

New Horizons in Periodontal Therapy

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Presenter Disclosures for Betsy Reynolds, RDH, MS

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Agenda

- Landmarks in Periodontal Therapy
- Relationship Between Oral and Systemic Conditions
- Microbial and Immunological Challenges
- Periodontal Therapy Considerations
- Wrap-Up

1980's: Role of Immune Status

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

Key Points:

- Most autoimmune disorders are AB-mediated
- Multifactorial
- Increase incidence with age
- Genetic predisposition is common (much more likely to affect females)

Autoimmunity disproportionately affects women—ratios vary by disease but, overall, almost 80% of people with autoimmune disorders are female

Autoimmune disorders can affect virtually ANY site in the body—including the oral cavity

Examples of Autoimmune Disorders

- Rheumatoid arthritis
- Scleroderma
- Systemic lupus erythematosus
- Psoriasis
- Crohn's disease

Rheumatoid Arthritis

Rheumatoid arthritis is mainly characterized by inflammation of the joints and can lead to long-term joint damage, resulting in chronic pain, loss of function and disability

Affecting 1.5 million Americans, RA most often affects people in middle age (although it can begin at any stage of life) and often starts with only minor joint pain and stiffness in the beginning

Clinical Considerations

- In a 2001 Australian study, people who had rheumatoid arthritis were more than TWICE as likely to have periodontal disease with moderate to severe bone loss as the control subjects— additionally, RA sufferers averaged 11.6 missing teeth compared to 6.7 in the control group

- In a more recent study, German researchers found that RA status and age were significant predictors of periodontal disease—they discovered that patients with RA were EIGHT times more likely to have periodontal disease compared to control patients
- At this point, researchers are not saying the relationship between the two diseases is causal—however, some scientists think a bacterial infection may trigger the disease process in some of the people with rheumatoid arthritis

Headliners: Metagenomic Study Finds Differences in Oral, Gut Microbiomes of Rheumatoid Arthritis Patients; Jun Wang et al; BGI; Results appearing in Nature Medicine; 7/27/15; accessed on 8/4/15 at: <https://www.genomeweb.com/sequencing-technology/metagenomic-study-finds-differences-oral-gut-microbiomes-rheumatoid-arthritis>

The oral and gut microbiomes of people with rheumatoid arthritis apparently differ from those of healthy people

Jun Wang and his colleagues of BGI (the largest genomic research facility in the world) found that, while the etiology of rheumatoid arthritis remains elusive, the research team believe that both genetic and environmental (including microbial) factors appear to influence disease development

The investigators analyzed fecal, dental, and salivary samples from people with RA and controls—the oral and gut microbiomes of people with RA differed from controls in both the composition and functions of the microbes present

‘Our [study] supports the notion that RA represents a state of chronic inflammation that might be provoked or aggravated by the overgrowth of pathogenic bacteria or a lack of immune-modulating commensal bacteria. These findings are a first step toward microbiome-based therapeutics and patient stratification in preclinical and clinical phases of RA.’--Wang

Lactobacillus salivarius was found in all three tested sites in RA patients—interestingly, this microbe has gained attention in recent years as a promising probiotic species (defined as ‘...living micro-organisms which upon ingestion in certain numbers exert health benefits beyond inherent nutrition’)

CAUTION!

- Research findings vary greatly when it comes to *Lactobacillus salivarius*
- While some studies have reported oral administration of *L. salivarius* improved bad breath, showed beneficial effects on bleeding on probing from the periodontal pocket, and inhibited the reproduction of pathogenic bacteria, other investigations have shown conflicting findings as to the benefits of this probiotic in caries or periodontal inflammation prevention

Headliners: Rheumatoid Arthritis Patients Are Using Medical Marijuana; Reported by David Downs; 7/8/15; accessed on 8//15 at: <http://blog.sfgate.com/smellthetruth/2015/07/08/rheumatoid-arthritis-patients-are-using-medical-marijuana-heres-why/>

More and more aging baby boomers are dealing with the long-term ramifications of chronic RA—and are increasingly turning to medical marijuana to treat the multiple forms of pain (including neuropathic pain) associated with RA cartilage degradation

Arthritis pain is reported as one of the most common reasons for persons using medical herbal cannabis in North America—severe arthritis is the condition justifying legal use of cannabis in over half of all authorizations in Canada

Cannabinoid receptors are present throughout the body and are embedded in cell membranes—they are believed to be more numerous than any other receptor system in the body

Knowledge of these receptors—CB1 and CB2—has greatly enhanced the overall knowledge of how cannabinoids synergistically interact with other cannabinoids and endocannabinoids to produce sometimes profound systemic effects

2-arachidonoylglycerol (2-AG)

As the most abundant endocannabinoid, 2-AG is a full agonist for cannabinoid receptors (CB1 and CB2)—although, as a potent immune modulator, 2-AG is often recognized as the primary agonist for the CB2 receptor

CB2 receptors occur mainly in peripheral locations of the cells and organs associated with the immune system and are involved in control of inflammatory reactions—upon stimulation by 2-AG, inhibition of the release of proinflammatory cytokines and increased release of anti-inflammatory cytokines is seen--
Source: Zubrzycki M et al: A New Face of Endocannabinoids in Pharmacotherapy; accepted for publication 16 DEC 2013; accessed on 26 OCT 2017 at:

http://www.jpp.krakow.pl/journal/archive/04_14/articles/02_article.html

2-AG was shown to inhibit the overexpression of inflammatory cytokines such as tumor necrosis factor alpha (TNF- α), IL-1 β , and inducible nitric oxide synthase (iNOS)

Source: Ben Li et al: Endocannabinoid 2-arachidonoylglycerol protects inflammatory insults from sulfur dioxide inhalation via cannabinoid receptors in the brain; appearing in Journal of Environmental Sciences; Volume 51, January 2017, Pages 265–274. Accessed on 26 OCT 2017 at:

<http://www.sciencedirect.com/science/article/pii/S1001074216302340>

Complex tasks coordinated by the body and brain (such as appetite, sleep, and pain perception) are also influenced by 2-AG because of its effects on the CB1 receptors

Summary of 2-AG Functions:

- Immune function***
- Bone health***
- Pain***
- Mood
- Metabolism
- Reproduction
- Memory
- Movement
- Sleep
- Neuroprotection

Scleroderma

Scleroderma is a chronic, degenerative, autoimmune disorder that leads to the over-production of collagen in the body's connective tissue—the word 'scleroderma' means 'hardening of the skin' and refers to one of the possible physical effects of the disease

The National Institute of Arthritis and Musculoskeletal and Skin Disease, recognizes that although scleroderma is often referred to as if it were a single disease, in fact, it is really a symptom of a group of diseases that involve the irregular growth of collagen

Oral manifestations of Scleroderma include:

- Microstomia***
- Xerostomia
- Raynaud's phenomenon***
- Periodontal diseases (uniform widening of the PDL)***
- Mucosal and skin disease
- Osseous resorption***

Mandibular resorption in systemic sclerosis is relatively uncommon and is reported only in 10% of cases

Headliners: Drugs That Reverse Fibrosis in Scleroderma Step Closer; Richard Neubig; lead investigator; professor and chairperson; Department of Pharmacology and Toxicology; Michigan State University; results published in the Journal of Pharmacology and Experimental Therapeutics; 4/14; accessed online 8/4/15 at: <http://www.medicalnewstoday.com/articles/275144.php>

Researchers say they have discovered a promising target for new drugs that might be able to reverse the fibrosis process in scleroderma—a core genetic pathway that that throws the main switch for all the signaling pathways in scleroderma

By validating this core switch ('MRTF/SRF gene transcription pathway') as a viable drug target, the researchers are hoping to improve treatment strategies and drug dosing—significantly changing the quality of life for scleroderma patients and greatly lengthening the lives of systemic patients

Lupus Erythematosus ('LE')

In lupus, the regulation of immune system goes awry and the body produces autoantibodies that attack host cells resulting in inflammation that causes redness, pain and swelling in the affected parts of the body

Also referred to as 'systemic lupus erythematosus', this autoimmune disorder attacks healthy organs and tissues, including the joints, skin, blood cells, lungs, heart, kidneys and brain

Ninety percent of people with lupus are female, and the disease typically starts between the ages of 15 and 40

Lupus is two to three times more common among African Americans, Hispanics, Asians, and Native Americans than among Caucasians

Although the cause for lupus is unknown, it likely requires an environmental stimulus in presence of many susceptibility genes

Headliners: Differing Chemical Tags on DNA Hint Why Lupus Is Not Identical in Twins; As reported by Tina Hesman Saey; appearing in Science News; 1/16/10

Lupus apparently can tell identical twins apart by the distinguishing marks the pairs carry on their DNA—the finding suggests that environmental factors determine whether genetically susceptible twins will contract systemic lupus erythematosus

Researchers have previously identified at least 17 different genes involved in lupus—if genes alone were responsible for determining whether a person gets lupus, then every time one identical twin got the disease, the other would, too

But that does not happen: Between 40% and 75% of the time, when one twin develops the disease, the other stays healthy—leading investigators to assume that some environmental factor must trigger the disease—Bruce Richardson; rheumatologist; University of Michigan Medical School (Ann Arbor)

Key Points:

- Lupus produces widely varying symptoms
- Lupus can cause short periods of symptoms alternating with healthy periods—or it can progress into a life-threatening disorder affecting the heart, kidneys, and other organ systems

Symptoms MAY include:

- Fatigue
- Joint pain
- Shortness of breath
- Butterfly Rash
- Visual impairment
- Photosensitivity
- Skin lesions
- Cardiac conditions

- Seizures
- Oral ulcerative lesions

Almost all people with LE have joint pain and most develop arthritis—frequently affecting joints of the fingers, hands, wrists, and knees

The ‘hallmark lesion’ of lupus is a malar—or ‘butterfly’—rash which presents as an erythematous rash across the bridge of the nose

Inflammation of various parts of the heart may occur as pericarditis, endocarditis, or myocarditis—chest pain and arrhythmias may result

Oral lesions occur in 10%-40% of patients

Lesions typically appear on the buccal mucosa and exhibit lichenoid characteristics

Headliners: Lupus: Spike Seen in Hospital Admissions for Infections; Michael M. Ward, MD; lead investigator; National Institute of Arthritis and Musculoskeletal and Skin Diseases; Bethesda, MD; results appearing in Arthritis Care & Research.; 8/14; As reported by Nancy Walsh; Senior Staff Writer; MedPage Today; accessed on 8/4/15 at:

<http://www.medpagetoday.com/Rheumatology/Lupus/52814>

In a national study, investigators found rates of hospitalization for serious infections among patients with systemic lupus erythematosus are substantially higher than in the general population—and have been rising in recent years

For instance, the relative risk among SLE patients of hospitalization for opportunistic infections compared with non-SLE patients rose from 8.8 in 1996 to 24.1 in 2011

Serious infections have been estimated to account for up to 37% of all hospitalizations among patients with SLE—as well as two-thirds of avoidable hospitalizations and one-third of deaths

‘We found strikingly high relative risks of hospitalizations for serious infections, which underscores the high burden of infections in SLE. [Infections remain a major concern in SLE and] adoption of guidelines for the prevention and management of infections, as have been successfully used in other diseases, are urgently needed.’ --study authors

Psoriasis

Psoriasis is the most common autoimmune disease in the United States—affecting more than 7.5 million people

Psoriasis is not a contagious skin disorder and occurs when the immune system sends out faulty signals that speed up the growth cycle of skin cells

Different types of psoriasis display characteristics such as pus-like blisters (pustular psoriasis), severe sloughing of the skin (erythrodermic psoriasis), drop-like dots (guttate psoriasis) and smooth inflamed lesions (inverse psoriasis)

The most common form—plaque psoriasis—appears as raised, red patches or lesions covered with a silvery white buildup of dead skin cells (called scale)

Psoriasis can occur on any part of the body and is associated with other serious health conditions, such as diabetes, heart disease and depression

Oral Psoriasis

Although rare, oral psoriasis occurs and can have a variety of manifestations

Epithelial turnover time is significantly increased in psoriatic plaques and may be as rapid as 3 to 7 days—normal epithelial turnover is 28 days

Some have suggested that this abnormally increased turnover time in psoriasis approximates that of the normal regenerative time of the oral epithelium, and this possibility may account for the apparent lack of changes in the oral mucosa of patients with psoriasis

Patients exhibiting oral psoriatic lesions will most often have severe forms of psoriasis such as generalized pustular psoriasis

Clinical Tip:

- The diagnosis of oral psoriasis should be based on good clinical and histologic evidence, and, in general, the clinical course of the oral lesions should parallel that of the skin disease

Patient Recommendations:

- Eat the right foods (elimination of sugar or sugar syrups, grain that is not 100% whole, and most saturated fats and ALL trans fats can be beneficial)
- Ingest omega-3, purified omega 7 or a couple of teaspoons of olive oil daily will reduce inflammation
- Get at least 7-8 hours of sleep nightly
- Cortisone cream may be prescribed
- A daily vitamin D3 supplement may help
- Use of a home humidifier (make sure it stays clean!)

Headliners: Cyndi Lauper's Psoriasis: Pop Star Is 'PsO' Ready To Open Up About Her Skin Disease; Reported by Emma Hernandez; 8/3/15; accessed on 8/4/15 at: <http://scribol.com/anthropology-and-history/the-insane-body-piercings-of-phukets-vegetarian-festival/14?image=14>

Pop icon Cyndi Lauper has teamed up with the National Psoriasis Foundation and Novartis Pharmaceuticals on the 'I'm PsO Ready' campaign to spread awareness of psoriasis

- "I am usually a very vocal and open person, but I think sharing your psoriasis story is very personal and takes a lot of courage. Raising awareness and educating others is critical. It is very easy to feel isolated. Through 'I'm PsO Ready,' I want people living with the condition to understand that we don't have to be embarrassed, we don't have to cover up and we don't have to settle for life the way it is."

The 'I'm PsO Ready' information campaign is part of the 'More To PsOriasis' initiative, intended to spread awareness about the disease and allow people to communicate their struggles so that they can educate others about what life is like living with psoriasis—it also aims to encourage people suffering with the disease to seek treatment

www.moretopsoriasis.com

Bottom Line:

- Like other autoimmune diseases, psoriasis cannot be cured—symptoms can be managed to a certain extent and exacerbations can be minimized to a degree

Crohn's Disease

Crohn's disease involves inflammation in the gastrointestinal tract and may affect the large or small intestine, rectum and/or mouth

Crohn's Disease by the Numbers--Source: Accessed on 8/4/15 at:

<http://www.healthline.com/health/crohns-disease/things-doctors-want-you-to-know-about-crohns>

1. There Are Flare and Remission Phases

Most people with Crohn's disease cycle through flare-ups and remissions—during remission phase, Crohn's sufferers feel pretty normal

Common symptoms of a Crohn's flare-up include:

- Abdominal pain (which typically worsens after meals)
- Diarrhea
- Painful bowel movements
- Blood in stool
- Weight loss
- Anemia
- Fatigue

2. More People Are Diagnosed Each Year

Roughly 700,000 Americans have been diagnosed with Crohn's disease—and that number continues to rise--Source: the Crohn's & Colitis Foundation of America (CCFA)

KEY: Men and women are equally affected!

Symptoms of the disease can start at any age, although, it most often shows up in adolescents and young adults between the ages of 15 and 35

3. No One Knows Exactly What Causes Crohn's

Most researchers believe CD results from an interaction of three factors:

- Genetic or hereditary factors
- Environmental triggers (such as medications, pollution, excessive antibiotic use, diet, and infections***)
- A wayward immune system that starts attacking its own GI tissue

Many believe that a virus or bacteria may be involved in the development of Crohn's disease causing the initial damage to the lining of the GI tract—however, it is not yet known which organism might be involved

4. Smoking Can Make Symptoms Worse

Research is suggesting that there may be a connection between cigarette use and Crohn's disease—not only can smoking cause people to have worse or more frequent symptoms but some data suggests that cigarette smoking may even increase the chance of developing Crohn's disease

'Smoking has been reported to affect the overall severity of the disease, with smokers having a 34% higher recurrence rate than nonsmokers.' --Akram Alashari, M.D.; surgeon and critical care physician; University of Florida

5. Crohn's Disease May Increase the Risk of GI Cancer

The risk of colorectal cancer is about three times higher in people with Crohn's disease

6. Non-judgmental Support is Important

Emotional support is vitally important to those battling Crohn's—listen to their feelings and be supportive

The main symptoms of Crohn's include abdominal pain, pain when passing stools, persistent diarrhea, fatigue, fever and weight loss—additional symptoms include joint pain and swelling, eye inflammation, mouth ulcers, constipation, rectal bleeding and other problems

The oral mucosa is commonly affected in Crohn's disease with up to one third of patients reported to have oral changes (the rate of oral lesions is higher in children)

KEY: Oral changes precede the diagnosis of Crohn's disease in the majority of cases

Nodular or diffuse soft swelling, a cobblestone appearance of the mucosa, mucosal tag lesions, ulcers, angular cheilitis, and aphthous-like ulcerations are often seen in cases of Crohn's disease

Lip swelling is one of the most common oral manifestations of the disease

Granulomatous cheilitis has been recognized as an early manifestation of Crohn's disease—it may follow, coincide with or precede the onset of Crohn's disease

KEY: Significant swelling of the lower lip due to granulomatous cheilitis could be the first manifestation of Crohn's disease, preceding intestinal symptoms!

Exacerbation of the lip lesion can be associated with a relapse of the underlying intestinal disease

Orofacial Signs of Malabsorption

- Folic acid deficiency (glossy, painful tongue and cheilitis)
- Iron deficiency
- Zinc deficiency (oral candidiasis, glossitis)
- Vitamin A deficiency (heightened keratinization of mucous membranes)

- Vitamin B complex deficiency (stomatitis, glossitis, angular cheilitis)
- Vitamin C deficiency (scurvy)
- Vitamin K deficiency (gingival bleeding)

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

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)

‘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 infections????

Unfortunately, Porphyromonas gingivalis is not the only autoimmunity trigger contender

Headliners: Women Smokers at Greater Risk for Rheumatoid Arthritis; Iowa Women’s health Study; research findings published in Annals of the Rheumatic Diseases; 8/06

Smoking nearly **DOUBLES** the odds of rheumatoid arthritis in women who do not have genetic risk factors (‘HLA-DRB1 SE’) for the disease

1990’s

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)

Other effects of systemic medications:

- Alteration of inflammatory response (corticosteroids)
- Increase bleeding tendencies (anticoagulants)
- **Xerostomia***

Whole saliva contains at least EIGHT different antimicrobial factors that are substantially diminished with xerostomia

They include:

- Lysozyme
- **Lactoferrin**
- Salivary peroxidases
- Myeloperoxidase
- Agglutinins and aggregating agents
- **Histidine**
- Proline-rich proteins
- IgA

Lactoferrin

Lactoferrin is a substance belonging to a family of chemicals called cytokines that are responsible for coordinating immune responses involved in preventing disease and infection

Lactoferrin has the unique ability to bind to iron—an essential mineral used not only by host cells but also a wide array of pathogens and tumors depend on iron for reproduction and growth

Presented with an infectious challenge or tumor, a healthy body will respond by producing lactoferrin in copious quantities in the vicinity of the infection or tumor where it binds systemic iron and renders it unavailable to the bacteria or malignant cells

Lactoferrin does not remove iron from the body itself and, over time, degrades to release the iron back into the body

Another attribute of lactoferrin involves its antimicrobial ability—special sections of lactoferrin molecules are themselves directly toxic to bacteria, yeast and molds

Lipopolysaccharide (LPS), a pathogen produced by periodontal bacteria, not only stimulates the progress of periodontal disease but also increases the level of cholesterol and triglycerides in the blood

Researchers have discovered that lactoferrin is one of the most promising ingredients for neutralizing these actions of LPS

It also appears that lactoferrin inhibits replication of some viruses—including HIV and some of the herpes family of viruses

In addition, lactoferrin has demonstrated positive control of *Candida albicans* —especially when combined with fluconazole in treating resistant candidiasis in HIV+ patients

Histatin

Histatins are a family of salivary proteins with bactericidal and fungicidal activities that contribute to the innate defense of the oral cavity

Histatins are present in the serous granules of the parotid and submandibular glands

Histatins are important for the initial stage of wound healing in which fast wound coverage is important for healing without infection, inflammation, or fibrosis development

Histatin's presence in acquired pellicle prevents adhesion by *Streptococcus mutans*

Histatins play a MAJOR role in inhibition of candidiasis

Challenges for the 2000's

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

Over 20% of adults are affected by clinical symptoms of viral infections and canker sores

An estimated 55 million Americans suffer from 'canker sores'

Most are women of higher SES

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

In recent years, a growing body of scientific evidence suggests an exquisite link between oral inflammation and the development of systemic disorders

Cardiovascular Disease

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

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

Stress

Stress is the way we react physically, mentally, and emotionally to various conditions, changes, and demands in our lives

Our minds react with concern, worry, or fear

Our bodies react by secreting stress chemicals and hormones

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 such as **cortisol**

Glucocorticoids inhibit the release of certain cytokines such as interferons and interleukins

Headliners: Stressful Times Have People Grinding Their Teeth; As reported by Camille Sweeney; New York Times News Service; appearing in the Idaho Statesman; 10/12/09

‘We’re finding in a lot of double-income families, we have the people who have lost jobs and are worried, and then we have the spouse, who still has the job, with the added pressure and uncertainty. This can cause some real grinding at night.’--Dr. Gerald McCracken; San Diego dentist

Some grinders will brux up to 40 minutes of every hour during sleep—which can quickly erode enamel, fracture teeth, affect bite, damage the temporomandibular joint, and cause pain in the jaw, face, and ears

With or without economic hardship, 10% to 15% of adult Americans moderately to severely grind their teeth—and, along with genetics, stress has been recognized as a source for nocturnal bruxing--Source: Dr. Matthew Messina; dentist; consumer adviser for the American Dental Association

KEY: Because the body reacts to stress with a spurt of energy that enables a person to run or fight, people who are under stress burn that excess energy off somewhere—some do it at night by clenching or grinding their teeth--Source: Messina

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

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 linked 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

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!

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 10% 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

Headliners: U.S. Antidepressant Use Jumps 65% in 15 Years; Laura Pratt; lead investigator; CDC's National Center for Health Statistics (NCHS); results released 15 AUG 2017; as reported by HealthDay News; 15 AUG 2017; accessed on 23 OCT 2017 at: <http://klinikkok.com/uncategorized/u-s-antidepressant-use-jumps-65-percent-in-15-years/>

According to the CDC, the number of Americans who say they have taken an antidepressant over the past month rose by 65% between 1999 and 2014.

The 2017 report is based on replies by more than 14,000 Americans—aged 12 and older—to a federal government health survey conducted between 2011 and 2014 (results were compared to those from prior surveys stretching back to 1999).

By 2014, about one in every eight Americans over the age of 12 reported recent antidepressant use. Women are nearly TWICE as likely as men to be taking the medications—with antidepressants used by 16.5% of females compared to just under 9% of males.

"Despite our society being progressive, there are still ongoing gender stigma related to seeking treatment for depression. It is more 'OK' for a woman to be depressed and seek out treatment for this, whereas men are supposed to be tough, suck it up and move on. One other possible confounder is that males, in my experience, are more upset by the sexual side effects associated with antidepressants—such as erectile dysfunction and delayed ejaculation—and could make them more reluctant to take these medications."--Source: Dr. Seth Mandel; director of psychiatry; Northwell Health's Huntington Hospital (Huntington, NY)

The researchers noted that 'one-fourth of all people [surveyed] who took antidepressants over the past month reported having taken them for 10 years or more'

'People have become increasingly stressed and depressed in our society. Social media continues to paradoxically cause people to be more isolated and out of touch with their feelings. In addition, direct-to-consumer advertising, coupled with an evolving societal mindset to just take a pill to make things better, both contributed to the growth in antidepressant use over this time period.'--Source: Dr. Seth Mandel; director of psychiatry; Northwell Health's Huntington Hospital (Huntington, NY)

Patients treated with antidepressant drugs often experience 'dry mouth'

- It was postulated that these drugs may cause salivary gland hypofunction or may alter the threshold for the perception of dry mouth—or they may do both
- Older patients appeared to be more at risk of a drug-induced dry mouth due to greater salivary gland hypofunction

Source: Daly, Christopher: Oral and Dental Effects of Antidepressants. Australian Prescriber 39.3 (2016); accessed on 13 NOV 2017 at:
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4919175/>

Direct Effects of Glucocorticoids on Bone = Increased bone resorption + Decreased bone formation

Diabetes

'Diabetes may well become the defining issue of global health for the next decade. We are not at the peak of this wave yet and, unlike high blood pressure and cholesterol, we still don't have great treatments for diabetes.'--Majid Ezzati, MEng, PhD; Chair of Global Environmental Health; Imperial College (London)

Headliners: Three-year-old Among Youngest Ever to be Diagnosed with Type 2 Diabetes; As reported by Allison Vuchnich; Senior Network Correspondent; Global News; posted 18 SEP 2015; accessed 4 APR 2016 at: <http://globalnews.ca/news/2228110/three-year-old-among-youngest-ever-to-be-diagnosed-with-type-2-diabetes/>

At only three years old, an American toddler was one of the youngest patients ever to be diagnosed with Type 2 diabetes—Type 2 diabetes is associated with obesity, poor diet and lack of exercise

'This is a global problem. Type 2 diabetes is no longer limited to adults. Now when I see any obese child I screen the patient for Type 2 diabetes.'--Dr. Michael Yafi; treating physician; in a comment to Reuters

KEY: Of the two types of diabetes, Type 2 diabetes displays the closest medical link between chronic inflammation and diabetes

Evidence has consistently indicated that diabetes is a risk factor for increased severity of gingivitis and periodontitis—and, conversely, periodontitis may be a risk factor for worsening glycemic control among patients with diabetes and may increase the risk of diabetic complications

Periodontal diseases involve activation of the broad axis of innate immunity through upregulation of proinflammatory cytokines from monocytes and neutrophils—including interleukin (IL)-1 β , IL-6, IL-8, tumor necrosis factor alpha (TNF- α) and prostaglandin E2***

These 'locally' produced cytokines move into the systemic circulation, where they may perpetuate an elevated inflammatory state—worsening the patient's diabetes through increasing insulin resistance and glucose levels

The inflammatory mediators originating from periodontal sources can interact systemically with lipids, free fatty acids and advanced glycation end products (AGEs)—all of which are characteristic of diabetes. This interaction induces or perpetuates activation of the intracellular pathways which are associated with insulin resistance—specifically, the activation of inflammatory pathways in immune cells (monocytes or macrophages), endothelium cells, adipocytes, hepatocytes and muscle cells promotes and contributes to an increase in overall insulin resistance

Insulin resistance makes it difficult to achieve metabolic control in patients with both type 2 diabetes and periodontitis

Headliners: Inflammation Markers May Be More Accurate Than Weight at Predicting Type 2 Diabetes Posted 29 Aug 2013 on Diabetes.co.uk; accessed on 4 Apr 2016 at:

<http://www.diabetes.co.uk/news/2013/Aug/inflammation-markers-may-be-more-accurate-than-weight-at-predicting-type-2-diabetes-93240187.html>

Researchers from University College Cork evaluated data on 2,047 people who took part in the Cork and Kerry Diabetes and Heart Disease Study—specifically, the study reviewed data on a number of inflammatory markers including C-reactive protein, TNF- α , interleukin 6, plasminogen activator inhibitor-1, adiponectin levels and white blood cell counts

Their findings: Participants with higher white blood cell counts and levels of acute-phase response proteins were more likely to have metabolic disorders such as insulin resistance and evidence of heart disease than participants that were obese and non-obese

Additionally, those participants that were obese and healthy demonstrated healthy levels of inflammation markers

Headliners: Inflammatory Markers and Risk of Type 2 Diabetes: A systematic review and meta-analysis; Xia Wang, MD, PHD et al; received April 12, 2012; accepted July 26, 2012; posted on Diabetes Care (American Diabetes Association); accessed on 4 Apr 2016 at:

<http://care.diabetesjournals.org/content/36/1/166.full>

This meta-analysis provided further evidence that elevated levels of IL-6 and CRP are significantly associated with increased risk of type 2 diabetes

Headliners: Oral Mucosal Lesions in Non-Oral Habit Diabetic Patients and Association of Diabetes Mellitus with Oral Precancerous Lesions; Source: Rajan Sainia, lead study author; study results appearing in Diabetes Research and Clinical Practice; 89(3): p.320-326. September 2010

Researchers found a significantly greater proportion of subjects with diabetes (45%) had one or more oral mucosal lesions ('OML') in comparison to non-diabetics (38.3%)

Diabetic patients demonstrated a significantly greater prevalence of geographic tongue, denture stomatitis and angular cheilitis than non-diabetics ($p < 0.05$)

The results also showed an association between occurrence of one or more OML and metabolic control of diabetic patients ($p < 0.05$)

Treating type 1 diabetes and some cases of type 2 diabetes has long required painful and frequent insulin injections or a mechanical insulin pump for insulin infusion

But researchers from the University of North Carolina and NC State have now developed what could be a much more patient-friendly option: artificial cells that automatically release insulin into the bloodstream when glucose levels rise

Researchers reported a single injection of the artificial beta cells ('A β Cs') into diabetic mice lacking beta cells quickly normalized the animals' blood glucose levels and kept those levels normal for up to five days

'Our plan now is to further optimize and test these synthetic cells in larger animals, develop a skin patch delivery system for them, and ultimately test them in people with diabetes.'--Source: Zhen Gu, PhD; lead investigator; professor; Joint UNC/NC State Department of Biomedical Engineering; study results accessed on 11/13/2017 at: <https://www.sciencedaily.com/releases/2017/10/171030131454.htm>

At least six million people in the United States use insulin as a diabetes treatment (either by injection or a mechanical pump)—delivery of insulin orally has been challenging due to the proteinaceous nature of the molecule (it is destroyed by digestive enzymes and acids before it reaches the bloodstream when administered in pill form)

Oral Inflammation and Cancer

Inflammation caused by specific oral pathogens has led to some breakthrough findings in the war on cancer

HPV is a virus from the papillomavirus family that affects human skin and mucous membranes (including the throat and oral cavity)

There are many, many types of HPV—some types can cause verrucae (warts) and a few strains have been shown to increase the risk of certain cancers (cervix, penis, vagina, anus and oropharyngeal area***)

The HPV 16 and 18 strains—which are known to cause nearly all cases of cervical cancer—raise the risk of developing oropharyngeal (throat) cancer

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 demonstrated that the periodontitis and HPV-infection appear to work in tandem to boost the chances of developing tongue cancer the following year

‘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

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)

The death rate associated with oral cancer is particularly high not because it is hard to discover or diagnose, but due to the cancer being routinely discovered late in its development

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

Manual palpation in combination with intraoral camera use is the ticket!

Often it is only discovered when the cancer has metastasized to another location—most likely the lymph nodes of the neck

Oral cancer is particularly dangerous because in its early stages it may not be noticed by the patient, as it can frequently prosper without producing pain or symptoms they might readily recognize

There are several types of oral cancers, but around 90% are squamous cell carcinomas

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

High-risk HPV strains cause cancer by using special proteins to disrupt healthy cells—it makes cells unable to repair themselves and unable to control how they are duplicated

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

The human papilloma virus, particularly version 16, has been shown to be sexually transmitted between partners—and is conclusively implicated in the increasing incidence of young non-smoking oral cancer patients

Based on peer reviewed published data, in people under the age of 50, HPV may even be replacing tobacco as the primary causative agent in the initiation of the disease process

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

From a gender perspective, for decades this has been a cancer which affected 6 men for every woman—that ratio has now become 2 men to each woman

Porphyromonas Gingivalis

As a non-motile, Gram-negative, rod-shaped, anaerobic organism, *P. gingivalis* has surface fimbriae which allow the bacteria to adhere ('stick') to epithelial AND tooth surfaces making it a very important pathogen for periodontal diseases

The main feature of periodontal diseases is inflammation of oral tissues in response to Gram negative pathogenic bacteria such as *Porphyromonas gingivalis*—an increase in secretion of gingival crevicular fluid ('GCF') accompanies the inflammatory response

The rise in GCF raises the local pH which allows periopathic bacteria such as *P. gingivalis* to overgrow and crowd out other microbes

P. gingivalis, as a hemin-dependent bacteria, enjoys the hemin that is abundantly found in GCF—the increased production of GCF accompanying inflammation of periodontal tissues provides a competitive advantage to the so-called 'red-complex' bacteria (of which *P. gingivalis* is a member) over commensals

A recent investigation demonstrated that *Porphyromonas gingivalis* was present in 61% of study participants with esophageal squamous cell carcinoma (ESCC)--Source: Gao S et al: Presence of *Porphyromonas gingivalis* in esophagus and its association with the clinicopathological characteristics and survival in patients with esophageal cancer; *Infect Agent Cancer* (2016); 11: 3. Published online 2016 Jan 19; accessed on 3/14/16 at: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4717526/>

The researchers also found the presence of *P. gingivalis* correlated with other factors—including cancer cell differentiation, metastasis and overall survival rate

There are two likely explanations: either ESCC cells are a preferred niche for *P. gingivalis* to thrive or the infection of *P. gingivalis* facilitates the development of esophageal cancer

'These findings provide the first direct evidence that *P. gingivalis* infection could be a novel risk factor for ESCC and may also serve as a prognostic biomarker for this type of cancer. These data, if confirmed, indicate that eradication of a common oral pathogen may contribute to a reduction in the significant number of people suffering with ESCC. It would suggest that improving oral hygiene may reduce ESCC risk; screening for *P. gingivalis* in dental plaque may identify susceptible subjects; and using antibiotics or other anti-bacterial strategies may prevent ESCC progression.'--Source: Huizhi Wang; University of Louisville; School of Dentistry

Research has documented that the higher the levels of C-reactive Protein ('CRP'), the poorer the prognosis for a variety of malignancies (multiple myeloma, melanoma, lymphoma, sarcoma as well as cancer of the ovaries, kidney, pancreas and gastrointestinal system)

Oral Health and Nutrition

Position Paper of the Academy of Nutrition and Dietetics: eatrightPRO; Volume 113 (5); p. 693-701; 5/2013; accessed on 8/15/2017 at: <http://www.eatrightpro.org/resource/practice/position-and-practice-papers/position-papers/oral-health-and-nutrition>

The organization urges you to visit **eatright.org** for more information on healthful eating or to find a registered dietitian nutritionist

It is the position of the Academy of Nutrition and Dietetics that nutrition is an integral component of oral health—the Academy supports integration of oral health with nutrition services, education and research

The provision of medical nutrition therapy—including oral and overall health—is incorporated into the Standards of Practice for registered dietitians and dietetic technicians

‘Inclusion of didactic and clinical practice concepts that illustrate the role of nutrition in oral health is essential in education programs for both professional groups’

Oral health and nutrition have a multifaceted relationship—oral infectious diseases as well as acute, chronic and systemic diseases with oral manifestations impact an individual's functional ability to eat and their nutrition status

Likewise, nutrition and diet can affect the development and integrity of the oral cavity and progression of oral diseases

As knowledge of the link between oral and nutrition health increases, dietetics practitioners and oral health care professionals must learn to provide screening, education and referrals as part of comprehensive client/patient care

‘Collaborative endeavors between dietetics, dentistry, medicine and allied health professionals in research, education and delineation of practice roles are needed to ensure comprehensive health care. The multifaceted interactions between diet, nutrition and oral health in practice, education and research in both dietetics and dentistry merit continued, detailed delineation.’--Position statement of the Academy of Nutrition and Dietetics

In order to maintain the integrity of the periodontal ligament, collagen synthesis and degradation must be equal

Unlike bone where formation is dependent on one type of cell (‘osteoblast’) and breakdown is achieved by another (‘osteoclast’), the remodeling of collagen is the sole responsibility of the fibroblast

KEY: Because of the exceptionally high rate of collagen turnover in the periodontal ligament, any interference in fibroblast function rapidly produces a loss of tooth support

Collagen in Review:

- Collagen is the most common protein in the human and is found in all connective tissue and hard structures such as bone, teeth and cartilage
- It has a triple-helix formation which gives it stability—the formation of the helical structure of collagen is dependent on vitamin C
- Prolyl hydroxylase is an enzyme which is required to form hydroxyproline which stabilizes the collagen's triple-helix structure by forming interstrand hydrogen bonds
- In order to function properly, this enzyme requires **vitamin C**

Unlike most other animals, humans (as well as guinea pigs) cannot synthesize L-ascorbic acid (vitamin C) and require dietary supplies of this nutrient in order to maintain healthy collagen and happy fibroblasts. The clinical manifestations of vitamin C deficiency are primarily due to abnormal collagen synthesis—collagen lacking hydroxyproline is more fragile and contributes to the clinical manifestations of this nutritional insufficiency

Oral Manifestations of Scurvy

- Gingival swelling with purplish, spongy edema
- Gingival bleeding
- Friable tissue
- Infections common

Typically, scurvy carries an excellent prognosis if diagnosed and treated appropriately—a supplement of 250 mg ascorbic acid by mouth four times daily in addition to a diet rich in FRESH fruit and vegetables generally relieves symptoms within two weeks

Patients at Risk for Vitamin C Deficiency:

- Infants fed only cow's milk during first year of life
- Adults 55+ years of age (especially males; 'tea-and-toast diets')
- Cigarette smokers
- Pregnant and lactating women
- Thyrotoxicosis (excess thyroid hormone)
- Anorexia
- Type 1 diabetes
- Diseases of the small intestine (Crohn, Whipple, celiac disease; also gastric bypass) NOTE: Vitamin C is absorbed in the small intestine
- Boiling fruit products
- Low SES
- Chronic inflammation

Headliners: Images Probe Artery-Hardening Plaques; Hutcheson JD et al; Nature Materials (2016); as reported by Tina Hesman Saey; Science News Magazine; 189 (4); 20 Feb 2016; accessed 5 Sep 2016 at: <https://www.sciencenews.org/article/images-probe-artery-hardening-plaques>

Collagen apparently also protects against loose bits of atherosclerotic plaque that can lead to cardiovascular events

Endothelial cells lining blood vessels secrete tiny spheres ('extracellular vesicles') filled with calcium and phosphate which fuse into calcified plaques under a protective collagen coating

The plaque poses little risk if the collagen layer is not disturbed

But when macrophages invade the area, they secrete chemicals that break down collagen and 'poke holes in the safety net'

As a result, the vesicles clump into smaller, less stable plaques that are more prone to 'breaking away' Researchers from Harvard Medical School were able to capture images of human arteries hardened by atherosclerotic plaque—the images illustrate the importance of collagen within the plaque

In the study, researchers found different arrangements of plaque deposited along arterial walls—stable plaques demonstrated an outer layer of collagen which protected the plaque; smaller clumps of collagen-covered plaques were more vulnerable to breaking away

MICROBIAL CHALLENGES

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

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 do we attack a plaque biofilm??????

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

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

Cementum

Less is known about cementum than any other supportive tissue

We do know that without root cementum, fiber attachment cannot occur

Bone

Boning Up on 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

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

THANK YOU!!!