss the need to massage the pectoral muscles to treat TMD—an administrative law judge disagreed, suspended his dental license, and charged him with two misdemeanor counts of battery and sexual battery

### **Stress Buster Headliners: A Little Charcoal in the Operatory May Be the Ticket!**

Ever notice how happy you feel after spending time outside?

It may be due to negative ions that enter the bloodstream and increase the body's output of serotonin

To keep levels of this neurotransmitter high when an outside break is not an option, try placing several lumps of plain charcoal in a bowl in your work area

Charcoal emits infrared rays that morph moisture molecules in the air into negative ions—giving you a quick mood boost without leaving your chair!

### **Behavioral Lifestyles and Periodontal Disease Risk**

- **Dietary choices**
- Use of tobacco, alcohol, and other recreational drugs
- Work schedule
- Family care

**Headliners: Strokes among middle-aged women skyrocket; Dr. Amytis Towfighi; neurology specialist, University of Southern California; reported by Marilyn Marchione; The Associated Press; Idaho Statesman; 2/21/08**

Strokes have **TRIPLED** in recent years among middle-aged women in the U.S.—a trend doctors are partially blaming on the obesity epidemic  
Compared to the federal health survey conducted from 1999 to 2004, the increase in stroke incidence occurred despite the fact that **MORE** women in the recent survey were on medications to control cholesterol and blood pressure (primarily prescribed to lower stroke risk)

Women's waistlines are nearly **TWO INCHES** bigger than they were a decade ago and BMI's rose from 27 in the first survey to 29 in the recent investigation

Belly fat stood out—the portion of women with abdominal obesity rose from 47% in the earlier study to 59% in the current survey

Adipose tissue attracts macrophages—which heightens the inflammatory response

Scientists have found that in deep apple fat tissue, macrophages constitute up to 40% of the cells!!!

Macrophages penetrate adipose tissue causing **BOTH** sets of cells to literally spew out damaging inflammatory compounds

'If you have excess fat, even in small amounts, the body starts mounting an immune response almost as if the body perceives excess calories as an invading organism.' --Dr. Gokhan Hotamisligil; Harvard School of Public Health

## **MICROBIAL CHALLENGES**

Bacteria rarely live alone—instead, they prefer to grow in crowds and squat on surfaces where they form communities known as biofilms

Biofilm research is still a relatively ‘new’ science—one that is uncovering amazing findings that will enable us to understand and better cope with the chronic infections they are responsible for causing

What is a BIOFILM?

A 3-Dimensional ‘community’ of bacteria attached to a surface which demonstrates:

- Fluid interaction
- Channels / pores
- Complex structure

More tenacious to mechanically remove and less susceptible to antimicrobial agents

Together these properties contribute to infection

### **Biofilm TIDBITS:**

- Biofilm bacteria can shrink to a spore-like state in order to wait for a hospitable environment
- Many topical antimicrobials kill surface bacteria (leaving the ‘deep dwellers’ a buffet!)
- Close proximity of bacterial cells in the biofilm allows for exchange of molecular signals that regulate behavior\*\*\*\*

### **Some ‘Community Activities’:**

- Bacteria can ‘talk’ to one another—regardless of species!—by utilizing autoinducer-2 for quorum sensing
- Certain biofilms (notably Pseudomonas) can produce a toxin that is almost bioidentical to rattlesnake venom
- Research has found biofilms that ‘glow’ (if an amoebae takes a bite, it will die!)

**KEY: When organized in biofilms, bacteria produce substances which individual bacteria alone cannot produce**

So how to we attack a plaque biofilm??????

Biofilm Adherence vs. Shear

Ultrasonic (office) and sonic (home) technology may just be our best weapon against biofilms

## **Pathological Microbiology**

Bacteria are grouped according to their MORPHOLOGICAL and BIOCHEMICAL / METABOLIC DIFFERENCES

Also classified according to immunologic and genetic characteristics

STAINING allows clinician to determine SHAPE of organism

Necessary because bacteria are colorless and invisible to light

The most useful is the GRAM STAIN:

Separates organisms into 2 groups (gram + and gram -)

Different stains are the result of differences in the CELL WALLS

## SUMMARY

### **Gram + Bacteria**

Thick

Contains teichoic acid

Vulnerable to penicillin and lysozyme

2 layers

Low lipid content

NO periplasmic space/porin channel

NO endotoxin\*

### **Gram - Bacteria**

Thin

Contains murein lipoprotein

High lipid

Periplasmic space

Porin channel

Endotoxin (LPS)- lipid A

Resistant to lysozyme and penicillin attack

Most disease causing microbes are gram - rods or gram - pleomorphic bacteria

- Eight disease-causing exceptions:
  - Two gram + cocci
- Four gram + rods
- One gram - cocci
- One gram - spiral shaped organism

### **Gram + cocci:**

Non-mobile

Do NOT form spores

Medically important:

- Streptococcus (“strips”)
- Staphylococcus (“clusters”)

### **Streptococcus**

Usually arranged in chains or pairs

All streptococcus are CATALASE NEGATIVE (unable to combat hydrogen peroxide)

Three groups:

- Beta-hemolytic (completely lyse RBC's)
- Alpha-hemolytic (partially lyse RBC's)
- Gamma-hemolytic (unable to lyse RBC's)

### **Beta-hemolytic streptococcus**

- Produces hemolysins
- Arranged into Lancefield groups (A-U)
- Group A streptococcus are important human pathogens
- Many strains are anti-phagocytic
- Group A streptococcus (‘GAS’)
- ‘Microbial post-it notes’

Causative for:

- Streptococcal pharyngitis
- Pyogenic infections
- Tonsillitis
- Scarlet fever/ Rheumatic fever

**Beta-hemolytic Group A streptococcus**

S. Pyogenes produces streptokinase (dissolves clots) and hyaluronidase (“spreading factor”)

Streptococcus pyogenes is one of the most frequent pathogens of humans  
It is estimated that between 5-15% of individuals harbor the bacterium, usually in the respiratory tract, without signs of disease

When the bacteria are introduced or transmitted to vulnerable tissues, a variety of types of suppurative infections can occur

As the body tries to fight off a strep infection, it can sometimes produce antibodies that attack both the strep bacteria and healthy cells

**Microbe Headlines: ‘Flesh-eating bug ate my face!’ one British tabloid screamed in the 1990’s**

The story took off like wildfire, with gruesome descriptions of limbs rotting in front of peoples eyes, faces melting away, and emergency amputations to save lives

Just another tabloid rumor, or something people should be losing sleep over?

There has been a recent increase in variety, severity and sequelae of Streptococcus pyogenes infections, and a resurgence of severe invasive infections, prompting descriptions of ‘flesh eating bacteria’ in the news media

In rare instances the bacteria can invade the body with wrath, causing a very serious infection called **necrotizing fasciitis**

Necrotizing fasciitis is a rare and extremely life-threatening illness, which requires extensive treatment

This can sometimes necessitate amputation or result in severe disfigurement

**Headliners: Lose 70 Pounds in 15 Days with Flesh-Eating Bacteria!**

According to the article, a ‘new, mutated’ strain of Streptococcus pyogenes cuts through fat ‘like a buzz saw’—eliminating ‘an incredible 3 inches of ugly, unsightly flab per hour’!

‘I went from 210 pounds to 140 pounds in 15 days with the help of fat-eating bacteria. Now when my husband invites those young starlets in bikinis to hang out by the pool, I don’t feel so insecure.’ --Wife of a well-known producer

A word or two about trustworthy sources...

**Microbe Headlines: Degrading a Defense: Bacteria use enzyme to escape trap; ScienceNews; 2/25/06**

Like a cloak of invisibility, an enzyme released by Strep A bacteria lets them slip away from the body’s staunchest defenders

Neutrophils attack bacteria by eating them OR they can release ‘neutrophil extracellular traps’ (‘NETs’)—the fibrous NETs are made up of DNA and toxic compounds that can catch and kill pathogenic microbes

Disease-producing bacteria such as GAS produce an enzyme that degrades the traps—likely DNases

Researchers speculate that this discovery could guide a new approach to fighting disease—although finding ways to target only pathogenic DNase must come first

‘Manipulating this one factor has a big effect on the disease-causing potential of bacteria. [Rather than killing the bacteria with resistance-promoting antibiotics,] we’re basically allowing the immune system to do its job.’--Victor Nizet; University of California (San Diego); lead researcher

In addition to Lancefield groups, there are further classification strategies for those pesky micro critters: **VIRIDANS GROUP STREPTOCOCCI**

- Big, heterogeneous group of strep bacteria
- No Lancefield group
- Not bile soluble

“Viridis” is Latin for GREEN; (produces greenish tint on blood agar)

Most viridans strep are alpha-hemolytic

Normal inhabitants of the nasopharynx and gingival crevices

The viridans streptococci cause 3 main types of infections:

- Dental infections
- Endocarditis
- Abscesses

#### **Dental infections:**

Some of the viridans streptococci (especially *S. mutans*) can bind to teeth by dextrans and ferment sugar, which produces acid and dental caries

#### **Endocarditis:**

Dental manipulations send viridans streptococci into the bloodstream where they can implant on the endocardial surface of the heart (most commonly on damaged valves) by producing an extracellular dextran

#### **Abscesses**

Subgroup of the viridans variety known as *S. intermedius* and *S. anginosus* are microaerophilic and are part of the normal GI tract

Most common VIRIDANS:

- *S. mutans* (pit and fissure caries)
- *S. sobrinus* (smooth surface caries)
- *S. salivarius* (septicemia)
- *S. mitis* (endocarditis)
- ***S. sanguis* (plaque colonization and endocarditis)\*\*\***

### Features of **S. Sanguis**

- Production of glycans from sucrose
- Platelet binding
- Binding to extracellular matrix proteins
- Binding to salivary proteins
- Ability to specifically co-aggregate with other oral microflora
- Genetic competence

*S. sanguis* directly binds to oral surfaces and serves as a tether for the attachment of a variety of other oral microorganisms which colonize the tooth surface, form dental plaque, and contribute to the etiology of both caries and periodontal disease

*S. sanguis* has been long recognized as a leading cause of bacterial endocarditis, a disease of high morbidity which is fatal if untreated

### **Microbe Headlines: Penicillin resistance is being observed in this group of organisms**

Such antibiotic resistance is both surprising and disquieting because the viridans streptococci (including *S. sanguis*) historically are classified as ‘penicillin sensitive’ and for many years were believed to be unable to become resistant to  $\beta$ -lactam antibiotics

Because the viridans streptococci organisms are often implicated in endocarditis, penicillin resistance is extremely alarming

## **STAPHYLOCOCCUS**

GENERALLY harmless inhabitant of the normal flora community

Has POWERFUL arsenal of enzymatic and exotoxin weapons

Important characteristics of *Staphylococcus*:

- Non-mobile
- Non-spore forming
- Gram + grapelike clusters
- Facultative aerobe
- Typical lesion = abscess

### **Staphylococcus aureus**

- Produces coagulase and hyaluronidase
- Produces pigmented compounds called carotenoids
- MAJOR producer of leukocidins (destroy phagocytes)
- Destroyed phagocytes make up bulk of pus

During the 1970s a strain of *Staphylococcus aureus* resistant to the antibiotic methicillin, was isolated and consequently vancomycin (the most powerful antibiotic in our arsenal) became the primary antibiotic used to combat staphylococcus infection

In 1997 a strain of *S. aureus* resistant to vancomycin was isolated, and people are once again exposed to the threat of untreatable staphylococcus infection

Indeed, microbes have an uncanny ability to adapt to their environment—even one laced with antibiotics

Consequently, the most fiercely antibiotic-resistant microbes will thrive where antibiotic use is heaviest

In the U.S., 2 million people acquire bacterial infections each year—90,000 die as a result

About 70% of those infections are resistant to at least one drug!!!

### **A Primer on Bacterial Resistance**

The BIG difference between animals and bacteria is that a new generation comes along every few years in large beasts--but as often as every 20 minutes in microbes!

That speeds up the ‘evolutionary cycle’ considerably--allowing for ‘survival mutations’

Another advantage that microbes have is that they are extremely promiscuous—even though they can reproduce asexually by splitting in two, they often link up with other microbes of the same species or even a different species

In doing so, microbes are capable of swapping bits of genetic material (their DNA) before reproducing

There are other ways bacteria can pick up genes—the DNA can come from viruses which have acquired it while infecting other microbes

Some types of bacteria can soak up DNA that spills out of dead or dying bacteria

This versatility means bacteria can acquire useful traits without having to wait for mutations in the immediate family

The process is even faster with antibiotic resistance than it is for other traits because the drugs wipe out the resistant bacterium’s competition

**Headliners: An Old Bug Has Learned Lethal New Tricks; Delthia Ricks; Newsday; as reported in the Idaho Statesman; 5/12/07**

Methicillin-resistant staphylococcus aureus (‘MRSA’) now thwarts everything in penicillin’s class—and threatens to do the same with other antibiotics

‘MRSA is a big problem in hospitals but [it] is becoming an equally large problem in the community. Many people who come into the hospital with a soft tissue infection have MRSA.’ --Dr. Bruce Farber, Chief of Infectious Diseases, North Shore University Hospital

**Headliners: Deadly Staph: Drug-resistant germ may kill more people than AIDS; Rob Stein; The Washington Post; 10/17/07**

The CDC calculated that MRSA is responsible for 94,000+ infections and nearly 19,000 deaths each year— meaning MRSA infects 31 out of every 100,000 Americans--JAMA; 10/17/07

The CDC estimates make MRSA much more common than flesh-eating strep, bacterial pneumonia and meningitis COMBINED

And because the CDC estimates include only the most serious MRSA infections, researchers are even more troubled

‘This is the first study that’s been able to capture the data in a comprehensive fashion. This is a significant public health problem. We should be very worried.’--Scott K. Fridkin; medical epidemiologist; Centers for Disease Control and Prevention

### **Any hope on the horizon???**

Throughout Europe, physicians have been battling severe MRSA for years—with success reported when maggots were used in treating infected diabetic foot ulcers

**Headlines: Sticky Treatment for Staph Infections; Cooper R; University of Wales Institute at Cardiff; as reported in ScienceNews; 6/9/07**

Manuka honey made by bees pollinating a New Zealand bush has the potential to reverse MRSA infections according to several case reports. The honey seems to interfere with cell division—making it effective against not only MRSA but a wide variety of resistant and non-resistant pathogens

Throughout Europe, physicians have been battling severe MRSA for years—with success reported when maggots were used in treating infected diabetic foot ulcers

**Microbe Headlines: Alligator Blood May Lead to Powerful New Antibiotics; Amitabh Avasthi; National Geographic News; 4/7/08**

Chemists in Louisiana found that peptides in blood from the American alligator can successfully destroy 23 strains of bacteria—including strains known to be resistant to antibiotics

‘We are in the process of separating and identifying the specific peptides in alligator blood. Once we sequence these peptides, we can obtain their chemical structure to potentially [create new] drugs.’--Lancia Darville, study co-author; Louisiana State University; presentation remarks at the 235th national meeting of the American Chemical Society in New Orleans; 4/08

The study team thinks that pills and creams containing alligator peptides could be available at local pharmacies within 7 to 10 years

### **Meet Mr. Neisseria**

**Headliners: Gonorrhea Is Increasingly Drug-Resistant, Officials Say As reported by Jia-Rui Chong; Los Angeles Times; 4/13/07**

*Neisseria gonorrhoeae* is the causative agent of the sexually-transmitted disease (STD) gonorrhea

Approximately 1 in 348 people in the U.S. are infected with *Neisseria gonorrhoeae*—in Canada, approximately 1 in 500 people are infected but the rate of infection is rising faster than in the U.S. (particularly in the western provinces)

Highly drug-resistant gonorrhea has been spreading rapidly across the U.S. and now accounts for 13% of ALL cases of this STD (up from 1% in 2001)

The CDC in April 2007 urged doctors to stop using a powerful class of antibiotics—fluoroquinolones—that until now has been the primary treatment for the disease

The agency now recommends a single class of antibiotics—cephalosporins ‘We have a very efficient class of drugs left, but if they go away and resistance marches on to other antibiotics, then we’re really in trouble.’ -- Dr. John M. Douglas, Jr.; director; CDC Division of Sexually Transmitted Disease Prevention

### **Actinomyces**

Normal flora of the upper respiratory, gastrointestinal and female genital tracts

Low virulence potential, only causing opportunistic disease following disruption of mucosal barriers by trauma, surgery or infection

### **Actinomycosis**

Also known as ‘Lumpy jaw’, actinomycosis is a chronic infection, commonly of the face and neck, that produces abscesses and open draining sinuses

Actinomycosis is usually caused by the bacterium called *Actinomyces israelii*, which is a common and normally nonpathogenic organism found in the nose and throat

Because of the bacterium's normal location in the nose and throat, actinomycosis most commonly appears in the face and neck

And since it is normal for people to carry this organism, the infection is not contagious

*Actinomyces* produces disease when it is introduced into the facial tissues by trauma, surgery, or infection (a common cause is dental abscess or oral surgery)

Once in the tissue, it forms an abscess, producing a hard, red-to-reddish-purple lump, often on the jaw—hence, the name ‘lumpy jaw’

Eventually, the abscess breaks through the skin surface to produce a draining sinus tract

Actinomycosis may occasionally occur in the chest (pulmonary actinomycosis) and abdomen or other areas of the body

Microcolonies within the abscesses are macroscopic masses of filamentous bacterial cells that are "cemented" together by calcium phosphate known as sulfur granules due to their yellow or orange appearance

Chronic suppuration results in granuloma formation and a fibrotic "walling off" of the lesion ultimately resulting in bone involvement

### **Meet *Prevotella intermedia***

*Prevotella* organisms are normal inhabitants of the oral, respiratory, intestinal, and urogenital cavities

**Microbe Headlines: *Prevotella intermedia* LOVES progesterone and estrogen!**

The gram-negative, anaerobic *Prevotella intermedia* have the ability to substitute estrogen and progesterone for menadione (vitamin K) as an essential growth factor

Elevated plasma concentrations of ovarian hormones—estrogen and progestins—during pregnancy, puberty, the menstrual cycle, and oral contraceptive use are associated with an increased incidence of gingival inflammation and exudate

## **VIRUSES**

Unique characteristics:

- Energy-less
- Must have HOST CELL
- Composed of protein core (CAPSID) surrounding genetic material
- Outer lipid bilayer (ENVELOPE) or “naked”
- Complete virus is called virion
- “Small” (0.02-0.3 microns)
- Various host ranges
- Specificity is determined by viral attachment capabilities
- Helical or icosahedral

Host cell outcomes:

- Death
- Transformation
- Latent infection
- Chronic slow infections

### **Classification of VIRUSES**

- Type and structure of nucleic acids (RNA or DNA--never both!!!!)
- Method of replication
- Host range

### **RNA Viruses**

Can be either positive or negative strand RNA based on relation to mRNA

Must provide replicase and transcriptase

Examples of RNA viruses:

- Hepatitis A
- Rhino virus
- Influenza virus
- Mumps
- Measles
- Rabies
- HIV

### **DNA Viruses**

Has both positive and negative strands

CANNOT be translated into proteins until it is transcribed into mRNA

Examples of the DNA crowd:

- **Human papilloma virus**
- Herpes Simplex 1 and 2
- Varicella-zoster
- CMV
- Epstein-Barr virus
- Smallpox

**Headliners: Canada Leads Research on HPV & Periodontitis Link!**

Researchers from UB and Roswell Park Cancer Institute published the first study showing an association between long-standing periodontitis and risk of tongue cancer in 2007—the UB researchers also recently demonstrated that the two infections appear to work in tandem to boost the chances of developing tongue cancer

Results of this research was presented on April 4, 2008 at annual American Association of Dental research meeting in Dallas, Texas ‘Evidence of periodontitis-HPV synergy has important practical implications because there is a safe treatment for periodontitis, but no treatment for HPV infection. If these results are confirmed by other studies, this has a tremendous relevance in predicting and intervening in the initiation and prognosis of HPV-related diseases, including head and neck cancers.’ --Mine Tezal, D.D.S., Ph.D., assistant professor in the Department of Oral Diagnostic Sciences, UB dental school, and research scientist at Roswell Park Cancer Institute

**A word or two about oral cancer**

More than 34,000 Americans will be diagnosed with oral or pharyngeal cancer this year—it will cause over 8,000 deaths, killing roughly 1 person per hour, 24 hours per day

Of those 34,000 newly diagnosed individuals, only half will be alive in 5 years—this is a number which has not significantly improved in decades The death rate for oral cancer is higher than that of cancers which we hear about routinely such as cervical cancer, Hodgkin's lymphoma, laryngeal cancer, cancer of the testes, endocrine system cancers such as thyroid, or skin cancer (malignant melanoma)

In order to discover pathology, you must first look for it

The **human papilloma virus (HPV)** is one of the most common virus groups in the world to affect the skin and mucosal areas of the body With over eighty identified types of HPV, we now know that different kinds of the human papilloma virus are known to infect different parts of the body by infecting the epithelial cells of skin and mucosa

There are forms of HPV (specifically HPV-16, HPV-18, HPV-31, and HPV-45) which are sexually transmitted and are a serious problem

The most dangerous sexually transmitted HPV's (16 and 18) are known to cause up to 95% of cervical cancers—now these two HPV's are also being linked to oral cancer

It has now been confirmed that in a younger age group, including those who have never used tobacco products, have oral cancer which is HPV viral based

**Headliners: Disturbing Link: Oral Sex & Throat Cancer; Cathy Becker; reporting for ABC News; posted 10/15/08 at abcnews.com; accessed 11/17/09**

Teresa Dillon was surprised to learn four years ago that what she deemed as an average sore throat actually was stage 2 cancer on her tonsil ‘People think the face of oral cancer is a 70-year-old man who's been chewing tobacco and drinking whiskey all his life. But the face of oral cancer now is—it's me, a young woman, healthy, nonsmoking, fit.’ -- Teresa Dillon

But what really shocked the waitress and then 38-year-old was that HPV may have caused her illness

Dillon is part of a new trend that is puzzling scientists—while most HPV infections clear on their own, there is an alarming surge of oral cancers linked to the virus

Johns Hopkins researchers reported in a study published in the February 2008 Journal of Clinical Oncology that between 1973 and 2004 the incidence of HPV-related oral cancers among people in their 40s nearly doubled—today 39% percent of oral cancer cases are related to HPV-- American Cancer Society.

‘These are patients that are young. They are in their 30s and 40s. They are nonsmokers, and they don't drink alcohol excessively. And every time we look we are able to find HPV-16 in their tissue, in the biopsy specimen.’ -- Dr. Robert Haddad, a Dana Farber Cancer Institute head and neck surgeon The virus is transmitted by direct contact—HPV is transmitted only in the location it attaches to and never travels through the bloodstream—how it is infecting the mouth reflects a disturbing trend

‘There is absolutely a link between oral sex and oral cancer.’ --Dr. Ellen Rome, Cleveland Clinic

Although no proof exists yet, there is a chance that HPV can be transmitted mouth to mouth: ‘We can't rule out the virus could be transmitted in saliva by other types of contact — like for instance sharing a drink or sharing a spoon.’ --Dr. Maura Gillison, Johns Hopkins Kimmel Cancer Center

Infection with the virus usually happens in adolescence—and, while oral sex today isn't necessarily more prevalent than it was in the past, it certainly is more accepted

And some often presume it is free of risks—a 2005 study in the Journal Pediatrics found that teens think oral sex is less risky to their health than vaginal sex

Dillon, who after six months of grueling chemotherapy is now in remission, said she wishes she had known the risk as a teen: ‘You have to be careful. Know who you're with and you have to take precautions. You need to educate yourself. You need to know what's going on.’ (Dillon)

**Headliners: Saliva May Help Spot Oral Cancer Early; Robert Preidt, reporting for HealthDay; 8/25/09**

In a major step towards early diagnosis of oral cancer, researchers have found that saliva contains at least 50 microRNAs that could aid detection. Researchers measured microRNA levels in the saliva of 50 people with oral squamous cell carcinoma and 50 healthy people.

They identified at least 50 microRNAs that may be associated with oral cancer.

The levels of two of those— miR-125a and miR-200a—were significantly lower in the cancer patients than in healthy people, the researchers found. 'It is a Holy Grail of cancer detection to be able to measure the presence of a cancer without a biopsy, so it is very appealing to think that we could detect a cancer-specific marker in a patient's saliva.' --Dr. Jennifer Grandis; professor of otolaryngology and pharmacology; University of Pittsburgh School of Medicine and Cancer Institute; and senior editor of Clinical Cancer Research.

**Headliners: The Worst Germs Aren't Where You'd Think; Charles Gerba, PhD.; coauthor; The Germ Freak's Guide to Outwitting Colds and Flu (HCI, 2005); as reported by First; 11/20/06**

According to the author, 80% of infections come from touching shared surfaces in high traffic areas.

**Germ Haven #1: Credit and Debit Card Machines**

Up to 3,000 customers go through a single Wal-Mart store checkout line on a busy day—many will touch the buttons and stylus on the credit/debit card machines.

It is estimated that the average ATM keypad houses 10 MILLION bacteria. Also, public pens at restaurants, medical offices, banks, gas stations, etc. can be covered in millions of pathogens.

Solution: Carry your own pen.

**Germ Haven #2: The Cart at the Department Store**

Many studies have shown that grocery carts failed more hygiene tests than public restrooms did—with evidence of blood, saliva, mucus and even fecal matter on the handles and baby seats.

'But the shopping carts at department stores and superstores where thousands of people shop every day are equally—if not more—hazardous since they are rarely cleaned.' --Charles Gerba.

**Germ Haven #3: The door to ENTER the restroom**

Many folks are avoiding contact with the door handle on the way OUT of the restroom by using a paper towel to open the door.

However, new research found that the door handle to ENTER the restroom is far dirtier: It's covered in 200% more viruses and bacteria!

This Travel Toiletry Package (TT Pack) contains one set of sanitary items to make using a public restroom bearable (Toilet seat cover, germicidal wipe, paper towel, tissue, hand wipe and disposable glove).

Microbes will continue to provide perplexing and daunting challenges...  
We need to keep abreast of current scientific breakthroughs and new product developments

As clinicians, our goal is to regenerate ALL of the components of the periodontium through periodontal therapy

The members of the Periodontium:

- Gingiva
- Periodontal ligament
- Cementum
- Bone

### **Gingiva**

**Headliners: The Effects of Anabolic Androgenic Steroid Abuse on Gingival Tissues; Onur Ozcelik, D.D.S., Ph.D.et al.; Journal of Periodontology 2006; 77:1104-1109**

The gingiva is affected by sex hormones, and clinical changes in periodontal tissue have been observed during puberty, pregnancy, menopause, and with the use of oral contraceptives

However, according to the study authors, 'no clinical research has been performed about the effects of anabolic androgenic steroid abuse on gingival tissues'

Previous research has shown that 4% to 6% of American young adult athletes have tried steroids—and few male bodybuilders, go without steroids

Study investigators found that, compared with their steroid-free counterparts, the steroid users were found to have a higher incidence of gingival enlargement

According to the investigators, steroid abuse is also associated with psychiatric and behavioral problems (such as depression, mania, psychosis, and aggression) which may increase one's risk for periodontal disease

'Because the non-medical use of anabolic androgenic steroid remains prevalent and seems to increase despite legislation, dentists and periodontists should be familiar with the adverse effects of these synthetic derivatives of testosterone on the gingival tissues.'--Ozcelik

### **Periodontal Ligament**

Consists of collagen fibers and fibroblasts

Numerous small blood capillaries

Fibers extend into matrix of bone AND cementum ('Sharpey's fibers')

Collagen in review:

- Collagen is synthesized by FIBROBLASTS
- Vitamin C is required for synthesis

Without Vitamin C, fibroblasts become constipated

Plaque antigens have the same effect on fibroblasts

**Headliners: New Bond in the Basement Tethers Body's Tissues Together; Billy Hudson; lead researcher and biochemist; Science; 9/4/09; as reported by Rachel Ehrenberg; Science News; 9/26/09**

Basement membranes have long been recognized as important for a body's structural integrity by acting to tether tissues together  
Basement membranes also play a crucial signaling role—sort of like a thermostat for cellular health

'If the basement membrane misbehaves, then the cell misbehaves.'--  
Raghu Kalluri; matrix biologist specialist; Harvard Medical School; Boston, MA

A major component of basement membranes is type IV collagen—a triple-stranded 'rope' capped with amino acid globules

The amino acid globule of one strand of collagen connects to a globule on another strand to help form a matrix—the nature of the bonds, however, was poorly understood

With newer technology involving higher microscopic resolution, the researchers were able to determine that the globular bonds were covalent sulfur-nitrogen bonds (known as 'sulfilimine bonds')—not disulfide bonds as most had originally suspected

It is thought that disrupting these bonds could help attack tumors—nearly HALF of a tumor's weight is derived from the collagen-basement membrane

Additionally, because basement membranes surround all blood vessels, the membranes act like train tracks that allow tumor cells to spread perhaps breaking the sulfilimine bonds would collapse the blood vessels and halt tumor growth

### **Cementum**

Less is known about cementum than any other supportive tissue

We do know that without root cementum, fiber attachment cannot occur  
News Flash: In the race to learn more about cementum, researchers uncover amazing cellular happenings!

Recent studies have indicated that the cementum matrix contains several growth factors and noncollagenous proteins that promote the attachment, migration, and growth of fibroblasts, osteoblasts and other cells

Cementum-derived attachment protein ('CAP') is a collagenous protein that promotes the attachment of fibroblasts and other periodontal cells  
CAP promotes the adhesion of periodontal cells which are able to form cementum-like mineralized tissue in culture

### **Bone**

Generation of BONE through grafting procedures is fast becoming a periodontal therapy option for a variety of defects

Types of Bone Grafts

- Autograft
- Allograft
- Xenograft

**Alloplasts**

Refers to synthetic, chemically derived bone substitute

Most often a form of calcium phosphate

May be absorbable or nonabsorbable

**Autografts**

Often referred to as the 'gold standard'

Bony tissue transplanted from one site to another within the same individual

May be extraoral (typically iliac cancellous bone and marrow) or intraoral (maxillary tuberosity)

**Allografts**

Defined as a tissue graft between individuals of the same species but of non-identical genetic composition

Bone source is typically cadaver bone that has undergone several treatment sequences to avoid disease transmission and decrease immune reactions

**Xenografts**

Tissue graft between two different species

Typically bovine-derived

Calcium phosphate is responsible for the mechanical strength and development of bone

Once processed, the material is termed anorganic bovine bone mineral (ABM)

**Alloplasts**

Refers to synthetic, chemically derived bone substitute

Most often a form of calcium phosphate

May be absorbable or nonabsorbable

**Headliners: 'Boning Up: Tissue for Grafts Grown Inside the Body' Science News; Vol. 168; 7/30/05**

The outside of the periosteum is smooth but the side that is in contact with the surface of the bone is 'sticky'—it supports a layer of stem cells that produces new bone

In laboratory studies, scientists inserted a bubble of calcium-containing gel between the periosteum and bone

The researchers hypothesized that separating the periosteum from the bone (mimicking an injury) along with supplying important nutrients for osteoblast-precursors (the calcium), the stem cells would be stimulated to create new bone

And guess what happened??? Within 2 weeks of the experiment, a soft layer of immature bone filling the space occupied by the calcium gel was observed

And that's not all: 6 to 8 weeks later, the bone had hardened into a mature form with mechanical properties similar to those of adult bone tissue

**Headliners: Serotonin: What the Gut Feeds the Bones; As reported by Laura Bell; Science News; 6/6/09**

It was discovered almost a decade ago that serotonin—the ‘feel good’ hormone also involved in learning and sleep—might be bad news for bone health

In Fall 2008, researchers found that the intestinal tract acts as a serotonin-bone command center—studying the ‘crosstalk’ between the skeleton and GI system may help in treating osteoporosis

Here’s what is happening:

- Eating a meal stimulates a specific enzyme (‘Tph1’) to make serotonin in the gut
- Platelets move the newly made serotonin throughout the body and into the bone

KEY: In excess, serotonin can inhibit pre-osteoblasts from becoming osteoblasts while osteoclastic function is not affected

Following the discovery of a serotonin connection to the bone-forming osteoblasts, researchers began to worry about the more than 8% of

Americans who take SSRIs (‘Selective Serotonin Reuptake Inhibitors’)

In an osteoporosis study involving ~6000 older men, those taking SSRIs had lower average bone density than those not on the antidepressants

A related study of postmenopausal women found that bone density declined in those taking SSRIs TWICE as fast as it did in women not taking the medication

‘I think the major question right now is—if depressed people are going to be treated with SSRIs, are we subjecting them to risk of fracture?’--

Michael Blizotes, Oregon Health & Science University; Portland, OR

**Thank You, Manitoba!**

**(Extra KUDOS to Mary Bertone)**