

# Bibliography and Online Oral-Systemic References

*Compiled by: G. Lee Ostler DDS*



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## General Interest - Misc

1. **How your dentist can save your life: The dentist may be the most important doctor you see this year.** [The immune system fights gum infections to keep oral bacteria from spreading to other parts of the body. It usually succeeds, but not always. Gum-disease bacteria can enter the bloodstream and move to the heart, creating life-threatening infections in previously damaged heart valves. What's more, scientists believe the resulting inflammation releases infection-fighting compounds that can inadvertently damage other tissues.] December 2005 – Readers Digest. <http://www.rd.com/content/openContent.do?contentId=19084>
2. **ADA/Colgate Begin “Oral Systemic Education Campaign”.** [Many in the oral health community have long recognized the relationship of oral health to general health. There are a number of articles that have recently been published in the scientific literature that add to the existing body of peer-reviewed published information on the association of periodontal disease and systemic conditions including heart disease, stroke, diabetes and the birth of pre-term and low birth-weight babies. To help spread the word among dental and medical professionals and the public, the ADA and Colgate are developing a new campaign that demonstrates why the mouth is an integral part of the body.] January 2006.  
<http://www.ada.org/prof/resources/pubs/adanews/adanewsarticle.asp?articleid=1611>
3. **January 2006- CIGNA begins “Dental Oral Health Maternity Program”.** [CIGNA Dental has followed the research that shows women with periodontal (gum) disease may be at increased risk for pre-term babies. That's why we are launching our new CIGNA Dental Oral Health Maternity Program, which enhances benefits for pregnant members with CIGNA medical and fully-insured dental coverage.]  
[http://www.cigna.com/health/consumer/dental/oral\\_health\\_maternity\\_program.html](http://www.cigna.com/health/consumer/dental/oral_health_maternity_program.html)
4. **ADA, AMA collaborate on oral and systemic health. February 2006- First Joint ADA-AMA Conference.** [Oral health conditions and other health conditions are more closely related than many may once have thought, and viewing them as separate matters no longer makes sense. “This kind of research is life and death,” said Dr. Louis F. Rose, a periodontist and physician. “We can't overstate it, but we must inform the public.”]  
<http://www.ada.org/prof/resources/pubs/adanews/adanewsarticle.asp?articleid=1815>
5. **March 2006- Consumer Articles increase- Save Your Smile and Health.** [Teeming with bacteria from rotting food, it's a gateway to infection, inflammation and systemic disease. It's your mouth. Ignore it at your own risk. That risk may be greater than you realize. Skipping basic oral hygiene and dental checkups not only can lead to a dingy smile but to serious health problems. Over the past few years, researchers have been focusing on the connections between periodontal disease and cardiovascular disease, stroke, diabetes and problems in pregnancy. Diabetes and periodontal disease appear to be a two-way street, with each disorder exacerbating the other. Studies have shown that treating gum disease can make diabetes easier to manage. Chronic gum disease in pregnant women is also linked to preeclampsia, a serious disorder characterized by high blood pressure, as well as to low-birth-weight babies.] Mary Beth Faller, The Arizona Republic Mar. 21, 2006.  
<http://www.azcentral.com/health/news/articles/0321dentalsins0321.html>
6. **Aetna And Columbia Announce Results From Study Showing Relationship Between Periodontal Treatment And A Reduction In The Overall Cost Of Care For Three Chronic Conditions.** [Periodontal care appears to have a positive effect on the cost of medical care, with earlier treatment resulting in lower medical costs for members with diabetes, coronary

artery disease (CAD), and stroke.] March 2006- Aetna-Columbia U. Research-  
[http://www.aetna.com/news/2006/pr\\_20060317.htm](http://www.aetna.com/news/2006/pr_20060317.htm)

7. **Mouth Body Connection.** [In July of 1998, the American Academy of Periodontology launched an effort to educate the public about new findings which support what dental professionals had long suspected: Infections in the mouth can play havoc elsewhere in the body. Periodontal bacteria can enter the blood stream and travel to major organs and begin new infections. Research is suggesting that this may: Contribute to the development of [heart disease](#), the nation's leading cause of death, Increase the risk of [stroke](#), Increase a woman's risk of having a [preterm, low birth weight baby](#), or Pose a serious threat to people whose health is compromised by [diabetes](#), [respiratory diseases](#), or [osteoporosis](#).] American Academy of Periodontology <http://www.perio.org/consumer/mbc.top2.htm>
8. **US Department of Health and Human Services: Oral Health in America: A Report of the Surgeon General – Executive Summary** [The terms oral health and general health should not be interpreted as separate entities. Oral health is integral to general health; this report provides important reminders that oral health means more than healthy teeth and that you cannot be healthy without oral health.] Rockville, MD: National Institute of Dental and Craniofacial Research, National Institutes of Health, 2000  
<http://www2.nidcr.nih.gov/sgr/execsumm.htm#message>

## **Periodontal Disease**

9. **Activation of protease-activated receptors by gingipains from *Porphyromonas gingivalis* leads to platelet aggregation: a new trait in microbial Pathogenicity.** [The bacterium *Porphyromonas gingivalis* is a major etiologic agent in the pathogenesis of adult periodontitis in humans. Cysteine proteinases produced by this pathogen, termed gingipains, are considered to be important virulence factors. To further expand knowledge of the interaction between gingipains and the clotting cascade, this study examined their effects on cellular components of the coagulation system. Results indicate the existence of a novel pathway of host cell activation by bacterial proteinases. This mechanism not only represents a new trait in bacterial pathogenicity, but may also explain an emerging link between periodontitis and cardiovascular disease.] Lourbakos A, Yuan, Y, et.al., HEMOSTASIS, THROMBOSIS, AND VASCULAR BIOLOGY, *Blood*, 15 June 2001, Vol. 97, No. 12, pp. 3790-3797.  
<http://www.bloodjournal.org/cgi/content/abstract/97/12/3790>
10. **The Concept of “Risk” and the Emerging Discipline of Periodontal Medicine.** [While the link between systemic disease and periodontitis was thought to be unidirectional, mounting evidence in the last decade suggests that the relationship may be bi-directional. Periodontitis triggers both local and systemic host inflammatory responses. A central hypothesis of periodontal medicine states that periodontal infection presents a chronic inflammatory burden at the systemic level. In addition to their products, whole bacterial pathogens can enter local host tissues where pocket epithelial integrity has been lost. Perio pathogens have evolved virulence factors that allow for direct tissue invasion. Systemic exposures to gram-negative pathogens, LPS and other products can trigger mediator expression and inflammatory events with consequences related to other organ systems. PGE2 causes oxidative stress, smooth muscle contraction and LDL oxidation. Cytokines IL-1b, TNF $\alpha$  and interleukin 6 (IL-6) can stimulate endothelial adhesion, hyperlipemia, metabolic wasting, hepatic release of acute phase reactants and connective tissue catabolism. Many of these events have been implicated in the natural histories of systemic conditions like cardiovascular disease and preterm low-birth

weight.] Paquette DW, Madianos P., *The Journal of Contemporary Dental Practice*, Vol. 1 No. 1, Fall 1999. <http://www.thejcdp.com/issue001/paquette/paquette.pdf>

11. **Causes of Periodontal Disease.** [The main cause of periodontal disease is bacterial plaque, a sticky, colorless film that constantly forms on your teeth. Other causes include: Smoking, genetics, pregnancy, nutrition, stress, medications, clenching/grinding teeth, and diabetes.] <http://www.perio.org/consumer/2a.html>
12. **Cementum and Periodontal Wound Healing and Regeneration.** [For new cementum and attachment formation during periodontal regeneration, the local environment must be conducive for the recruitment and function of cementum-forming cells, and that the wound matrix is favorable for repair rather than regeneration.] <http://crobm.iadrjournals.org/cgi/content/abstract/13/6/474>
13. **Dental disease and risk of coronary heart disease and mortality.** [Among all 9760 subjects included in the analysis those with periodontitis had a 25% increased risk of coronary heart disease relative to those with minimal periodontal disease. Poor oral hygiene, determined by the extent of dental debris and calculus, was also associated with an increased incidence of coronary heart disease. In men younger than 50 years at baseline periodontal disease was a stronger risk factor for coronary heart disease; men with periodontitis had a relative risk of 1.72. Both periodontal disease and poor oral hygiene showed stronger associations with total mortality than with coronary heart disease. CONCLUSION--Dental disease is associated with an increased risk of coronary heart disease, particularly in young men.] DeStefano F, Anda RF et al, *Brit Med J* 306:688-691, 1993, [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=8471920&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8471920&dopt=Abstract)
14. **Early Carotid Atherosclerosis in Subjects with Periodontal Diseases.** [The present results indicate that periodontal disease is associated with the development of early atherosclerotic carotid lesions.] Söder P, Söder B, *Stroke*. 2005;36:1195. <http://stroke.ahajournals.org/cgi/content/full/36/6/1195>
15. **Effect of treating periodontitis on C-reactive protein levels.** [Periodontitis seems to increase C-reactive protein only in some individuals, presumably the ones reacting to it with a systemic inflammatory reaction. Periodontal treatment decreases C-reactive protein levels in these individuals and it may thus decrease their risk of coronary heart disease.] Mattila K, Vesanen M, *BMC Infect Dis*. 2002 Dec 10;2:30. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=12475397&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12475397&dopt=Abstract)
16. **Elevation of Systemic Markers Related to Cardiovascular Diseases in the Peripheral Blood of Periodontitis Patients.** [Periodontitis is a common, often undiagnosed, chronic infection of the supporting tissues of the teeth, epidemiologically associated with cardiovascular diseases. Since C-reactive protein (CRP) and other systemic markers of inflammation have been identified as risk factors for cardiovascular diseases, we investigated whether these factors were elevated in periodontitis. Periodontitis results in higher systemic levels of CRP, IL-6, and neutrophils. These elevated inflammatory factors may increase inflammatory activity in atherosclerotic lesions, potentially increasing the risk for cardiac or cerebrovascular events.] *J Periodontology* 2000 Oct; 71(10):1528-34. <http://www.joponline.org/doi/abs/10.1902/jop.2000.71.10.1528>
17. **Molecular Pathogenicity of the Oral Opportunistic Pathogen *Actinobacillus Actinomycetemcomitans*.** [Periodontitis is mankind's most common chronic inflammatory disease. The main causative organism of this disease is *Actinobacillus actinomycetemcomitans*.

This organism also produces a plethora of proteins able to inhibit eukaryotic cell cycle progression and proteins and peptides that can induce distinct forms of proinflammatory cytokine networks.] Henderson B, Nair SP, et. al., *Annual Review of Microbiology* Vol. 57: 29-55 <http://arjournals.annualreviews.org/doi/abs/10.1146/annurev.micro.57.030502.090908>

18. **Periodontal Disease: An Overview for Physicians.** [Periodontitis is now seen as resulting from a complex interplay of bacterial infection and host response, often modified by behavioral factors. Susceptibility to periodontitis increases with age, and all individuals are susceptible to severe periodontal disease.] Fenesy KE, Dept of Oral Pathology, Biology and Diagnostic Sciences, New Jersey Dental School, Univ. of Medicine and Dentistry of New Jersey, Newark, NJ. [http://www.mssm.edu/msjournal/65/08\\_fenesy.pdf](http://www.mssm.edu/msjournal/65/08_fenesy.pdf)
19. **Periodontal Disease and Risk of Cerebrovascular Disease.** [Periodontal disease is an important risk factor for total CVA and, in particular, nonhemorrhagic stroke.] Wu T et al, *Arch Intern Med.* 2000; 160:2749-2755. <http://archinte.ama-assn.org/cgi/content/abstract/160/18/2749>
20. **Periodontal disease and systemic health--what you and your patients need to know.** [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=12005375&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12005375&dopt=Abstract)
21. **Periodontal Infections Contribute to Elevated Systemic C-Reactive Protein Level.** [Periodontitis is a local inflammatory process mediating destruction of periodontal tissues triggered by bacterial insult. However, this disease is also characterized by systemic inflammatory host responses that may contribute, in part, to the recently reported higher risk for cardiovascular disease (CVD) among patients with periodontitis. Moderate elevation of C-reactive protein (CRP) has been found to be a predictor of increased risk for CVD. Elevated CRP levels in periodontal patients have been reported by several groups. In this study, we examined whether CRP plasma levels are increased in periodontitis and if there is a relation to severity of periodontal disease and to the periodontal microflora. there are elevated levels of CRP associated with infection with subgingival organisms often associated with periodontal disease, including *P.g.*, *P.i.*, *C.r.*, and *B.f.* Recent investigations emphasized the role of moderate elevated CRP plasma levels as a risk factor for CVD. The positive correlation between CRP and periodontal disease might be a possible underlying pathway in the association between periodontal disease and the observed higher risk for CVD in these patients.] Noack et al, *J Periodontol.* 2001 Sep;72(9):1221-7. <http://www.joponline.org/doi/abs/10.1902/jop.2000.72.9.1221?cookieSet=1&journalCode=jop>
22. **Periodontal Therapy Lowers Levels of Heart Disease Inflammation Markers.** [Treating periodontal disease with scaling and root planing combined with a topical antibiotic gel can significantly lower the levels of two inflammatory proteins associated with a heightened risk of heart disease. People who have high levels of CRP in their blood are at high risk of heart disease. Results showed that in people who had elevated levels of CRP at baseline, removal of dental plaque bacteria by scaling or scaling combined with topical antibiotics produced a statistically significant reduction, bringing CRP levels close to the low-risk level.] Grossi, S, et al. SUNY Buffalo, *ADA News* 04/21/2004. <http://www.ada.org/prof/resources/pubs/adanews/adanewsarticle.asp?articleid=841>
23. **Periodontitis and Systemic Inflammation: Control of the Local Infection is Associated with a Reduction in Serum Inflammatory Markers.** [Severe periodontitis is associated with elevated inflammatory markers in otherwise healthy populations. periodontitis seems to contribute to systemic inflammation. The potential significance of the reported findings relates to the magnitude of the observed decreases in CRP, the high prevalence of periodontitis in the

population, and the fact that periodontitis can be treated.] D' Aiuto F., Parkar M, et al.  
<http://jdr.iadrjournals.org/cgi/content/full/83/2/156>

24. **Purification and characterization of a potent 70-kDa thiol lysyl- proteinase (Lys-gingivain)** from *Porphyromonas gingivalis* that cleaves kininogens and fibrinogen. { These data suggest that lys-gingivain is a very potent proteinase that would be fully functional in anaerobic periodontal crevices and might participate in the pathogenesis of periodontitis.}  
<http://www.jbc.org/cgi/content/abstract/268/11/7935>
25. **Relationship Between Periodontal Disease and C-Reactive Protein Among Adults in the Atherosclerosis Risk in Communities Study.** [Extensive periodontal disease and BMI are jointly associated with increased CRP levels in otherwise healthy, middle-aged adults, suggesting the need for medical and dental diagnoses when evaluating sources of acute-phase response in some patients. ] <http://archinte.ama-assn.org/cgi/content/abstract/163/10/1172>
26. **Relationship Between Periodontal Disease, Tooth Loss, and Carotid Artery Plaque.** [Chronic infections, including periodontal infections, may predispose to cardiovascular disease. Data suggest that tooth loss is a marker of past periodontal disease in this population and is related to subclinical atherosclerosis, thereby providing a potential pathway for a relationship with clinical events.] *Stroke*. 2003;34:2120.  
<http://stroke.ahajournals.org/cgi/content/abstract/34/9/2120?etoc%20>
27. **Short-term Effects of Intensive Periodontal Therapy on Serum Inflammatory Markers and Cholesterol.** [Analysis of these data indicates that periodontitis causes moderate systemic inflammation in systemically healthy subjects.] D' Aiuto F., Nibali, L, et al  
<http://jdr.iadrjournals.org/cgi/content/abstract/84/3/269>
28. **Soluble antagonists to interleukin-1 (IL-1) and tumor necrosis factor (TNF) inhibits loss of tissue attachment in experimental Periodontitis.** [The inflammatory response is effective in preventing large-scale colonization of the gingival tissues by bacteria that lie in close proximity to the tooth surface or within the gingival sulcus. It has been postulated that the host-response in some individuals may lead to an over-reaction to invading oral pathogens resulting in the destruction of periodontal tissues.] <http://www.blackwell-synergy.com/links/doi/10.1034/j.1600-051x.2001.028003233.x/abs/>
29. **Spokesman for the American Heart Association confirms the link between Perio and Heart Disease –** *Healthday News*, November 29 2005- ["People who have chronic infections -- and gum disease is one of the major chronic infections -- are at increased risk later in life for atherosclerosis (hardening of the arteries) and coronary heart disease," said American Heart Association spokesman Dr. Richard Stein]  
[http://health.yahoo.com/news/141399;\\_ylt=Ahq5pJAqH2GCLGes3r4j7NX3tMUF](http://health.yahoo.com/news/141399;_ylt=Ahq5pJAqH2GCLGes3r4j7NX3tMUF)
30. **The antimicrobial treatment of periodontal disease: changing the treatment paradigm.** [This review highlights some of the evidence for the specific plaque hypothesis, and the questions that should be addressed if antimicrobial agents are to be used responsively and effectively.] *Critical Reviews in Oral Biology & Medicine*, Vol 10, 245-275.  
<http://crobm.iadrjournals.org/cgi/content/abstract/10/3/245>
31. **The antimicrobial treatment of periodontal disease: changing the treatment paradigm.** [The recent observations that periodontal infections increase the risk of specific systemic health problems, such as cardiovascular disease, argue for the prevention and elimination of these periodontal infections. W.J. Loesche, *Critical Reviews in Oral Biology & Medicine*, Vol 10, 245-275. <http://crobm.iadrjournals.org/cgi/content/abstract/10/3/245>

32. **The oral-medical connection - Exploring our role as health care providers.** [Periodontal disease is a chronic infectious disease that has been postulated to affect other chronic conditions through various pathways, including the generation of inflammatory mediators, by direct effect of bacterial colonization, or as a result of toxins produced by periodontal pathogens. Thousands of articles have discussed periodontal disease and its association with heart disease, stroke, pneumonia, preterm births, low-birth weight babies, osteopenia, osteoporosis and diabetes mellitus.] Michael Glick, Editor, *J Am Dent Assoc*, Vol 136, No 6, 716-718.  
<http://jada.highwire.org/cgi/content/full/136/6/716>
33. **Transmission of *Porphyromonas gingivalis* between spouses.** [*P. gingivalis* can be transmitted between spouses.] <http://www.blackwell-synergy.com/doi/abs/10.1111/j.1600-051X.1993.tb00370.x>

## **Alzheimer's**

34. **Association of antioxidants with memory in a multiethnic elderly sample using the Third National Health and Nutrition Examination Survey.** [Oxidative stress has been implicated both in the aging process and in the pathological changes associated with Alzheimer's disease. Antioxidants, which have been shown to reduce oxidative stress in vitro, may represent a set of potentially modifiable protective factors for poor memory, which is a major component of the dementing disorders. The authors investigated the association between serum antioxidant (vitamins E, C, A, carotenoids, selenium) levels and poor memory performance in an elderly, multiethnic sample of the United States. The sample consisted of 4,809 non-Hispanic White, non-Hispanic Black, and Mexican-American elderly who visited the Mobile Examination Center during the Third National Health and Nutrition Examination Survey, a national cross-sectional survey conducted from 1988 to 1994. Memory is assessed using delayed recall (six points from a story and three words) with poor memory being defined as a combined score less than 4. Decreasing serum levels of vitamin E per unit of cholesterol were consistently associated with increasing levels of poor memory after adjustment for age, education, income, vascular risk factors, and other trace elements and minerals. Serum levels of vitamins A and C, beta-carotene, and selenium were not associated with poor memory performance in this study.] Perkins AJ, Hendrie HC, et al. *Am J Epidemiol*. 1999 Jul 1;150(1):37-44.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=10400551&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10400551&dopt=Abstract)
35. **Inflammatory Markers and Cognition in well-functioning African-American and White Elders.** [Serum markers of inflammation, especially IL-6 and CRP, are prospectively associated with cognitive decline in well-functioning elders. These findings support the hypothesis that inflammation contributes to cognitive decline in the elderly.] Yaffe, K, Lindquist K, et al. *Neurology* 2003;61:76-80.  
<http://www.neurology.org/cgi/content/abstract/61/1/76>
36. **Inflammation Linked to Cognitive Decline.** [Inflammation is increasingly being implicated as a major factor contributing to several age-related diseases, including Alzheimer's and dementia. Now, researchers at the San Francisco VA Medical Center (SFVAMC) have found a link between inflammation and early cognitive decline in otherwise healthy individuals.] *J Neurology* July 8, 2003 Yaffe, K, <http://www.ncire.org/yaffe6.html>

## Cancer

37. **C-reactive protein and the risk of incident colorectal cancer.** [Plasma CRP concentrations are elevated among persons who subsequently develop colon cancer. These data support the hypothesis that inflammation is a risk factor for the development of colon cancer in average-risk individuals.] Erlinger TP, Platz EA, et.al., *JAMA* vol.291 No.5, Feb 4,2004.  
<http://jama.ama-assn.org/cgi/content/abstract/291/5/585>
38. **C-reactive protein is significantly associated with prostate-specific antigen and metastatic disease in prostate cancer.** [The strong association of CRP with PSA, independent of tumor stage, suggests that inflammation might be fundamental in prostate cancer, and that chronic inflammation may be a legitimate target for prostate cancer chemoprevention and treatment.] Lehrer S, Diamond EJ, et.al. *BJU Int.* 2005 May;95(7):961-2.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=15839913&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15839913&dopt=Abstract)
39. **Inflammation Marker Predicts Colon Cancer.** [C-reactive protein, a marker of inflammation circulating in the blood already associated with increased risk of heart disease, can also be used to identify a person's risk of developing colon cancer, according to a Johns Hopkins study. People with higher levels of CRP in their blood were more likely to develop colorectal cancers than those with low levels of CRP. Higher levels of C-reactive protein are linked to an increased risk of several apparently distinct, chronic diseases: heart disease, stroke, diabetes, and now colon cancer. The odds of developing colorectal cancers increased progressively with higher concentrations of CRP.] Johns Hopkins Medicine Office of Communications and Public Affairs. Feb. 3, 2004 *JAMA*.  
[http://www.hopkinsmedicine.org/Press\\_releases/2004/02\\_10\\_04.html](http://www.hopkinsmedicine.org/Press_releases/2004/02_10_04.html)
40. **Oral Cancer & Periodontal Disease.** [UB study links gum disease with oral cancer risk. Oral tumors were four times more prevalent and pre-cancerous lesions were twice as prevalent in people with periodontal disease (as assessed by clinical attachment loss) than in those without periodontal disease. These findings suggest strongly that infection is associated with oral cancer. Research shows an association between H. pylori and stomach cancer, human papillomavirus and cervical cancer, and cytomegalovirus and Kaposi's sarcoma.] Tezal Mine, Grossi SG., [http://www.eurekalert.org/pub\\_releases/2003-03/uab-us1031303.php](http://www.eurekalert.org/pub_releases/2003-03/uab-us1031303.php)

## Cardiovascular Disease

41. **Angiographically Confirmed Coronary Heart Disease and Periodontal Disease in Middle-Aged Males.** [There was an association between coronary heart disease and poor periodontal status in the middle-aged males investigated. This association was independent of diabetes and all other cardiovascular risk factors investigated.] Briggs JE, McKeown PP, *J Periodontol* 2006.77.1.95.  
[http://www.joponline.org/doi/abs/10.1902/jop.2006.77.1.95?prevSearch=keywordsfield%3AC-reactive\\_protein](http://www.joponline.org/doi/abs/10.1902/jop.2006.77.1.95?prevSearch=keywordsfield%3AC-reactive_protein)
42. **Atherogenesis in perspective: Hypercholesterolemia and inflammation as partners in crime.** [A historical perspective on atherosclerosis allows us to reflect on the once controversial hypotheses in the field. Plaque formation was once thought to be dependent upon hypercholesterolemia alone, or solely in response to injury. More recently, inflammatory cascades were thought to be at the root of lesion development. A more realistic view may be that atherosclerosis is neither exclusively an inflammatory disease nor solely a lipid disorder: it is both.] Daniel Steinberg, *Nature Medicine* 8, 1211 - 1217 (2002),  
<http://www.nature.com/nm/journal/v8/n11/full/nm1102-1211.html>

43. **Association between dental health and acute myocardial infarction.** [Dental health was significantly worse in patients with acute myocardial infarction than in controls.] Mattila KJ, Nieminen MS, et.al., *Brit Med J* 189; 298:779-81.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=2496855&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2496855&dopt=Abstract)
44. **Association Between Nanobacteria and Periodontal disease.** [Because NB can be identified by using culture, monoclonal antibodies, and electron microscopy techniques, and because they were detected in both dental pulp stones and CA, NB should be considered a potential causative agent to be screened in related diseases. We propose that NB may provide a potential bridge between periodontal diseases and peripheral artery disease.] Çiftçiođlu N, McKay DS, *Circulation*. 2003;108:e58. <http://circ.ahajournals.org/cgi/content/full/108/8/e58>
45. **Atherosclerosis — An Inflammatory Disease.** [Atherosclerosis is an inflammatory disease. [Inflammation and infection are factors that induce or promote inflammation and arterogenesis.] Ross R, *NEJM Vol.340:115-126 Jan 14, 1999*,  
<http://content.nejm.org/cgi/content/short/340/2/115>
46. **Atherosclerosis: The New View.** [Scientists now agree that inflammation fuels the development and progression of atherosclerosis. The old view – that fat builds up on passive arterial walls- does not fit recent evidence. Inflammation can also cause certain plaques to rupture. Blood clots tend to form over ruptured plaques and can then occlude arteries, leading to such atherosclerotic complications as heart attack and stroke. Excess LDL can trigger arterial inflammation. The presence of CRP in the blood signifies that inflammation is present somewhere in the body.] Peter Libby MD, *Scientific American, May 2002, p50-59*.  
<http://www.ahs.uwaterloo.ca/~kh346/pdf/libby.pdf>
47. **Blood Pressure, C-Reactive Protein, and Risk of Future Cardiovascular Events.** [CRP and blood pressure are independent determinants of cardiovascular risk, and their predictive value is additive. CRP showed a linear relationship with blood pressure across all categories of blood pressure. Both CRP and blood pressure were independent determinants of cardiovascular risk, and in combination, each parameter had additional predictive value. data suggest that increasing levels of blood pressure may stimulate a proinflammatory response and that endothelial inflammation may also herald the changes in arterial wall that characterize the hypertensive state. Inflammatory processes are now recognized to play a fundamental role in atherogenesis. C-reactive protein (CRP) has been found to be a robust predictor of incident cardiovascular disease. In this regard, the American Heart Association and the Centers for Disease Control and Prevention have recently issued a class IIa recommendation for the measurement of CRP in primary prevention among those at intermediate risk.] Blake GJ, Rifai N. et. al., *Circulation*. 2003;108:2993. <http://circ.ahajournals.org/cgi/content/full/108/24/2993>
48. **C-Reactive Protein and the Risk of Developing Hypertension.** [C-reactive protein levels are associated with future development of hypertension, which suggests that hypertension is in part an inflammatory disorder.] Sesso HD, Buring JE, et. al., *JAMA*. 2003;290:2945-2951.  
<http://jama.ama-assn.org/cgi/content/abstract/290/22/2945>
49. **C-reactive protein is increased in patients with degenerative aortic valvular stenosis.** [The goal of this study was to assess the presence of systemic inflammation in degenerative aortic valvular stenosis. Local inflammatory changes, resembling those observed in atherosclerosis, have been recently reported in degenerative aortic valvular stenosis. It is presently unknown whether systemic signs of inflammation, similar to those observed in atherosclerosis, may be present in this disorder. C-reactive protein (CRP) was measured by enzyme immunoassay in 141 subjects: 62 with trileaflet degenerative valvular aortic stenosis and 79 volunteers with similar demographic and clinical characteristics. IgG antibodies against *Helicobacter pylori*

(enzyme-linked immunosorbant assay) and *Chlamydia pneumoniae* (microimmunofluorescence assay) were also measured. Systemic signs of inflammation, similar to those found in atherosclerosis, are present in patients with degenerative aortic valve stenosis. They do not seem to be linked to *C. pneumoniae* or *H. pylori* infection.] Galante A, Pietroiusti A, et.al. *J Am Coll Cardiol*, 2001; 38:1078-1082. <http://content.onlinejacc.org/cgi/content/abstract/38/4/1078>.

50. **C-Reactive Protein Stimulates MMP-1 Expression in U937 Histiocytes Through Fc $\gamma$ RII and Extracellular Signal-Regulated Kinase Pathway: An Implication of CRP Involvement in Plaque Destabilization.** [These findings suggest that CRP may promote matrix degradation and thus contribute to plaque vulnerability.] Williams TN, et.al., *Arteriosclerosis, Thrombosis, and Vascular Biology*. 2004;24:61. <http://atvb.ahajournals.org/cgi/content/abstract/24/1/61>
51. **Coagulation and Thrombosis in Cardiovascular Disease: Plausible Contributions of Infectious Agents.** [By initiating a procoagulant response, infectious agents can indirectly trigger a prothrombotic response. Alternatively, some microbes can directly trigger platelet aggregation in vitro and in animal models, suggesting direct prothrombotic potential in human cardiovascular disease. Activation of coagulation and thrombosis characterizes the pathological response to infectious agents in human disseminated intravascular coagulation and infective endocarditis. Given the underlying biological plausibility, the cumulative lifetime burden of chronic pathogens may be expected to create risk of atherosclerosis and thrombosis, and, indirectly, signs of cardiovascular disease.] Herzberg MC, *Annals of Periodontology*, 2001, Vol. 6, No. 1, Pages 16-19. <http://www.joponline.org/doi/abs/10.1902/annals.2001.6.1.16>
52. **Current Concepts of the Pathogenesis of the Acute Coronary Syndromes.** [These various findings all highlight the central role of inflammation as a determinant of the biology underlying the acute thrombotic complications of atherosclerosis. Inflammation has emerged as a leading pathophysiologic mechanism (for thrombosis and acute myocardial infarction). In addition to local effects of inflammation at the level of the atherosclerotic lesion itself, systemic aspects of the inflammatory response may alter thrombotic risk. Inflammation upsets the prevailing homeostatic balance. Increased fibrinogen and plasminogen activator inhibitor circulate at higher concentrations in inflammatory states. A given plaque disruption could have a greater chance to produce an occlusive thrombus under such conditions.] Libby P. *Circulation*. 2001;104:365. <http://circ.ahajournals.org/cgi/content/full/104/3/365>
53. **Deep periodontal pockets linked with ECG abnormalities.** [Patients with deep periodontal pockets have an increased risk for electrocardiographic abnormalities, suggesting a heightened risk of cardiovascular disease. Elevated levels of the inflammatory compounds C-reactive protein, interleukin-6 and neutrophils associated with periodontitis may cause inflammatory changes to atherosclerotic lesions, increasing the risk of cardiac events, the researchers concluded.] ADA News Release. <http://www.ada.org/prof/resources/pubs/adanews/adanewsarticle.asp?articleid=956>
54. **Dental disease, fibrinogen and white cell count; links with myocardial infarction?** [Inflammatory dental disease may be a determinant of fibrinogen level and white cell count in the general population, and that fibrinogen and white cell count may be two mediators of the link between dental disease and myocardial infarction.] Kweider M, Lowe GD, et. al, *Scott med J*. 1993 Jun;38(3):73-4. Department of Oral Surgery, Dental Hospital & School, Glasgow. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=8356427&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8356427&dopt=Abstract)
55. **Dental Disease, Coronary Heart Disease and Stroke, and Inflammatory Markers.** [In addition to "classical" risk factors for coronary heart disease (CHD) and stroke, "emerging" risk predictors (which may also play roles in pathogenesis) include measures of chronic infections

and of chronic, low-grade activation of inflammation and of hemostasis. As all dental healthcare professionals know (but probably fewer medical practitioners and their patients), the oral cavity is a major site of chronic infection and inflammation, particularly periodontal disease. In recent years there has been increasing interest in the "periodontal-systemic connection" between dental health parameters and the risks of cardiovascular disease, respiratory disease, diabetes mellitus, osteoporosis, and adverse pregnancy outcomes.] Lowe G, *Circulation* 2004;109:1076-1078. <http://circ.ahajournals.org/cgi/content/full/109/9/1076> .

56. **Detection of *Porphyromonas gingivalis* DNA in Aortic Tissue by PCR.** [These results might indicate a link between periodontopathogens entering the cardiovascular system and cardiovascular disease.] *Journal of Periodontology*, 2002, Vol. 73, No. 8, Pages 868-870. Stelzel M, Conrads G, et al. <http://www.joonline.org/doi/abs/10.1902/jop.2002.73.8.868>
57. **Early Carotid Atherosclerosis in Subjects With Periodontal Diseases.** [The present results indicate that periodontal disease is associated with the development of early atherosclerotic carotid lesions.] Soder P, Soder B. *Stroke*. 2005;36:1195. <http://stroke.ahajournals.org/cgi/content/full/36/6/1195>
58. **Effect of aortic valve replacement on c-reactive protein in nonrheumatic aortic stenosis.** [Plasma levels of C-reactive protein were higher in 20 patients with bicuspid or trileaflet degenerative aortic stenosis than in 31 normal controls and in 19 patients with pure aortic regurgitation. C-reactive protein decreased from before to 6 months after aortic valve replacement for aortic stenosis. These observations suggest that aortic stenosis is an inflammatory disease.] Gerber IL, Stewart RA, et.al. *Am J Cardiol*. 2003 Nov 1;92(9):1129-32. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=14583374&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14583374&dopt=Abstract).
59. **Evaluation of the Incidence of Periodontitis-Associated Bacteria in the Atherosclerotic Plaque of Coronary Blood Vessels.** Unstable atherosclerotic plaque is a dangerous clinical condition, possibly leading to acute coronary deficiency resulting in cardiac infarction. Questions about the role of inflammatory factors in the formation of pathological lesions in the endothelium of coronary vessels have often been raised. This condition may be caused by bacteria that are able to initiate clot formation in a blood vessel, destabilizing an atherosclerotic plaque that is already present. The sources of these pathogens are chronic inflammatory processes occurring in the host, including periodontal disease, which is one of the most frequent conditions. The aim of this study was to evaluate the incidence of selected anaerobic bacteria in subgingival and atherosclerotic plaque in patients treated surgically because of coronary vessel obliteration. ...In patients with the severe form of chronic periodontitis, it seems that clinical attachment loss is not associated with bacterial permeability into coronary vessels. What is important is the presence of an active inflammatory process expressed by a significantly higher bleeding index in those patients in whom the examined bacterial species were found in atherosclerotic plaque.] Zaremba M, Górska R, et.al. *Journal of Periodontology* 2007, Vol. 78, No. 2, Pages 322-327. <http://www.joonline.org/doi/abs/10.1902/jop.2006.060081>
60. **Heart disease and stroke.** [Researchers have found that people with periodontal disease are almost twice as likely to suffer from coronary artery disease as those without periodontal disease. Additional studies have pointed to a relationship between periodontal disease and stroke. In one study that looked at the causal relationship of oral infection as a risk factor for stroke, people diagnosed with acute cerebrovascular ischemia were found more likely to have an oral infection when compared to those in the control group.] <http://www.perio.org/consumer/mbc.heart.htm>

61. **Human atherosclerotic plaque contains viable invasive *actinobacillus actinomycetemcomitans* and *porphyromonas gingivalis*, Arteriosclerosis.** [Human atherosclerotic plaque contains viable invasive *actinobacillus actinomycetemcomitans* and *porphyromonas gingivalis*.] Kozarov et al. *Arteriosclerosis, Thrombosis, and Vascular Biology*. 2005;25:e17.  
<http://atvb.ahajournals.org/cgi/reprint/25/3/e17?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=1&author1=kozarov&andorexacttitle=and&andorexacttitleabs=and&andorexactfulltext=and&searchid=1&FIRSTINDEX=0&sortspec=relevance&volume=25&resourcetype=HWCIT>
62. **Identification of periodontal pathogens in atheromatous plaques.** [Periodontal pathogens are present in atherosclerotic plaques where, like other infectious microorganisms such as *C. pneumonia*, they may play a role in the development and progression of atherosclerosis leading to coronary vascular disease and other clinical sequela.]. Haraszthy V.I., Zambon J.J., et al. *J Periodontol*. 2000 Oct;71(10):1554-60  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed&cmd=Retrieve&list\\_uids=11063387&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed&cmd=Retrieve&list_uids=11063387&dopt=Abstract)
63. **Infections and their role in atherosclerotic vascular disease.** [Infectious agents may play a role in the pathogenesis of atherosclerosis by several mechanisms of action and at different stages. Microorganisms could infect vascular endothelial cells directly, initiating the inflammatory response needed for the initial process of inducing atherosclerosis. Furthermore, even if the induction or initial injury to the endothelium was caused by another inciting agent or factor (for example, hypercholesterolemia or hypertension), infectious agents could accelerate or enhance the process through several mechanisms of action. They include further recruitment and stimulation of proinflammatory cytokines and tissue growth factors in the arterial wall, as well as enhancement of lipid (low-density lipoprotein, or LDL) accumulation through stimulation of macrophage scavenger or LDL-receptors. Microbes could indirectly influence the development and progression of atherosclerosis by a systemic effect without directly invading the arterial endothelium. Release of endotoxin or lipopolysaccharide into the circulation could indirectly damage vascular endothelium or the immune response, and systemic cytokine release could result in lipid profile predisposing to atherosclerosis or could predispose the arterial environment to a procoagulant state, resulting in acute thrombus on a pre-existent unstable or critical plaque, thus causing an acute ischemic event. Infectious agents may play an important role in atherogenesis, but the jury is not in. Further studies are needed to prove causality of atherogenesis from *C. pneumoniae* and to establish an association between cardiovascular disease and periodontitis. There is, however, sufficient evidence from biological mechanisms and animal models to warrant interventional studies on periodontitis and development of cardiovascular events.] Fong IW, *J Am Dent Assoc*, Vol 133, No suppl\_1, 7S-13S.  
[http://jada.ada.org/cgi/content/full/133/suppl\\_1/7S](http://jada.ada.org/cgi/content/full/133/suppl_1/7S)
64. **Invasion of Aortic and Heart Endothelial Cells by *Porphyromonas gingivalis*.** [Invasion of host cells is believed to be an important strategy utilized by a number of pathogens, which affords them protection from the host immune system. The connective tissues of the periodontium are extremely well vascularized, which allows invading microorganisms, such as the periodontal pathogen *Porphyromonas gingivalis*, to readily enter the bloodstream. These results indicate that *P. gingivalis* can actively invade endothelial cells and that fimbriae are required for this process. *P. gingivalis* invasion of endothelial cells may represent another strategy utilized by this pathogen to thwart the host immune response.] <http://intl-iai.asm.org/cgi/content/abstract/66/11/5337>

65. **Live Oral Bacteria Found in Arterial Plaque.** [There are live periodontal bacteria in human atherosclerotic tissue.] March 22, 2005 Ann Progulsk-Fox, chief investigator, U of FL College of Dentistry. <http://www.napa.ufl.edu/2005news/plaque.htm>
66. **Microbiological Effects of Scaling and Root Planing.** [The endpoint of clinical therapy is the elimination of inflammation. To achieve this, open debridement may be required in addition to scaling and root planing, and treatment may be aided by chemotherapeutic agents. Scaling and root planing results in systemic effects (including bacteremia) and local effects which include decreases in the levels of calculus, pathogenic microorganisms and clinical inflammation. Additional therapy may be required to achieve clinical health.] Haake SK, Isaacs D. (Note: <http://www.dent.ucla.edu/pic/members/microscaling/>)
67. **New research finds link between gum disease, acute heart attacks.** [Heart attack survivors who suffer advanced gum disease show significantly higher levels of C-reactive protein in their blood than patients without gum disease, new University of North Carolina at Chapel Hill research indicates.] UNC News Services, <http://www.unc.edu/news/archives/nov00/deliar111300.htm> ; <http://www.sciencedaily.com/releases/2000/11/001113071724.htm>
68. **Oral care for patients with cardiovascular disease and stroke.** [Many systemic diseases and conditions have oral manifestations that may be the initial signs of clinical disease. The mouth is a portal of entry as well as the site of disease for microbial infections that affect general health status. Sufficient evidence exists to conclude that oral lesions, especially advanced periodontic pathologies, place certain patients at increased risk of developing cardiovascular disease and stroke.] Rose LF, Mealey B. *J Am Dent Assoc*, Vol 133, No suppl\_1, 37S-44S. [http://jada.ada.org/cgi/content/full/133/suppl\\_1/37S](http://jada.ada.org/cgi/content/full/133/suppl_1/37S)
69. **Periodontal infections and cardiovascular disease – the heart of the matter.** [Evidence continues to support an association among periodontal infections, atherosclerosis and vascular disease. Most studies reported positive associations between periodontal disease and cardiovascular disease after accounting for the effects of multiple risk factors such as age, sex, diabetes, cholesterol levels, blood pressure, obesity, smoking status, dietary patterns, race/ethnicity, education and socioeconomic status. Carotid atherosclerosis as measured by intima-media thickening increased with higher levels of the periodontal bacteria. The mounting evidence points to an association of periodontal disease at the biological, clinical, radiographic and microbiological levels in relation to clinical and subclinical vascular disease. The emergence of periodontal infections as a potential risk factor for CVD is leading to a convergence in oral and medical care that can only benefit the patients and public health.] Demmer RT, Desvarlieux M., *JADA*, Vol.137, Oct 2006 Supplement, pp.15s-20s. [http://jada.ada.org/content/vol137/suppl\\_2/index.dtl](http://jada.ada.org/content/vol137/suppl_2/index.dtl)
70. **Pathogen-related oral spirochetes from dental plaque are invasive.** [These findings indicate that gingival tissues may be a port of entry for previously unrecognized invasive spirochetes in humans.] *Infect Immuno* 59:3377-80, 1991. Riviere GR et al. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=1894352&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=1894352&dopt=Abstract)
71. **Periodontal disease and cardiovascular disease - Epidemiology and possible mechanisms.** [Mild forms of periodontal disease affect 75 percent of adults in the United States, and more severe forms affect 20 to 30 percent of adults. Because periodontal disease is common in the population, it may account for a significant portion of the proposed infection-associated risk of cardiovascular disease.] Genco R, Offenbacher S. *J Am Dent Assoc*, Vol 133, No suppl\_1, 14S-22S. [http://jada.ada.org/cgi/content/full/133/suppl\\_1/14S](http://jada.ada.org/cgi/content/full/133/suppl_1/14S)

72. **Periodontal Disease and Heart Health.** [According to the American Academy of Periodontology, people with periodontal disease are almost twice as likely to have coronary artery disease (also called heart disease). And one study found that the presence of common problems in the mouth, including gum disease (gingivitis), cavities, and missing teeth, were as good at predicting heart disease as cholesterol levels.] April, 2005, WebMD. <http://www.webmd.com/content/Article/104/107270.htm?printing=true>
73. **Periodontal Disease and Risk of Cerebrovascular Disease** [Periodontal disease is an important risk factor for total CVA and, in particular, nonhemorrhagic stroke.] Wu T, Trevisan M, et al. *Arch Intern Med.* 2000;160:2749-2755. <http://archinte.ama-assn.org/cgi/content/abstract/160/18/2749>
74. **Periodontal Disease May Increase Risk of Stroke.** [People with periodontal disease are more likely to have thickened carotid arteries, which can lead to stroke, according to a study released at the American Academy of Neurology's 51st annual meeting in Toronto.] American Academy of Neurology 51<sup>st</sup> annual meeting Toronto CA, 4/21/1999, Mitchell Elkind, MD, Columbia Univ, New York. <http://www.pslgroup.com/dg/f896a.htm>
75. **Periodontal infections and atherosclerosis: mere associations?** [The influence of periodontitis on lipoprotein metabolism has emerged as a new, important factor. Recent studies provide experimental proof that periodontitis may predispose to atherosclerosis.] Pussien PJ et al. *Current Opinion in Lipidology.* 15(5):583-588, Oct 2004. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=15361795&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15361795&dopt=Abstract)
76. **Periodontal Infections and Coronary Heart Disease.** [Chronic inflammation from any source is associated with increased cardiovascular risk. Periodontitis is a possible trigger of chronic inflammation. We investigated the possible association between periodontitis and coronary heart disease (CHD), focusing on microbiological aspects. Our findings suggest an association between periodontitis and presence of CHD. Periodontal pathogen burden, and particularly infection with *A actinomycetemcomitans*, may be of special importance.] Spahr A, Klein E, et al., *Arch Intern Med.* 2006;166:554-559. <http://archinte.ama-assn.org/cgi/content/short/166/5/554>
77. **Periodontitis: a risk factor for coronary heart disease?** [New findings are presented which indicate that the extent of the periodontal infection, a measure reflecting microbial burden, also is related to onset of new CHD events. Our previously published model describing the potential biological mechanisms underlying the associations found is reviewed. This model places the associations into a context of an intrinsic or acquired hyperinflammatory monocyte trait that results in a more intense inflammatory response to lipopolysaccharide (LPS) challenges, such as periodontal infections. This hyperinflammatory response may promote atheroma formation and thromboembolic events. finally, new findings from ongoing animal studies are presented, indicating that high fat diets in atherosclerotic-susceptible mice induce greater inflammatory responses to *Porphyromonas gingivalis* challenges. We conclude that the available evidence does allow an interpretation of periodontitis being a risk factor for atherosclerosis/CHD. Current findings regarding the associations between oral conditions and atherosclerosis/CHD imply that the criteria for causality may be met in the not-too-distant future.] Beck JD, Offenbacher S. *Ann Periodontol.* 1998 Jul;3(1):127-41. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=9722697&dopt=Citation](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9722697&dopt=Citation)
78. **Relation of circulating C-reactive protein to progression of aortic valve stenosis.** [C-reactive protein (CRP) is a marker of inflammation and predicts outcome in apparently healthy

subjects and patients with coronary artery disease. Systemic inflammation is present in patients with aortic valve stenosis (AS). The aim of this prospective study was to assess whether CRP levels predict the progression of AS severity. Blood samples for high-sensitivity CRP measurements and echocardiographic data were obtained in 43 patients (70% men; mean age 73 +/- 8 years) with asymptomatic degenerative AS at study entry. On the basis of repeat echocardiographic assessment at 6 months, patients were grouped as (1) slow progressors (a decrease in aortic valve area [AVA] <0.05 cm<sup>2</sup> and/or an increase in aortic peak velocity <0.15 m/s) and (2) rapid progressors (a decrease in AVA > or =0.05 cm<sup>2</sup> and/or an increase in aortic peak velocity > or =0.15 m/s). Plasma CRP levels were significantly higher in rapid progressors than slow progressors (median 5.1 [range 2.3 to 11.3] vs 2.1 [range 1.0 to 3.1] mg/L, p = 0.007). In multivariate analysis, CRP levels >3 mg/L were independently associated with rapid AS progression (odds ratio 9.1, 95% confidence interval 2.2 to 37.3). In conclusion, CRP levels are higher in patients with degenerative AS who show rapid valve disease progression. These findings suggest that inflammation may have a pathogenic role in degenerative AS.] Sanchez PI, Santos JL, et.al. *Am J Cardiol.* 2006 Jan 1;97(1):90-3. Epub 2005 Nov 10.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=16377290&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=16377290&dopt=Abstract)

79. **Relationship of Periodontal Disease to Carotid Artery Intima-Media Wall Thickness.** [Periodontitis has been linked to clinical cardiovascular disease but not to subclinical atherosclerosis. The purpose of this study was to determine whether periodontitis is associated with carotid artery intima-media wall thickness. These results provide the first indication that periodontitis may play a role in the pathogenesis of atheroma formation, as well as in cardiovascular events.] <http://atvb.ahajournals.org/cgi/content/abstract/atvbaha;21/11/1816>
80. **Researchers link periodontal bacteria to atherosclerosis.** [Patients with periodontal disease are more likely to suffer from atherosclerosis than their counterparts with healthy gums, researchers from Columbia University Medical Center report. Bacteria that cause periodontal disease can migrate throughout the body via the bloodstream and stimulate the immune system, causing inflammation that results in the build up of deposits in the arteries.] ADA News Release. <http://www.ada.org/prof/resources/pubs/adanews/adanewsarticle.asp?articleid=1267>
81. **Role for Periodontal Bacteria in Cardiovascular Diseases.** [*P. gingivalis* exhibits several properties which could play a role in CVD as mediators of LDL oxidation, foam cell formation, and rupture of atherosclerotic plaque.] Kuramitsu HK, *Annals of Periodontology*, 2001, Vol. 6, No. 1, Pages 41-47. <http://www.joonline.org/doi/abs/10.1902/annals.2001.6.1.41>
82. **Study links gum disease, heart attack risk independent of smoking.** [Subjects under 55 with markers for periodontal disease showed a two- to four-times greater risk of having a heart attack, regardless of tobacco use.] ADA News Release. <http://www.ada.org/prof/resources/pubs/adanews/adanewsarticle.asp?articleid=939>
83. **The Association Between Cumulative Periodontal Disease and Stroke History in Older Adults.** [Based on the results of this study, there is evidence of an association between cumulative periodontal disease, based on PHS, and a history of stroke. However, it is unclear whether cumulative periodontal disease is an independent risk factor for stroke or a risk marker for the disease.] Lee HJ, Garcia RI, *Journal of Periodontology*, 2006, Vol. 77, No. 10, Pages 1744-1754. <http://www.joonline.org/doi/abs/10.1902/jop.2006.050339?journalCode=jop>
84. **The relationship between oral conditions and ischemic stroke and peripheral vascular disease.** [Studies to date suggest that oral conditions may be associated with increased risk of ischemic stroke and peripheral vascular disease.] Joshipura K. *J Am Dent Assoc*, Vol 133, No suppl\_1, 23S-30S. [http://jada.ada.org/cgi/content/full/133/suppl\\_1/23S](http://jada.ada.org/cgi/content/full/133/suppl_1/23S)

85. **The Role of Inflammatory and Immunological Mediators in Periodontitis and Cardiovascular Disease.** [Oral pathogens and inflammatory mediators (such as interleukin [IL]-1 and tumor necrosis factor [TNF]- $\alpha$ ) from periodontal lesions intermittently reach the bloodstream inducing systemic inflammatory reactants such as acute-phase proteins, and immune effectors including systemic antibodies to periodontal bacteria.] DeNardin E, *Annals of Periodontology*, 2001, Vol. 6, No. 1, Pages 30-40.  
<http://www.joponline.org/doi/abs/10.1902/annals.2001.6.1.30>
86. **Treatment of Periodontitis and Endothelial Function.** [*Background* Systemic inflammation may impair vascular function, and epidemiologic data suggest a possible link between periodontitis and cardiovascular disease. *Methods* We randomly assigned 120 patients with severe periodontitis to community-based periodontal care (59 patients) or intensive periodontal treatment (61). Endothelial function, as assessed by measurement of the diameter of the brachial artery during flow (flow-mediated dilatation), and inflammatory biomarkers and markers of coagulation and endothelial activation were evaluated before treatment and 1, 7, 30, 60, and 180 days after treatment. *Results* Twenty-four hours after treatment, flow-mediated dilatation was significantly lower in the intensive-treatment group than in the control-treatment group (absolute difference, 1.4%; 95% confidence interval [CI], 0.5 to 2.3; P=0.002), and levels of C-reactive protein, interleukin-6, and the endothelial-activation markers soluble E-selectin and von Willebrand factor were significantly higher (P<0.05 for all comparisons). However, flow-mediated dilatation was greater and the plasma levels of soluble E-selectin were lower in the intensive-treatment group than in the control-treatment group 60 days after therapy (absolute difference in flow-mediated dilatation, 0.9%; 95% CI, 0.1 to 1.7; P=0.02) and 180 days after therapy (difference, 2.0%; 95% CI, 1.2 to 2.8; P<0.001). The degree of improvement was associated with improvement in measures of periodontal disease (r=0.29 by Spearman rank correlation, P=0.003). There were no serious adverse effects in either of the two groups, and no cardiovascular events occurred. *Conclusions* Intensive periodontal treatment resulted in acute, short-term systemic inflammation and endothelial dysfunction. However, 6 months after therapy, the benefits in oral health were associated with improvement in endothelial function.] Tonetti MS, D' Aiuto F, et.al. *New England Journal of Medicine* Vol 356:911-920, March 1, 2007, No.9. <http://content.nejm.org/cgi/content/abstract/356/9/911>
87. **UC Davis researchers discover receptor pathway for C reactive protein and its effects.** [Scientists have discovered how C-reactive protein, or CRP, is able to access endothelial cells. CRP is a known risk marker for heart disease. This is the first time that anyone has shown how CRP is able to get into the human aortic endothelial cells.]  
[http://www.eurekalert.org/pub\\_releases/2005-06/uocd-udr062105.php](http://www.eurekalert.org/pub_releases/2005-06/uocd-udr062105.php)
88. **UC Davis Study Identifies C-reactive Protein as Cause of Blood Clot Formation.** [A new study by UC Davis physicians is the first to conclusively link C-reactive proteins (CRP) to formation of blood clots, a major cause of heart attacks, strokes and other vascular disease. Until now, CRP had been recognized mainly as a risk marker of heart disease. CRP causes cells in the arteries, endothelial cells, to produce higher levels of an enzyme that inhibits the breakdown of clots. The enzyme, plasminogen activator inhibitor-1 (PAI-1) is also a strong risk marker for heart disease, especially in diabetics. ]  
[http://www.ucdmc.ucdavis.edu/news/CRP\\_study.html](http://www.ucdmc.ucdavis.edu/news/CRP_study.html)
89. **Valsartan, Blood Pressure Reduction, and C-Reactive Protein.** [Increased levels of high-sensitivity C-reactive Protein (hsCRP) are associated with incident hypertension as well as cardiovascular events, and angiotensinII is a potent proinflammatory mediator.] Ridker PM, Danielson E, et. al., *Hypertension*. 2006;48:1-7.  
<http://hyper.ahajournals.org/cgi/content/abstract/01.HYP.0000226046.58883.32v1?maxtoshow>

90. **VCU Study Suggests New Link Between Severe Periodontitis and Cardiovascular – Disease.** [Virginia Commonwealth University researchers have found that changes in the plasma lipoprotein profile of patients with severe periodontitis – a condition characterized by chronic infection and inflammation of the gums - may contribute to these patients' elevated risk for heart disease and stroke. Patients with periodontitis had elevated plasma levels of a particularly bad subclass of the low density lipoprotein (LDL) called small-dense LDL. Also the decrease of LDL associated PAF-AH activity in patients with severe periodontitis may increase cardiovascular risk in these patients.] RICHMOND, Va. (Dec. 1, 2005) <http://www.vcu.edu/uns/Releases/2005/dec/120105.html>

### **C-reactive Protein / Pro-inflammatory Mediators**

91. **Additive Value of Immunoassay-Measured Fibrinogen and High-Sensitivity C-Reactive Protein Levels for Predicting Incident Cardiovascular Events.** [Current guidelines suggest measuring high-sensitivity C-reactive protein (hs-CRP) as an aid to coronary risk assessment in adults without cardiovascular disease (CVD). Whether other inflammatory biomarkers, such as fibrinogen, add further prognostic information is uncertain. In this cohort of initially healthy women, baseline levels of fibrinogen measured with a high-quality immunoassay provided additive value to hs-CRP and traditional risk factors in predicting incident CVD.] Mora S, Rifai N, et.al. *Circulation*. 2006;114:381-387. <http://circ.ahajournals.org/cgi/content/abstract/114/5/381?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=1&andorexacttitle=and&andorexacttitleabs=and&andorexactfulltext=and&searchid=1&FIRSTINDEX=0&sortspec=relevance&volume=114&firstpage=381&resourcetype=HWCIT>
92. **Assessment of Hemostatic Risk Factors in Predicting Arterial Thrombotic Events.** [Arterial thrombosis results from endovascular injury and, to a lesser extent, alterations in hemostatic equilibrium. Endothelial cell injury with the elaboration of proinflammatory mediators stimulates the process of arterial thrombosis. Although this is most often the result of endovascular injury attributable to atherosclerotic disease, other disease states can elicit a similar response as well. Epidemiological studies have identified several acquired or inherited states that may result in endothelial damage or altered hemostatic equilibrium, thereby predisposing patients to arterial thrombosis. These include hyperhomocysteinemia, elevated C-reactive protein, antiphospholipid antibodies, elevated fibrinogen, Factor VII, plasminogen activator inhibitor-1 (PAI-1), hereditary thrombophilias, and platelet hyper-reactivity. At present, the literature supports a role for hyperhomocysteinemia, elevated C-reactive protein, and elevated fibrinogen as risk factors for arterial thrombosis.] David Feinbloom; Kenneth A. Bauer. *Arteriosclerosis, Thrombosis, and Vascular Biology*. 2005;25:2043. <http://atvb.ahajournals.org/cgi/content/abstract/25/10/2043>
93. **Comparison of C-Reactive Protein and Low-Density Lipoprotein Cholesterol Levels in the Prediction of First Cardiovascular Events.** [These data suggest that the C-reactive protein level is a stronger predictor of cardiovascular events than the LDL cholesterol level and that it adds prognostic information to that conveyed by the Framingham risk score.] Ridker, PM, et.al., *NEJM*, Nov 14, 2002 Vol. 347:1557-1565 No 20. <http://content.nejm.org/cgi/content/abstract/347/20/1557>
94. **CRP—Marker or Maker of Cardiovascular Disease?** [C-reactive protein (CRP) has emerged as an interesting novel and potentially clinically useful marker for increased cardiovascular risk. This is an attractive concept because atherosclerosis is a disease

characterized by chronic arterial inflammation and suggests the possibility that subclinical states of atherosclerosis can be identified by an increase in circulating markers of inflammation before acute events occur. Based on data obtained primarily from in vitro studies it has also been proposed that CRP in itself is actively contributing to disease progression and that it should be considered as true risk factor and consequently as a target for intervention. The association between moderately elevated CRP levels and an increased risk for development of cardiovascular disease is well established.] Jan Nilsson. *Arteriosclerosis, Thrombosis, and Vascular Biology*. 2005;25:1527. <http://atvb.ahajournals.org/cgi/content/full/25/8/1527>

95. **C Reactive protein and its relation to cardiovascular risk factors: a population based cross sectional study.** [The body's response to inflammation may play an important part in influencing the progression of atherosclerosis.] Mendall MA, Patel P, et. al. *BMJ* 1996;312:1061-1065 (27 April). <http://bmj.bmjournals.com/cgi/content/abstract/312/7038/1061>
96. **C-Reactive Protein and Incident Cardiovascular Events Among Men With Diabetes.** [Several large prospective studies have shown that baseline levels of C-reactive protein (CRP) are an independent predictor of cardiovascular events among apparently healthy individuals. However, prospective data on whether CRP predicts cardiovascular events in diabetic patients are limited so far. High plasma levels of CRP were associated with an increased risk of incident cardiovascular events among diabetic men, independent of currently established lifestyle risk factors, blood lipids, and glycemic control.] Schulze M, Rimm EB, et.al. *Diabetes Care* 27:889-894, 2004. [http://care.diabetesjournals.org/cgi/content/abstract/27/4/889?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&author1=Schulze&searchid=1081215809897\\_10507&stored\\_search=&FIRSTINDEX=0&sortspec=relevance&volume=27&firstpage=889&journalcode=diacare](http://care.diabetesjournals.org/cgi/content/abstract/27/4/889?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&author1=Schulze&searchid=1081215809897_10507&stored_search=&FIRSTINDEX=0&sortspec=relevance&volume=27&firstpage=889&journalcode=diacare)
97. **C-Reactive Protein and LDL Cholesterol Levels in Women.** [The authors concluded that increasing levels of C-reactive protein are an independent predictor of cardiovascular events and are even more strongly associated with cardiovascular risk than increased LDL cholesterol levels.] <http://www.aafp.org/afp/20030315/tips/27.html>
98. **C-Reactive Protein and the 10-Year Incidence of Coronary Heart Disease in Older Men and Women: The Cardiovascular Health Study.** [High C-reactive protein (CRP) is associated with increased coronary heart disease risk. Few long-term data in the elderly are available. In older men and women, elevated CRP was associated with increased 10-year risk of CHD, regardless of the presence or absence of cardiac risk factors. A single CRP measurement provided information beyond conventional risk assessment, especially in intermediate-Framingham-risk men and high-Framingham-risk women.] Cushman M, Arnold A, et.al. *Circulation*. 2005;112:25-31. <http://circ.ahajournals.org/cgi/content/abstract/112/1/25>
99. **C-Reactive Protein Increases Plasminogen Activator Inhibitor-1 Expression and Activity in Human Aortic Endothelial Cells.** [Inflammation plays a pivotal role in atherosclerosis. In addition to being a risk marker for cardiovascular disease, much recent data suggest that C-reactive protein (CRP) promotes atherogenesis via effects on monocytes and endothelial cells. The metabolic syndrome is associated with significantly elevated levels of CRP. Plasminogen activator inhibitor-1 (PAI-1), a marker of atherothrombosis, is also elevated in the metabolic syndrome and in diabetes, and endothelial cells are the major source of PAI-1. This study makes the novel observation that CRP induces PAI-1 expression and activity in HAECs and thus has implications for both the metabolic syndrome and atherothrombosis.] *American Heart Assoc Journal Circulation*, 2003;107:398-404. Devaraj S et.al, Univ of California, Davis Medical Center. <http://circ.ahajournals.org/cgi/content/abstract/107/3/398>

100. **C-Reactive Protein, a Sensitive Marker of Inflammation, Predicts Future Risk of Coronary Heart Disease in Initially Healthy Middle-Aged Men.** [Inflammatory reactions in coronary plaques play an important role in the pathogenesis of acute atherothrombotic events; inflammation elsewhere is also associated with both atherogenesis generally and its thrombotic complications. Recent studies indicate that systemic markers of inflammation can identify subjects at high risk of coronary events. These results confirm the prognostic relevance of CRP, a sensitive systemic marker of inflammation, to the risk of CHD in a large, randomly selected cohort of initially healthy middle-aged men. They suggest that low-grade inflammation is involved in pathogenesis of atherosclerosis, especially its thrombo-occlusive complications.] Koenig et al, *Circulation*. 1999;99:237-242. <http://circ.ahajournals.org/cgi/content/abstract/circulationaha;99/2/237>
101. **C-Reactive Protein Modulates Risk Prediction Based on the Framingham Score.** [The Framingham Coronary Heart Disease (CHD) prediction score is recommended for global risk assessment in subjects prone to CHD. Recently, C-reactive protein (CRP) has emerged as an independent predictor of CHD. We sought to assess the potential of CRP measurements to enhance risk prediction based on the Framingham Risk Score (FRS) in a large cohort of middle-aged men from the general population. Our results suggest that CRP enhances global coronary risk as assessed by the FRS, especially in intermediate risk groups. This might have implications for future risk assessment.] Koenig W, Löwel H, et.al. *Circulation*. 2004;109:1349-1353. <http://circ.ahajournals.org/cgi/content/abstract/109/11/1349>
102. **C-Reactive Protein, Subclinical Atherosclerosis, and Risk of Cardiovascular Events.** [C-reactive protein (CRP) is an independent determinant of risk of stroke among both men and women. Emerging data suggest that CRP may be a mediator as well as a marker of atherosclerosis. CRP induces expression of cellular adhesion molecules, interleukin-6, and endothelin-1 by endothelial cells. CRP also mediates monocyte chemoattractant protein-1 induction, and it has been shown to mediate uptake of LDL by macrophages. Furthermore, smooth muscle cells and macrophages in arterial tissue have been shown to produce CRP, a process that is substantially upregulated in atherosclerotic plaque.] Gavin J. Blake; Paul M. Ridker, <http://atvb.ahajournals.org/cgi/content/full/22/10/1512>
103. **C-Reactive Protein, the Metabolic Syndrome, and Risk of Incident Cardiovascular Events.** [Prospective data suggest that measurement of CRP adds clinically important prognostic information to the metabolic syndrome.] Ridker PM, Buring JE, et al. *Circulation*. 2003;107:391. <http://circ.ahajournals.org/cgi/content/abstract/107/3/391>
104. **Clinical Application of C-Reactive Protein for Cardiovascular Disease Detection and Prevention.** [C-reactive protein (CRP), a marker of inflammation that has been shown in multiple prospective epidemiological studies to predict incident myocardial infarction, stroke, peripheral arterial disease, and sudden cardiac death. CRP levels have also been shown to predict risk of both recurrent ischemia and death among those with stable and unstable angina, those undergoing percutaneous angioplasty, and those presenting to emergency rooms with acute coronary syndromes. CRP is an independent predictor of future cardiovascular events that adds prognostic information to lipid screening, to the metabolic syndrome, and to the Framingham Risk Score.] Ridker PM, *Circulation: Journal of the American Heart Association: Volume 107(3) 28 January 2003 pp 363-369*, <http://pt.wkhealth.com/pt/re/circ/fulltext.00003017-200301280-00017.htm;jsessionid=GdsbRvFtQ8wg71bkQySLXZIGXT5pcLhGS5mJTfPnvMWsJL5Zym3m!869285401!-949856145!8091!-1>
105. **Cytokine profile in synovial fluid from patients with internal derangement of the temporomandibular joint: a preliminary study.** [Temporomandibular joint disorders (TMD)

comprise a group of chronic painful conditions of mastication in the temporomandibular joint (TMJ). Although the association between TMD and internal derangement of the TMJ is well documented, the functional relevance is still unclear. Increased concentrations of inflammatory mediators have been identified in the synovial fluid of affected patients with TMD, suggesting an underlying degenerative or inflammatory process. The aim of this study was to generate a comprehensive cytokine expression profile in TMD. **Methods:** 15 samples from patients with internal derangement of TMJ were analysed using a novel cytokine array that enables the analysis of 79 different cytokines simultaneously. **Results:** Cytokine levels were correlated with the presence of joint effusion (JE) determined by MRI. In the majority of synovial fluid samples, angiogenin (Ang), fibroblast growth factor (FGF)-9, insulin-like growth factor-binding protein (IGFBP)-3, interleukin (IL)-1 $\alpha$ , IL-1 $\beta$ , IL-8, inducible protein (IP)-10, macrophage inflammatory protein (MIP)-1 $\beta$ , osteoprotegerin (OPG), transforming growth factor (TGF)- $\beta$ 2, tissue inhibitor of metalloproteinase (TIMP)-1, TIMP-2, tumour necrosis factor (TNF)- $\beta$  and vascular endothelial growth factor (VEGF) were detectable. Furthermore, the expression levels of Ang, brain-derived neurotrophic factor (BDNF), FGF-4, FGF-9, IGFBP-2, IL-8, MIP-1 $\beta$ , OPG, pulmonary and activation-regulated protein (PARC), TGF- $\beta$ 2, TIMP-2 and VEGF were significantly associated with the presence of JE; among these, nine cytokines (Ang, BDNF, FGF-4, FGF-9, IGFBP-2, MIP-1 $\beta$ , PARC, TGF- $\beta$ 2 and TIMP-2) were hitherto not described in TMD. **Conclusions:** This study confirmed previous reports of elevated cytokine levels in TMD. Additionally, we identified previously undescribed cytokines that were upregulated and correlated significantly with the presence of JE. We were able to identify novel cytokines that have hitherto not been described in TMD. Strategies targeting the identified cytokines may represent a novel therapy option in TMD.] Matsumoto K, Honda K, et al. *Dentomaxillofacial Radiology* (2006) 35, 432-441.

<http://dmfr.birjournals.org/cgi/content/abstract/35/6/432>

106. **Definition of Tumor necrosis factor.** [Tumor necrosis factor: A member of a superfamily of [proteins](#), each with 157 amino acids, which induce [necrosis](#) (death) of tumor cells and possess a wide range of proinflammatory actions. Tumor necrosis factor is a multifunctional [cytokine](#) with effects on [lipid metabolism](#), [coagulation](#), [insulin](#) resistance, and the function of [endothelial](#) cells lining blood vessels. Blocking the action of TNF has been shown to be beneficial in reducing the inflammation in inflammatory diseases.] <http://www.medterms.com/script/main/art.asp?articlekey=25458>
107. **Effect of treating Periodontitis on C-reactive protein levels: a pilot study.** [Periodontitis is associated with elevated levels of C-reactive protein and fibrinogen and it may be a coronary heart disease risk factor. Periodontitis seems to increase C-reactive protein only in some individuals, presumably the ones reacting to it with a systemic inflammatory reaction. Periodontal treatment decreases C-reactive protein levels in these individuals and it may thus decrease their risk of coronary heart disease.] Mattila K, Vesänen M, et al, *BMC Infectious Diseases* 2002, 2:30. <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=138813&rendertype=abstract>
108. **Elevation of Systemic Markers Related to Cardiovascular Diseases in the Peripheral Blood of Periodontitis Patients.** [Periodontitis is a common, often undiagnosed, chronic infection of the supporting tissues of the teeth, epidemiologically associated with cardiovascular diseases. Since C-reactive protein (CRP) and other systemic markers of inflammation have been identified as risk factors for cardiovascular diseases, we investigated whether these factors were elevated in periodontitis. Periodontitis results in higher systemic levels of CRP, IL-6, and neutrophils. These elevated inflammatory factors may increase inflammatory activity in atherosclerotic lesions, potentially increasing the risk for cardiac or

cerebrovascular events. Loos BG, Craandijk J, et al. *Journal of Periodontology*, October 2000, Vol. 71, No. 10, Pages 1528-1534.

<http://www.joponline.org/doi/abs/10.1902/jop.2000.71.10.1528>

109. **High-Sensitivity C-Reactive Protein Potential Adjunct for Global Risk Assessment in the Primary Prevention of Cardiovascular Disease.** [Inflammation plays a major role in atherothrombosis, and measurement of inflammatory markers such as high-sensitivity C-reactive protein (HSCRP) may provide a novel method for detecting individuals at high risk of plaque rupture. Several large-scale prospective studies demonstrate that HSCRP is a strong independent predictor of future myocardial infarction and stroke among apparently healthy men and women and that the addition of HSCRP to standard lipid screening may improve global risk prediction among those with high as well as low cholesterol levels. Because agents such as aspirin and statins seem to attenuate inflammatory risk, HSCRP may also have utility in targeting proven therapies for primary prevention. Inexpensive commercial assays for HSCRP are now available; they have shown variability and classification accuracy similar to that of cholesterol screening. Risk prediction algorithms using a simple quintile approach to HSCRP evaluation have been developed for outpatient use. Thus, although limitations inherent to inflammatory screening remain, available data suggest that HSCRP has the potential to play an important role as an adjunct for global risk assessment in the primary prevention of cardiovascular disease.] Ridker PM *Circulation*. 2001;103:1813.  
<http://circ.ahajournals.org/cgi/content/full/103/13/1813#F4>
110. **High-Sensitivity C-Reactive Protein; Potential Adjunct for Global Risk Assessment in the Primary Prevention of Cardiovascular Disease.** [Inflammation plays a major role in atherothrombosis, and measurement of inflammatory markers such as high-sensitivity C-reactive protein (hsCRP) may provide a novel method for detecting individuals at high risk of plaque rupture. Measurement of inflammatory markers such as HSCRP may provide a novel method for detecting individuals at high risk of plaque rupture. Several large-scale prospective studies demonstrate that hsCRP is a strong independent predictor of future myocardial infarction and stroke among apparently healthy men and women. Recent data describing CRP within atheromatous plaque, as a correlate of endothelial dysfunction, and as having a direct role in cell adhesion molecular expression raise the possibility that CRP may also be a potential target for therapy. Available data suggest that hsCRP has the potential to play an important role as an adjunct for global risk assessment in primary prevention of cardiovascular disease.] Paul M. Ridker MD. *Circulation*. 2001;103:1813,  
<http://circ.ahajournals.org/cgi/content/full/103/13/1813>
111. **High-Sensitivity Serum C-Reactive Protein Levels in Subjects With or Without Myocardial Infarction or Periodontitis.** [As expected, elevated serum hsC-rp concentration and serum WBC counts are associated with acute coronary heart disease. (2) Elevated serum hsC-rp values are associated with radiographically defined periodontitis in subjects with no evidence of CVD.] Persson G., Pettersson T., et al, *J Clin Perio* 32: 219–224, 2005.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=15766362&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15766362&dopt=Abstract)
112. **How the Blood Talks to the Brain Parenchyma and the Paraventricular Nucleus of the Hypothalamus During Systemic Inflammatory and Infectious Stimuli.** [There are exciting new developments regarding the molecular mechanisms involved in the influence of circulating proinflammatory molecules within cells of the blood-brain barrier (BBB) during systemic immune challenges. These molecules, when present in the circulation, have the ability to trigger a series of events in cascade, leading to either the mitogen-activated protein (MAP) kinases/nuclear factor kappa B (NF- $\kappa$ B) or the janus kinase (JAK)/signal transducer and activator of transcription (STAT) transduction pathways in vascular-associated cells of the

central nervous system (CNS). The brain blood vessels exhibit both constitutive and induced expression of receptors for different proinflammatory ligands that have the ability to stimulate these signaling molecules. Depending on the challenges and the cytokines involved, the transduction signal(s) solicited in cells of the BBB may orient the neuronal activity in a very specific manner in activating the transcription and production of soluble factors, such as prostaglandins (PGs). It is interesting to note that cytokines as well as systemic localized inflammation stimulate the cells of the BBB in a nonselective manner (i.e., within both large blood vessels and small capillaries across the brain). This nonselectivity raises several questions with regard to the localized neuronal activation induced by different experimental models of inflammation and cytokines. It is possible that the selectivity of the neuronal response is a consequence of the fine interaction between nonparenchymal synthesis of soluble mediators and expression of specific receptors for these ligands within parenchymal elements of different brain nuclei. This review will present the recent developments on this concept and the mechanisms that take place in cells of the BBB, which lead to the neuronal circuits involved in restoring the body's homeostasis during systemic immunogenic challenges. The induction of fever, the hypothalamic-pituitary adrenal (HPA) axis, and other autonomic functions are among the physiological outcomes necessary for the protection of the mammalian organism in the presence of foreign material.] Rivest S, Lacroix S, et.al. *Proceedings of the Society for Experimental Biology and Medicine* 223:22-38 (2000).  
<http://www.ebmonline.org/cgi/content/abstract/223/1/22>

113. **Humoral immune responses in gingival crevice fluid: local and systemic implications.** [ ] Ebersole, JL. *Periodontology* 2000. Volume 31 Issue 1 Page 135 - February 2003. <http://www.blackwell-synergy.com/doi/abs/10.1034/j.1600-0757.2003.03109.x?journalCode=prd>
114. **Inhibition of activator protein-1 transcription factor activation by [omega]-3 fatty acid modulation of mitogen-activated protein kinase signaling kinases.** [Background: Lipopolysaccharide (LPS)-stimulated macrophages (M[Phi]) produce excess tumor necrosis factor (TNF), and the direct inhibition of I[kappa]B phosphorylation and its subsequent separation from the nuclear factor [kappa]B (NF[kappa]B)-I[kappa]B complex has been experimentally supported as a mechanism for [omega]-3 fatty acid (FA) inhibition of this TNF response. However, TNF production is a "late" event in the LPS-induced M[Phi] inflammatory cascade, and in addition to NF[kappa]B-associated pathways, a separate transcription factor, activator protein-1 (AP-1) is an important pathway for M[Phi] proinflammatory cytokine production. The mitogen-activated protein kinase (MAPK) cascade regulates both NF[kappa]B-I[kappa]B and AP-1-associated gene transcription through several cross-amplifying phosphorylation kinases, specifically p44/42 [ie, extracellular signal-regulated kinase (ERK) 1/2], p38, and c/jun N-terminal kinase (JNK)/stress-activated protein kinase (SAPK). The activation of these kinases occurs in the proximal MAPK cascade and activation modulates AP-1 activation. In this set of experiments, it was hypothesized that inhibition of MAPK signaling phosphorylation kinases by [omega]-3 fatty acids in a model of LPS-stimulated M[Phi]s would alter the activation of the proinflammatory cytokine transcription factor AP-1. ...Conclusions: [omega]-3 FA inhibited p44/42 and JNK/SAPK phosphorylation; however, p38 remained unchanged. Phosphorylation of p44/42 and JNK/SAPK are the immediate prior steps in AP-1 activation. Attenuated AP-1 activation and subsequent attenuated gene-level proinflammatory cytokine elaboration is anticipated after inhibition of these MAPK intermediates and is confirmed by the reduction in AP-1 activity. These results provide further evidence for the transcriptional level regulation in the elaboration of proinflammatory cytokines by [omega]-3 FA in this M[Phi] model.] Babcock TA, Kurland A, et.al. *Journal of Parenteral and Enteral Nutrition* 27:176-181, 2003.  
[http://findarticles.com/p/articles/mi\\_qa3762/is\\_200305/ai\\_n9216984](http://findarticles.com/p/articles/mi_qa3762/is_200305/ai_n9216984)

115. **Interleukin-6, C-Reactive Protein, and Mortality Risk.** [There is an increased risk of death associated with elevated levels of IL-6 and CRP in nondisabled older persons. These findings may broaden our understanding of the health correlates and consequences of low-level inflammation, as well as providing a new way to identify high-risk subgroups for anti-inflammatory interventions.] Harris TB, Ferrucci Luigi, et al., *Am J Med.* 1999;106:506-512. <http://dceg.cancer.gov/pdfs/harris1065061999.pdf>
116. **Immunogenetic Susceptibility of Atherosclerotic Stroke; Implications on Current and Future Treatment of Vascular Inflammation.** [The understanding of the pathophysiology governing atherosclerosis supports a prominent role for inflammation pathways in plaque initiation and progression that result in stroke and myocardial infarction. Elevated levels of inflammatory markers in the blood, such as C-reactive protein and CD40 ligand/CD40, in concert with increased expression of adhesion molecules, chemokines, cytokines, matrix metalloproteinases (MMP), and inflammatory cells in the plaque, characterize the symptomatic atherothrombotic state.] Thomas J. DeGraba, MD *Stroke.* 2004;35:2712. [http://stroke.ahajournals.org/cgi/content/full/35/11\\_suppl\\_1/2712](http://stroke.ahajournals.org/cgi/content/full/35/11_suppl_1/2712)
117. **Inflammation Marker Predicts Colon Cancer. Feb. 4, 2004 JAMA.** [C-reactive protein, a marker of inflammation circulating in the blood already associated with increased risk of heart disease, can also be used to identify a person's risk of developing colon cancer, according to a Johns Hopkins study.] [http://www.hopkinsmedicine.org/Press\\_releases/2004/02\\_10\\_04.html](http://www.hopkinsmedicine.org/Press_releases/2004/02_10_04.html)
118. **Joint Effects of C-Reactive Protein and Glycated Hemoglobin in Predicting Future Cardiovascular Events of Patients With Advanced Atherosclerosis.** [C-reactive protein (CRP) and glycohemoglobin (HbA1c) are established risk factors for the development of cardiovascular disease. Inflammation, indicated by hs-CRP, and hyperglycemia, indicated by HbA1c, jointly contribute to the cardiovascular risk of patients with advanced atherosclerosis. Patients with both hs-CRP and HbA1c in the upper quartiles (>0.44 mg/dL and >6.2%, respectively) are at particularly high risk for poor cardiovascular outcome.] Schillinger et al, *Circulation.* 2003;108:2323. <http://circ.ahajournals.org/cgi/content/abstract/108/19/2323>
119. **Levels of soluble cytokine factors in temporomandibular joint effusions seen on magnetic resonance images.** [OBJECTIVE: To elucidate the correlations between joint effusion (JE) on T2-weighted magnetic resonance images (MRI) of the temporomandibular joint (TMJ) and the levels of various cytokine receptors, cytokine antagonists, and protein in the synovial fluid of patients with temporomandibular joint disorders (TMD). STUDY DESIGN: Fifty-five TMJs of 55 patients with TMD were scanned by MRI, and synovial fluid samples were obtained on the same day. The grade of JE was evaluated on a scale of 0 to 3: Grades 0 and 1 indicated absence, and grades 2 and 3 indicated the presence of JE. Correlations were evaluated between JE and the concentrations of soluble tumor necrosis factor receptors I and II (sTNFR-I and sTNFR-II, respectively), IL-6 soluble receptor (IL-6sR), IL-1 soluble receptor type II, and IL-1 receptor antagonist and protein in the synovial fluid of patients with TMD. RESULTS: The concentrations of sTNFR-I and protein in the group with JE (18 joints) were significantly higher than in the group without JE (37 joints). In addition, there were significant positive correlations between the grade of JE and the levels of sTNFR-I, sTNFR-II, and protein. CONCLUSIONS: sTNFRs and protein may play important roles in the pathogenesis of TMD. These mediators seem to influence the expression of JE, which may reflect synovial inflammation of the TMJ.] Kaneyama K, Segami N, et.al. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2005 Apr;99(4):411-8. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=15772591&dopt=Citation](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15772591&dopt=Citation)

120. **Lipopolysaccharide and interleukin 1 augment the effects of hypoxia and inflammation in human pulmonary arterial tissue.** [The combined effects of hypoxia and interleukin 1, lipopolysaccharide, or tumor necrosis factor alpha on the expression of genes encoding endothelial constitutive and inducible nitric oxide synthases, endothelin 1, interleukin 6, and interleukin 8 were investigated in human primary pulmonary endothelial cells and whole pulmonary artery organoid cultures. Hypoxia decreased the expression of constitutive endothelial nitric oxide synthase (NOS-3) mRNA and NOS-3 protein as compared with normoxic conditions. The inhibition of expression of NOS-3 corresponded with a reduced production of NO. A combination of hypoxia with bacterial lipopolysaccharide, interleukin 1 beta, or tumor necrosis factor alpha augmented both effects. In contrast, the combination of hypoxia and the inflammatory mediators superinduced the expression of endothelin 1, interleukin 6, and interleukin 8. Here, we have shown that inflammatory mediators aggravate the effect of hypoxia on the down-regulation of NOS-3 and increase the expression of proinflammatory cytokines in human pulmonary endothelial cells and whole pulmonary artery organoid cultures.] Ziesche R, Petkov V, et al. [Proc Natl Acad Sci U S A](#). 1996 Oct 29;93(22):12478-83.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=8901607&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8901607&dopt=Abstract)
121. **Markers of Inflammation and Cardiovascular Disease. Application to Clinical and Public Health Practice: A Statement for Healthcare Professionals From the Centers for Disease Control and Prevention and the American Heart Association** [Basic science and epidemiological studies have developed an impressive case that atherogenesis is essentially an inflammatory response to a variety of risk factors and the consequences of this response lead to the development of acute coronary and cerebrovascular syndromes. ... hs-CRP seems to add predictive value above that of currently established risk factors.... On the basis of the available evidence, the Writing Group recommends against screening of the entire adult population for hs-CRP as a public health measure.] <http://circ.ahajournals.org/cgi/content/full/107/3/499>
122. **New research finds link between gum disease, acute heart attacks.** [Heart attack survivors who suffer advanced gum disease show significantly higher levels of a protein in their blood called C-reactive protein (CRP) than such patients without gum disease, new University of North Carolina at Chapel Hill research indicates.] UNC News Service.  
<http://www.unc.edu/news/archives/nov00/deliar111300.htm>
123. **Non-HDL Cholesterol, Apolipoproteins A-I and B<sub>100</sub>, Standard Lipid Measures, Lipid Ratios, and CRP as Risk Factors for Cardiovascular Disease in Women.** [Current guidelines for cardiovascular risk detection are controversial with regard to the clinical utility of different lipid measures, non-high-density lipoprotein cholesterol (non-HDL-C), lipid ratios, apolipoproteins, and C-reactive protein (CRP). Non-HDL-C and the ratio of total cholesterol to HDL-C were as good as or better than apolipoprotein fractions in the prediction of future cardiovascular events. After adjustment for age, blood pressure, smoking, diabetes, and obesity, high-sensitivity CRP added prognostic information beyond that conveyed by all lipid measures.] Ridker P, Rafai N, et al. *JAMA*. 2005;294:326-333. <http://jama.ama-assn.org/cgi/content/abstract/294/3/326>
124. **Patterns of chemokines and chemokine receptors expression in different forms of human periodontal disease.** [Current knowledge states that periodontal diseases are chronic inflammatory reactions raised in response to periodontopathogens. Many cell types and mediators, including Th1 and Th2 lymphocytes, cytokines and chemokines, appear to be involved in the immunopathogenesis of periodontal diseases. Chemokines, a family of chemotactic cytokines, bind to specific receptors and selectively attract different cell subsets to

the inflammatory site. They can also interact with classical cytokines and modulate the local immune response. Chronic periodontitis patients exhibited a more frequent and higher expression of monocyte chemoattractant protein-1 (MCP-1) and its receptor CCR4, and higher expression of IL-10. It is possible that chemokines, in addition to the classical cytokines, are involved in the immunopathogenesis of periodontal disease, driving the migration and the maintenance of several inflammatory cell types such as polymorphonuclear leukocytes, dendritic cells (DCs), natural killer cells, macrophages, and subsets of lymphocytes in the gingival tissues. These cells are thought to participate in the inflammatory and immune reaction that takes place in periodontal disease, killing pathogens, presenting antigens, and producing cytokines. The selective recruitment of polarized lymphocyte subsets could result in differential cytokine production at the site of response, which is supposed to determine the stable or progressive nature of the lesion. Besides, the role of chemokines as activators and chemoattracts of osteoclasts may be involved in the determination of disease severity.] Garlet G.P, Martins W. et al., *Journal of Periodontal Research*, Volume 38, Number 2, April 2003, pp. 210-217(8).

<http://www.ingentaconnect.com/content/mksg/per/2003/00000038/00000002/art00015>

125. **Periodontal Disease, C-Reactive Protein and Overall Health.** [CRP levels are predictive of heart disease, and as a predictor for heart disease, is superior to and independent of cholesterol.] <http://www.perio.org/consumer/happy-heart.htm>
126. **Periodontal therapy lowers levels of heart disease inflammation markers.** [Treating periodontal disease with scaling and root planing combined with a topical antibiotic gel can significantly lower the levels of two inflammatory proteins associated with a heightened risk of heart disease.] Grossi S. ADA News Release.  
<http://www.ada.org/prof/resources/pubs/adanews/adanewsarticle.asp?articleid=841>
127. **Periodontal Treatment Reduces CRP and TNF- $\alpha$ .** [Periodontal treatment is effective in reducing CRP and TNF- $\alpha$  value, mechanisms independent of adiponectin. Thus, the results indicate that periodontal inflammation up-regulate CRP and TNF- $\alpha$ , although still for the most part in the healthy reference range. Elevated level of CRP and TNF- $\alpha$  might be associated with increased risk for future development of atherosclerosis in periodontal patients.] Iwamoto Y, Nishimura, F, et al., Okayama University Graduate School of Medicine and Dentistry, Japan.  
[http://iadr.confex.com/iadr/2003Goteborg/techprogram/abstract\\_30513.htm](http://iadr.confex.com/iadr/2003Goteborg/techprogram/abstract_30513.htm)
128. **Population Distributions of C-reactive Protein in Apparently Healthy Men and Women in the United States: Implication for Clinical Interpretation.** [Measurement of the acute-phase reactant C-reactive protein (CRP) has been used historically in the diagnosis and monitoring of active infection or inflammation. Recent prospective epidemiologic studies have demonstrated that CRP, at concentrations within the reference interval, is a strong predictor of myocardial infarction stroke, sudden cardiac death, and peripheral arterial disease in apparently healthy adults.] Nader Rifai<sup>1,2,a</sup> and Paul M. Ridker<sup>2,3</sup>. *Clinical Chemistry*. 2003;49:666-669.)  
<http://www.clinchem.org/cgi/content/full/49/4/666>
129. **Production of interleukin-1 and tumor necrosis factor by human peripheral monocytes activated by periodontal bacteria and extracted lipopolysaccharides.** [Whole Gram-negative bacteria associated with juvenile and adult periodontitis, and their respective extracted lipopolysaccharides (LPS), were tested for the ability to activate quiescent human peripheral blood monocytes. Results indicate that monocytes are activated by free LPS or LPS bound to Gram-negative pathogenic periodontal bacteria to produce monokines which may contribute to the destruction of periodontal bone.] R. A. Lindemann, J. S. Economou., *Journal of Dental Research*, Vol 67, 1131-1135.  
<http://jdr.iadrjournals.org/cgi/content/abstract/67/8/1131>

130. **Profiling the Cytokines in Gingival Crevicular Fluid Using a Cytokine Antibody Array.** [In this study, we detected several cytokines in GCF using a cytokine antibody array system, including both inflammatory cytokines and various growth factors. Therefore, periodontal disease may participate in the wound healing process and in tissue destruction via the inflammatory process.] Sakai A, Ohshima M, et. al., *Journal of Periodontology* 2006.050340. <http://www.joponline.org/doi/abs/10.1902/jop.2006.050340>
131. **Proinflammatory cytokines detectable in synovial fluids from patients with temporomandibular disorders.** [OBJECTIVE: To measure the levels of the proinflammatory cytokines, interleukin (IL)-1 beta, IL-6, tumor necrosis factor- (TNF) alpha, IL-8, and interferon- (IFN) gamma in synovial fluid samples taken from patients with temporomandibular disorders (TMD). STUDY DESIGN: We studied 6 asymptomatic volunteers and 51 patients with TMD. The IL-1 beta, IL-6, TNF-alpha, IL-8, and IFN-gamma levels in temporomandibular joint synovial fluid were measured using enzyme-linked immunosorbent assay. RESULTS: Measurable level of at least one cytokine in the synovial fluid was found in 40 (64.5%) of 62 joints in the patients: IL-1 beta and IFN-gamma were each detected in 18 (29.0%) of 62 joints; IL-6 in 13 (21.0%) of 62 joints; IL-8 in 11 (19.3%) of 57 joints; and TNF-alpha in only 5 (8.1%) of 62 joints. None of these cytokines was detectable in the synovial fluid in the control group. Furthermore, there was a strong correlation between the detection of IL-1 beta and pain in the joint area. CONCLUSIONS: These data clearly demonstrate increased levels of several proinflammatory cytokines in certain patients with TMD and suggest that these cytokines may play a role in the pathogenesis of synovitis and degenerative changes of the cartilaginous tissue and bone of the temporomandibular joint.] Takahashi T, Kondoh T, et.al. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 1998 Feb;85(2):135-41. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=9503445&dopt=Citation](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9503445&dopt=Citation)
132. **Prospective Study of C-Reactive Protein, Homocystine, and Plasma Lipid Levels as Predictors of Sudden Cardiac Death.** [These results confirm the prognostic relevance of CRP, a sensitive systemic marker of inflammation, to the risk of CHD in a large, randomly selected cohort of initially healthy middle-aged men. They suggest that low-grade inflammation is involved in pathogenesis of atherosclerosis, especially its thrombo-occlusive complications.] <http://circ.ahajournals.org/cgi/content/abstract/99/2/237>
133. **Psychosocial Factors and Inflammation in the Multi-Ethnic Study of Atherosclerosis.** [Psychosocial factors are associated with the development and progress of cardiovascular disease, but the pathological mechanisms remain unclear. Psychosocial risk factors for cardiovascular disease with concentrations of inflammatory markers, were examined. The extent to which these associations are mediated by behaviors, body mass index (BMI), and diabetes mellitus, was examined. Higher levels of cynical distrust were associated with higher levels of inflammatory markers. Higher levels of chronic stress were associated with higher concentrations of IL-6 and C-reactive protein. Depression was positively associated with the level of IL-6. Psychosocial factors are associated with higher levels of inflammatory markers, most consistently for cynical distrust. Results are compatible with a mediating role of BMI, behaviors, and diabetes.] Ranjit N, Diez-Roux A, et.al. *Arch Intern Med.* 2007;167:174-181. <http://archinte.ama-assn.org/cgi/content/abstract/167/2/174>.
134. **Relationship of Destructive Periodontal Disease to the Acute-Phase Response.** [Destructive periodontal diseases have been associated with an increased risk of atherosclerotic complications; however, the potential mechanisms are yet to be defined. Inflammation plays a central role in atherosclerosis since CRP, an acute-phase protein monitored as a marker of inflammatory status, has been identified as a major risk factor for atherosclerotic complications.

Recent reports that destructive periodontal diseases can increase CRP values present the possibility that the acute-phase response may link these 2 disease processes. These results suggest that destructive periodontal disease and disease progression are associated with changes in serum components consistent with an acute-phase response.] Craig RG, Yip JK., et al., *J Periodontol* 2003;74:1007-1016.

[http://www.joponline.org/doi/abs/10.1902/jop.2003.74.7.1007?prevSearch=keywordsfield%3AC-reactive\\_protein](http://www.joponline.org/doi/abs/10.1902/jop.2003.74.7.1007?prevSearch=keywordsfield%3AC-reactive_protein)

135. **Soluble Interleukin-6 receptor.** [Interleukin-6 (IL-6) is a multifunctional cytokine that regulates pleiotropic roles in immune regulation, inflammation, hematopoiesis, and oncogenesis. Its biological activities are shared by IL-6-family of cytokines such as leukemia inhibitory factor and oncostatin M. IL-6 exerts its biological activities through interaction with specific receptors expressed on the surface of target cells.] SBH Sciences.  
[http://www.sbhsciences.com/SIL6R\\_info.asp](http://www.sbhsciences.com/SIL6R_info.asp)
136. **Statin Therapy, LDL Cholesterol, C-Reactive Protein, and Coronary Artery Disease.** [Recent trials have demonstrated better outcomes with intensive than with moderate statin treatment. Intensive treatment produced greater reductions in both low-density lipoprotein (LDL) cholesterol and C-reactive protein (CRP), suggesting a relationship between these two biomarkers and disease progression.] Nissen SE, et al *NEJM* 352:29-38 January 6, 2005 Number 1  
[http://content.nejm.org/cgi/content/abstract/352/1/29?hits=20&andorexactfulltext=and&where=fulltext&searchterm=statin+C+Reactive+nissen&search\\_tab=articles&sortspec=Score%2Bdesc%2BPUBDATE\\_SORTDATE%2Bdesc&sendit=GO&excludeflag=TWEEK\\_element&searchid=1&FIRSTINDEX=0&resourcetype=HWCIT](http://content.nejm.org/cgi/content/abstract/352/1/29?hits=20&andorexactfulltext=and&where=fulltext&searchterm=statin+C+Reactive+nissen&search_tab=articles&sortspec=Score%2Bdesc%2BPUBDATE_SORTDATE%2Bdesc&sendit=GO&excludeflag=TWEEK_element&searchid=1&FIRSTINDEX=0&resourcetype=HWCIT)
137. **Targeting C-reactive protein for the treatment of cardiovascular disease.**  
[Complement-mediated inflammation exacerbates the tissue injury of ischemic necrosis in heart attacks and strokes, the most common causes of death in developed countries. Large infarct size increases immediate morbidity and mortality and, in survivors of the acute event, larger non-functional scars adversely affect long-term prognosis. There is thus an important unmet medical need for new cardioprotective and neuroprotective treatments. We have previously shown that human C-reactive protein (CRP), the classical acute-phase protein that binds to ligands exposed in damaged tissue and then activates complement<sup>1</sup>, increases myocardial and cerebral infarct size. ...Therapeutic inhibition of CRP is a promising new approach to cardioprotection in acute myocardial infarction, and may also provide neuroprotection in stroke. Potential wider applications include other inflammatory, infective and tissue-damaging conditions characterized by increased CRP production, in which binding of CRP to exposed ligands in damaged cells may lead to complement-mediated exacerbation of tissue injury.] Pepys MB, Hirschfield GM et.al., *Nature* 440, 1217-1221 (27 April 2006).  
<http://www.nature.com/nature/journal/v440/n7088/abs/nature04672.html>
138. **The Cholinergic Anti-inflammatory Pathway: A Missing Link in Neuroimmunomodulation.** [This review outlines the mechanisms underlying the interaction between the nervous and immune systems of the host in response to an immune challenge. The main focus is the cholinergic anti-inflammatory pathway, which we recently described as a novel function of the efferent vagus nerve. This pathway plays a critical role in controlling the inflammatory response through interaction with peripheral  $\alpha 7$  subunit-containing nicotinic acetylcholine receptors expressed on macrophages. We describe the modulation of systemic and local inflammation by the cholinergic anti-inflammatory pathway and its function as an interface between the brain and the immune system. The clinical implications of this novel mechanism also are discussed... Introduction: Inflammation is a normal response to disturbed homeostasis caused by infection, injury, and trauma. The host responds with a complex series

of immune reactions to neutralize invading pathogens, repair injured tissues, and promote wound healing. The onset of inflammation is characterized by release of pro-inflammatory mediators including tumor necrosis factor (TNF), interleukin (IL)-1, adhesion molecules, vasoactive mediators, and reactive oxygen species. The early release of pro-inflammatory cytokines by activated macrophages has a pivotal role in triggering the local inflammatory response. Excessive production of cytokines, such as TNF, IL-1 $\beta$ , and high mobility group B1 (HMGB1), however, can be more injurious than the inciting event, initiating diffuse coagulation, tissue injury, hypotension, and death. The inflammatory response is balanced by anti-inflammatory factors including the cytokines IL-10 and IL-4, soluble TNF receptors, IL-1 receptor antagonists, and transforming growth factor (TGF) $\beta$ . Although simplistic the pro-/anti-terminology is widely used in the discussion of the complex cytokine network. Apart from their involvement in local inflammation, TNF and IL-1 $\beta$  are signal molecules for activation of brain-derived neuroendocrine immunomodulatory responses. Neuroendocrine pathways, such as the hypothalamo-pituitary-adrenal (HPA) axis and the sympathetic division of the autonomic nervous system (SNS), control inflammation as an anti-inflammatory balancing mechanism. The host thereby mobilizes the immunomodulatory resources of the nervous and endocrine systems to regulate inflammation. Restoration of homeostasis as a logical resolution of inflammation does not always occur. Insufficient inflammatory responses may result in increased susceptibility to infections and cancer. On the other hand, excessive responses are associated with autoimmune diseases, diabetes, sepsis, and other debilitating conditions. When control of local inflammatory responses is lost, pro-inflammatory mediators can spill into the circulation, resulting in systemic inflammation that may progress to shock, multiple organ failure, and death. Effective therapies for diseases of excessive inflammation are needed.] Pavlov VA, Wang H, et.al. *Mol Med*. 2003 May-Aug; 9(5-8): 125–134.

<http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1430829>

139. **The Effect of Including C-Reactive Protein in Cardiovascular Risk Prediction Models for Women.** [A global risk prediction model that includes hsCRP improves cardiovascular risk classification in women, particularly among those with a 10-year risk of 5% to 20%. In models that include age, blood pressure, and smoking status, hsCRP improves prediction at least as much as do lipid measures.] Cook NR, Buring JE, et.al. *Annals of Internal Medicine*, Vol.145 Issue 1, P 21-29, 4 July 2006, <http://www.annals.org/cgi/content/abstract/145/1/21>
140. **The role of brain insulin in the neurophysiology of serious mental disorders: review.** [The purpose of this review is to indicate the role insulin plays in normal brain neurophysiology, together with the role insulin may play in the regulation of regional cerebral blood flow (rCBF). The relationship between sustained elevation of the inflammatory cytokines and brain insulin dysregulation, with respect to the serious mental disorders, is also discussed. It has been observed that, as the inflammatory cytokines increase, they exert a synergistic influence on insulin and somatostatin, by initially increasing and then decreasing insulin secretion. In the brain, increased levels of insulin result in increased glucose utilization and over-stimulation of the autonomic nervous system (ANS), while the inhibition of insulin secretion results in decreased glucose utilization and dysregulation of the hypothalamo-pituitary-adrenal (HPA) axis. It will further be argued that these alterations in brain insulin influence rCBF in the serious mental disorders such as schizophrenia and the affective disorders. It is hypothesized that insulin regulates rCBF either directly, or indirectly via GLUT4 in the hypothalamus now considered the glucose-sensing, insulin-sensing mechanism of the brain and the body. Thus, we shall propose that insulin plays an important role in normal neurophysiology and that sustained elevation of the inflammatory cytokines dysregulates insulin secretion, rCBF, ANS and the HPA-axis in serious mental disorders.] Holden RJ. *Med*

*Hypotheses*. 1999 Mar;52(3):193-200.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=10362277&dopt=Citation](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10362277&dopt=Citation)

141. **Tumor Necrosis Factor.** [Tumor necrosis factor is a multifunctional proinflammatory cytokine, with effects on lipid metabolism, coagulation, insulin resistance, and endothelial function.] <http://www.ncbi.nlm.nih.gov/entrez/dispmim.cgi?cmd=entry&id=191160>
142. **Tumor necrosis factor.** [TNF $\alpha$  is released by white blood cells, endothelium and several other tissues in the course of damage, e.g. by infection. Its release is stimulated by several other mediators, such as interleukin 1 and bacterial endotoxin. It has a number of actions on various organ systems, generally together with interleukins 1 and 6. On the liver: stimulating the acute phase response, leading to an increase in C-reactive protein and a number of other mediators. It attracts neutrophils very potently, and helps them to stick to the endothelial cells for migration. On macrophages: stimulates phagocytosis, and production of IL-1 oxidants and the inflammatory lipid prostaglandin E2 (PGE2). On other tissues: increasing insulin resistance.] [http://en.wikipedia.org/wiki/Tumor\\_necrosis\\_factor](http://en.wikipedia.org/wiki/Tumor_necrosis_factor)
143. **Tumor necrosis factor.** [Tumor necrosis factor alpha is a cytokine produced primarily by monocytes and macrophages. It is found in synovial cells and macrophages in the tissues. It shares many properties with another cytokine - interleukin 1. It is not unique to RA, but occurs in many inflammatory diseases, and also as a response to endotoxins from bacteria for example.] Drdoc on-line. <http://www.arthritis.co.za/tnf.htm>
144. **Vitamin C reduces level of C-reactive protein, finds UC Berkeley-led study.** [Vitamin C supplements can reduce levels of C-reactive protein, a marker of inflammation and chronic disease risk in humans, according to a new study led by researchers at the University of California, Berkeley. Participants who took about 500 milligrams of vitamin C supplements per day saw a 24 percent drop in plasma C-reactive protein (CRP) levels after two months. The study, published in the April issue of the Journal of the American College of Nutrition, is the first time vitamin C has been shown to decrease levels of CRP, a biomarker that has garnered increasing attention among health researchers in recent years. C-reactive protein is a marker of inflammation, and there is a growing body of evidence that chronic inflammation is linked to an increased risk of heart disease, diabetes and even Alzheimer's disease, said Gladys Block, UC Berkeley professor of epidemiology and public health nutrition and lead author of the study. If our finding of vitamin C's ability to lower CRP is confirmed through other trials, vitamin C could become an important public health intervention. Inflammation occurs as part of the body's defense against infection or injury. The body triggers the production of inflammatory cytokines, such as interleukin-6, that then set off the production of CRP by the liver.] Apr-2004, [http://www.eurekalert.org/pub\\_releases/2004-04/uoc--vcr041204.php](http://www.eurekalert.org/pub_releases/2004-04/uoc--vcr041204.php)

## **Diabetes**

145. [Periodontal problems can complicate the management of diabetes, and uncontrolled diabetes may aggravate periodontal disease. Recent studies indicate that the majority of the U.S. population has some periodontal disease including the most common form, chronic adult periodontitis, formerly known as pyorrhea.] <http://www.diabetesmonitor.com/b285.htm>
146. **Bidirectional Interrelationships Between Diabetes and Periodontal Diseases: An Epidemiologic Perspective.** [The evidence reviewed supports viewing the relationship between diabetes and periodontal diseases as bidirectional.] Taylor G. *Annals of*

147. **Clinical and Metabolic Changes After Conventional Treatment of Type 2 Diabetic Patients With Chronic Periodontitis.** [The aim of this study was to compare the response to conventional periodontal treatment between patients with or without type 2 diabetes mellitus from a clinical and metabolic standpoint. Both groups of patients showed a clinical improvement after basic non-surgical periodontal treatment. The diabetic patients showed improved metabolic control (lower HbA<sub>1c</sub>) at 3 and 6 months after periodontal treatment.] Faria-Almeida R, Navarro A, et. al, *Journal of Periodontology* 2006.050084.  
<http://www.joponline.org/doi/abs/10.1902/jop.2006.050084>
148. **C-Reactive Protein and Incident Cardiovascular Events Among Men With Diabetes.** [Several large prospective studies have shown that baseline levels of C-reactive protein (CRP) are an independent predictor of cardiovascular events among apparently healthy individuals. However, prospective data on whether CRP predicts cardiovascular events in diabetic patients are limited so far. High plasma levels of CRP were associated with an increased risk of incident cardiovascular events among diabetic men, independent of currently established lifestyle risk factors, blood lipids, and glycemic control.] Schulze M, Rimm EB, et.al. *Diabetes Care* 27:889-894, 2004.  
[http://care.diabetesjournals.org/cgi/content/abstract/27/4/889?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&author1=Schulze&searchid=1081215809897\\_10507&stored\\_search=&FIRSTINDEX=0&sortspec=relevance&volume=27&firstpage=889&journalcode=diacare](http://care.diabetesjournals.org/cgi/content/abstract/27/4/889?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&author1=Schulze&searchid=1081215809897_10507&stored_search=&FIRSTINDEX=0&sortspec=relevance&volume=27&firstpage=889&journalcode=diacare)
149. Dental considerations for the treatment of patients with diabetes mellitus. [The susceptibility to periodontal disease—often called the "sixth complication of diabetes mellitus"<sup>12</sup>—is the most common oral complication of diabetes. The patient with poorly controlled diabetes is at greater risk of developing periodontal disease. The dental team can improve the metabolic control of a patient's diabetes by maintaining optimal oral health.] Vernillo AT, *J Am Dent Assoc*, Vol 134, No suppl\_1, 24S-33S.  
[http://jada.ada.org/cgi/content/full/134/suppl\\_1/24S](http://jada.ada.org/cgi/content/full/134/suppl_1/24S)
150. **Detection and prevention of periodontal disease in diabetes.** [Recent studies in which the age relationship of periodontal disease is accounted for show that in type 2 diabetics, periodontal disease is more severe and more prevalent than in non-diabetics.] *Diabetes Monitor*. <http://www.diabetesmonitor.com/b116.htm>
151. **Effect of Periodontitis on Overt Nephropathy and End-Stage Renal Disease in Type 2 Diabetes.** [The purpose of this study was to investigate the effect of Periodontitis on development of overt nephropathy, defined as macroalbuminuria, and end-stage renal disease (ESRD) in type 2 diabetes. Periodontitis predicts development of overt nephropathy and ESRD in individuals with type 2 diabetes. Whether treatment of Periodontitis will reduce the risk of diabetic kidney disease remains to be determined.] Shultis, WA, Weil EJ, et.al. *Diabetes Care* 30:306-311, 2007. <http://care.diabetesjournals.org/cgi/content/abstract/30/2/306>
152. **Educational resources on diabetes mellitus.** [Multiple resources available on managing diabetes.] Eisenberg ES, *J Am Dent Assoc*, Vol 134, No suppl\_1, 59S-60S.  
[http://jada.ada.org/cgi/content/full/134/suppl\\_1/59S](http://jada.ada.org/cgi/content/full/134/suppl_1/59S)
153. **Glycated Hemoglobin Level Is Strongly Related to the Prevalence of Carotid Artery Plaques With High Echogenicity in Nondiabetic Individuals.** [Background— High levels of HbA<sub>1c</sub> have been associated with increased mortality and an increased risk of atherosclerosis assessed as carotid intima-media thickness or plaque prevalence. In the present population-based study, we examined the association between HbA<sub>1c</sub> and plaque prevalence

with emphasis on plaque echogenicity in subjects not diagnosed with diabetes. *Conclusions*—Metabolic changes reflected by HbA<sub>1c</sub> levels may contribute to the development of hard carotid artery plaques, even at modestly elevated levels.] Jorgensen Lone, Jenssen Trond, et.al. *Circulation*. 2004;110:466-47. <http://www.circ.ahajournals.org/cgi/content/full/110/4/466>

154. **Oral Complications in Diabetes.** [Periodontal disease is more severe and occurs with higher frequency in diabetic patients. <http://diabetes.niddk.nih.gov/dm/pubs/america/pdf/chapter23.pdf>
155. **Periodontal disease and diabetes – A two way street.** [A large evidence base suggests that diabetes is associated with an increased prevalence, extent and severity of gingivitis and periodontitis. Furthermore, numerous mechanisms have been elucidated to explain the impact of diabetes on the periodontium. While inflammation plays an obvious role in periodontal diseases, evidence in the medical literature also supports the role of inflammation as a major component in the pathogenesis of diabetes and diabetic complications. Research suggests that, as an infectious process with a prominent inflammatory component, periodontal disease can adversely affect the metabolic control of diabetes. Conversely, treatment of periodontal disease and reduction of oral inflammation may have a positive effect on the diabetic condition, although evidence for this remains somewhat equivocal.] Mealey BL, *JADA*, Vol.137, Oct.2006 Supplement, pp.26s-31s. [http://jada.ada.org/content/vol137/suppl\\_2/index.dtl](http://jada.ada.org/content/vol137/suppl_2/index.dtl)
156. **Periodontal disease, diabetes, and immune response: a review of current concepts.** [A reasonable interpretation of the present evidence indicates that diabetes, when a complication of periodontitis, acts as a modifying and aggravating factor in the severity of periodontal infection. Diabetics with periodontitis who were young and poorly controlled, those who were long-duration diabetics, especially those over 30 years old, demonstrated more attachment loss, bone loss, and deeper probing pocket depths than their nondiabetic controls. It seems that the earlier the onset of diabetes and the longer the duration, especially without consistent control, the more susceptible the individual will be to periodontal disease. Consequently, once a diabetic contracts periodontal disease, it is usually more destructive. Although plaque scores of diabetics may be comparable to or even less than those of nondiabetics, diabetics often exhibit higher gingival index scores. The elevation of this particular clinical parameter is indicative of the microangiopathy associated with diabetes. Diabetic microangiopathy contributes to compromised delivery of nutrients to surrounding tissues and poor elimination of metabolic waste products. The complications associated with diabetes such as macroangiopathy, microangiopathy (i.e., retinopathy), ketoacidosis, and hyperglycemia result in impaired wound healing, immunosuppression, and susceptibility to bacterial infection. Individuals ages 30 to 40 suffering from diabetic retinopathy had significantly more gingival inflammation than controls or diabetics without complications. Collagen metabolism is defective in diabetics and is one component underlying delayed wound healing. Animal studies have been instrumental in elucidating the details of delayed wound healing. Hyperglycemia was associated with increased collagenase and protease activity in the gingiva of rats. Vascular wound healing in rats, particularly new re-endothelialization across vascular anastomoses, was significantly impaired. Diabetic abnormalities in immune response include impaired neutrophil chemotaxis, phagocytosis, and adhesion. Decreased neutrophilic chemotactic response seems to be attributable to protein factors in diabetic serum that competitively bind neutrophil receptors, thereby preventing complement-mediated phagocytosis. Because diabetics are not able to eliminate circulating immune complexes (CIC) effectively, serum CIC levels are elevated. There are microbiological differences in the characteristic flora of NIDDM patients and IDDM patients with periodontitis. These differences are not associated with diabetic impaired immune response. Ultimately, bacterial plaque is the primary etiology of periodontal diseases. Evidently, the host's response to

bacterial plaque and ability to heal following surgery is altered by diabetic disease. Therefore, a thorough history regarding onset of diabetes, duration, and diabetic control would prove useful in the clinical management of diabetics presenting for treatment of periodontal disease.] Grant-Theule DA. *J West Soc Periodontol Periodontol Abstr.* 1996;44(3):69-77.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=9477864&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9477864&dopt=Abstract)

157. **Periodontal Disease and Mortality in Type 2 Diabetes.** [Periodontal disease may contribute to increased mortality associated with diabetes.] Harold Loe, Robert J. Genco,. Oral Complications in Diabetes.  
<http://care.diabetesjournals.org/cgi/reprint/28/1/27?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&fulltext=periodontal+disease&searchid=1&FIRSTINDEX=0&sortspec=relevance&resourceType=HWCIT>
158. **Periodontal disease linked to mortality in diabetes patients: study.** [Investigators from the National Institute of Diabetes and Kidney Disease found a positive association between severity of periodontal disease and mortality in diabetes patients. The investigators found that periodontal disease was a positive predictor for deaths from ischemic heart disease and diabetic nephropathy. After adjusting for factors such as duration of diabetes, hypertension, tobacco use and other factors, they noted that "subjects with severe periodontal disease had 3.2 times the risk of cardiorenal mortality" compared with the groups with no or mild to moderate periodontal disease combined.] ADA News Release.  
<http://www.ada.org/prof/resources/pubs/adanews/adanewsarticle.asp?articleid=1219>
159. **Periodontal Disease Predicts Mortality in Diabetics.** [www.DiabetesinControl.com](http://www.DiabetesinControl.com)  
*Diabetes Care* 2005;28:27-32 National Institute of Diabetes and Digestive and Kidney Disease, Phoenix, AZ.  
<http://www.diabetesincontrol.com/modules.php?name=News&file=print&sid=2402>
160. **Periodontal Disease Predicts Mortality in Diabetics.** [Those with severe periodontal disease had a 28.4 % death rate and those with no or little periodontal disease had a 3.7% death rate.] <http://www.defeatdiabetes.org/Articles/periodontal050124.htm>
161. **Poor Oral Health Puts Patients with Diabetes at Higher Risk of Death.** [Severe gum disease in patients with diabetes makes them twice as likely to die from kidney failure or heart disease. When the gums pull far away from the teeth due to severe gum disease, harmful bacteria from the mouth are allowed to enter the bloodstream, affecting these organs.] ADA news release, [http://www.ada.org/public/media/releases/0310\\_release07.asp](http://www.ada.org/public/media/releases/0310_release07.asp)
162. **Poorly controlled Type 2 diabetics twice as likely to develop periodontal disease.** [People with diabetes are more likely to have periodontal disease than people without diabetes, probably because diabetics are more susceptible to contracting infections. In fact, periodontal disease is often considered the sixth complication of diabetes. Those people who don't have their diabetes under control are especially at risk. Research has emerged that suggests that the relationship between periodontal disease and diabetes goes both ways - periodontal disease may make it more difficult for people who have diabetes to control their blood sugar.] American Academy of Periodontology. <http://www.perio.org/consumer/mbc.diabetes.htm>
163. **The Effect of Antimicrobial Periodontal Treatment on Circulating Tumor Necrosis Factor-Alpha and Glycated Hemoglobin Level in Patients With Type 2 Diabetes.** [Tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) may play an important role in insulin resistance. Antimicrobial therapy significantly reduced the number of microorganisms in periodontal pockets. The results indicate that anti-infectious treatment is effective in improving metabolic control in diabetics, possibly through reduced serum TNF- $\alpha$  and improved insulin resistance.] *J*

*Periodontol* 2001;72:774-778.

<http://www.joponline.org/doi/abs/10.1902/jop.2001.72.6.774?journalCode=jop>

164. **The Prevalence of Calcified Carotid Artery Atheromas on the Panoramic Radiographs of Patients with Type 2 Diabetes Mellitus.** [Type 2 diabetes mellitus, which affects 15 Million Americans, is associated with accelerated cervical carotid artery atherosclerosis and a heightened risk of stroke.] Friedlander AH, Maeder LA, Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2000;89:420-4.  
<http://www.journals.elsevierhealth.com/periodicals/ymoe/article/PIIS1079210400701223/abstract?source=aemf>
165. **The Relationship Between Periodontal Diseases and Diabetes: An Overview.** [This overview looks at the bidirectional relationship between periodontitis and diabetes.] Soskolne WA, Klinger A, et. al., *Annals of Periodontology* 2001.6.1.91.  
[http://www.joponline.org/doi/abs/10.1902/annals.2001.6.1.91?prevSearch=keywordsfield%3Adiabetes\\_mellitus](http://www.joponline.org/doi/abs/10.1902/annals.2001.6.1.91?prevSearch=keywordsfield%3Adiabetes_mellitus)
166. **The Severity of Periodontal Disease is Associated with the Development of Glucose Intolerance in Non-diabetics: The Hisayama Study.** [Inflammation is hypothesized to play a significant role in the development of type 2 diabetes. In the subgroup with normal glucose tolerance 10 years previously, subjects who subsequently developed impaired glucose tolerance were significantly more likely to have deep pockets. Deep pockets were closely related to current glucose tolerance status and the development of glucose intolerance.] *Dent Res* 83(6):485-490,2004. <http://jdr.iadrjournals.org/cgi/content/abstract/83/6/485?etoc>
167. **Treatment of Periodontal Disease and Control of Diabetes: An Assessment of the Evidence and Need for Future Research.** [Evidence points to an increased cytokine response in type 2 diabetes, especially the proinflammatory cytokines interleukin (IL)-1 beta, IL-6, and tumor necrosis factor (TNF)-alpha. Porphyromonas gingivalis, one of the microorganisms responsible for this infection, is able to invade endothelial cells and is a potent signal for monocyte and macrophage activation. Thus, once established in the diabetic host, this chronic infection complicates diabetes control and increases the occurrence and severity of microvascular and macrovascular complications. The evidence supports the notion that treatment of chronic periodontal infection is essential in the diabetic patient. Assessment of infection status in diabetic patients is fundamental for appropriate treatment decisions.] Grossi SG. *Annals of Periodontology* 2001, Vol. 6, No. 1, Pages 138-145.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=11887456&dopt=Citation](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11887456&dopt=Citation) ; <http://www.joponline.org/doi/abs/10.1902/annals.2001.6.1.138>
168. **Treatment of Periodontal Disease in Diabetics Reduces Glycated Hemoglobin.** [Periodontal disease is a common infection-induced inflammatory disease among individuals suffering from diabetes mellitus. Effective treatment of periodontal infection and reduction of periodontal inflammation are associated with a reduction in level of glycated hemoglobin. Control of periodontal infections should thus be an important part of the overall management of diabetes mellitus patients.] *J Periodontol* 1997;68:713-719, Sara Grossi, et.al, SUNY Buffalo  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=9287060&dopt=Citation](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9287060&dopt=Citation) <http://www.electronicipc.com/JournalEZ/detail.cfm?code=02250010680801>

## **Hypertension**

169. **Acute Systemic Inflammation Increases Arterial Stiffness and Decreases Wave Reflections in Healthy Individuals.** [This is the first study to show through a cause-and-effect relationship that acute systemic inflammation leads to deterioration of large-artery stiffness and to a decrease in wave reflections. These findings have important implications, given the

importance of aortic stiffness for cardiovascular function and risk and the potential of therapeutic interventions with anti-inflammatory properties.] Vlachopoulos C et.al., *Circulation* 2005 112: 2193 – 2200 <http://circ.ahajournals.org/cgi/content/abstract/112/14/2193>

170. **Arterial Stiffness in Chronic Inflammatory Diseases.** [Arterial stiffness is increased in chronic inflammatory disorders independent of the presence of atherosclerosis and is related to disease duration, cholesterol, and the inflammatory mediator C-reactive protein and the cytokine that stimulates its production, IL-6.] Roman M, Devereux RB, et.al., *Hypertension*. 2005;46:194. <http://hyper.ahajournals.org/cgi/content/abstract/46/1/194>
171. **Arterial Stiffness Is Related to Systemic Inflammation in Essential Hypertension.** [The acute phase-reactant high-sensitivity C-reactive protein, a marker of vascular inflammation and an atherosclerotic risk factor, is related to arterial stiffness in healthy subjects and in systemic vasculitis.] Mahmud A, et.al., *Hypertension*. 2005;46:1118. <http://hyper.ahajournals.org/cgi/content/abstract/46/5/1118>
172. **Blood Pressure, C-Reactive Protein, and Risk of Future Cardiovascular Events.** [CRP and blood pressure are independent determinants of cardiovascular risk, and their predictive value is additive. CRP showed a linear relationship with blood pressure across all categories of blood pressure. Both CRP and blood pressure were independent determinants of cardiovascular risk, and in combination, each parameter had additional predictive value. data suggest that increasing levels of blood pressure may stimulate a proinflammatory response and that endothelial inflammation may also herald the changes in arterial wall that characterize the hypertensive state. Inflammatory processes are now recognized to play a fundamental role in atherogenesis. C-reactive protein (CRP) has been found to be a robust predictor of incident cardiovascular disease. In this regard, the American Heart Association and the Centers for Disease Control and Prevention have recently issued a class IIa recommendation for the measurement of CRP in primary prevention among those at intermediate risk.] Blake GJ, Rifai N. et. al., *Circulation*. 2003;108:2993. <http://circ.ahajournals.org/cgi/content/full/108/24/2993>
173. **C-Reactive Protein and the Risk of Developing Hypertension.** [C-reactive protein levels are associated with future development of hypertension, which suggests that hypertension is in part an inflammatory disorder.] Sesso HD, Buring JE, et.al., *JAMA*. 2003;290:2945-2951. <http://jama.ama-assn.org/cgi/content/abstract/290/22/2945>
174. **C-Reactive Protein Is Related to Arterial Wave Reflection and Stiffness in Asymptomatic Subjects From the Community.** [Systemic inflammation leads to Endothelial dysfunction which leads to arterial stiffness and wave reflection. CRP, a marker of systemic inflammation, is associated with measures of arterial stiffness and wave reflection in asymptomatic subjects drawn from the community. Changes in arterial stiffness and wave reflection are seen in both acute inflammation and chronic inflammation. CRP levels are predictive of future development of hypertension. Subclinical systemic inflammation is linked to functional alterations of the arterial bed. Arterial stiffness is increased in people with chronic systemic inflammation.] Kullo IJ et.al., *American Journal of Hypertension Volume 18, Issue 8, August 2005, Pages 1123-1129.* [http://www.sciencedirect.com/science?\\_ob=ArticleURL&\\_udi=B6T0Y-4GWPPSS-K&\\_user=10&\\_handle=V-WA-A-W-WB-MSAYWA-UUW-U-AACBEWZDDU-AACACUDCDU-EZAUYYBAE-WB-U&\\_fmt=summary&\\_coverDate=08%2F31%2F2005&\\_rdoc=17&\\_orig=browse&\\_srch=%23toc%234875%232005%23999819991%23604286!&\\_cdi=4875&\\_view=c&\\_acct=C000050221&\\_version=1&\\_urlVersion=0&\\_userid=10&md5=40bdb7a0738f7c972a6417738de5aff7](http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6T0Y-4GWPPSS-K&_user=10&_handle=V-WA-A-W-WB-MSAYWA-UUW-U-AACBEWZDDU-AACACUDCDU-EZAUYYBAE-WB-U&_fmt=summary&_coverDate=08%2F31%2F2005&_rdoc=17&_orig=browse&_srch=%23toc%234875%232005%23999819991%23604286!&_cdi=4875&_view=c&_acct=C000050221&_version=1&_urlVersion=0&_userid=10&md5=40bdb7a0738f7c972a6417738de5aff7)

175. **High-sensitivity C-reactive protein affects central haemodynamics and augmentation index in apparently healthy persons.** [This study shows that plasma levels of hsCRP are positively correlated with AIX, central pulse pressure and central systolic blood pressure. Apparently healthy subjects with increased inflammatory markers have increased systemic arterial stiffness, which might reflect early atherosclerotic changes. Our results suggest that hsCRP and non-invasively measured arterial stiffness could serve as additional tools, beside conventional cardiovascular risk factors, for assessment of global arterial risk and preclinical atherosclerotic changes in arteries.] Kampus, Priit, *Journal of Hypertension*. 22(6):1133-1139, June 2004.  
<http://www.jhypertension.com/pt/re/jhypertension/abstract.00004872-200406000-00014.htm;jsessionid=GgKHTLvGHmcM3LHQ20mrl0dJCl8RcxQ79gZJLzSQgb0sv1hW8LDZ!-1734750035!-949856144!8091!-1>
176. **Oscillatory Shear Stress Stimulates Adhesion Molecule Expression in Cultured Human Endothelium.** [Altered arterial flow patterns increase expression of adhesion molecules. Surface intercellular adhesion molecule-1 induction by pro-inflammatory cytokine stimulation for 24 hours was found to be approximately five times the level detected after 24 hours of oscillatory shear stress. These results further indicate that atherosclerotic lesion initiation is likely related, at least in part, to unique signals generated by oscillatory shear stress and that the mechanism of upregulation is, to some extent, reduction/oxidation sensitive.] Chappell DC, Varner SE, et.al., *Circulation Research*. 1998;82:532-539.  
<http://circres.ahajournals.org/cgi/content/abstract/82/5/532>
177. **Plasma Hydrogen Peroxide Production in Human Essential Hypertension.** [Increased pulse pressure is associated with generation of pro-inflammatory reactive oxygen species.] Lacy F; Kailasam MT, et.al., *Hypertension*. 2000;36:878.)  
<http://hyper.ahajournals.org/cgi/content/abstract/36/5/878> .
178. **Significant association of C-reactive protein with arterial stiffness in treated non-diabetic hypertensive patients.** [C-reactive protein (CRP) has been known to be associated with vascular inflammation and hypertension. Pulse wave velocity may be correlated with CRP levels in treated hypertensive patients. hsCRP was associated with arterial stiffness, independent of age, systolic BP, gender, heart rate, glucose, lipid profiles and medications in treated hypertension. Therefore, hsCRP could be a useful marker of arterial stiffness in treated hypertension patients and a possible target for arterial inflammation in hypertension.] Jung-Sun Kim, Tae Soo Kang et al., *Journal of Atherosclerosis*, 2006.05.025,  
[http://www.sciencedirect.com/science?\\_ob=ArticleURL&\\_udi=B6T12-4K716DT-2&\\_coverDate=06%2F19%2F2006&\\_alid=457204692&\\_rdoc=1&\\_fmt=&\\_orig=search&\\_qd=1&\\_cdi=4878&\\_sort=d&\\_view=c&\\_acct=C000050221&\\_version=1&\\_urlVersion=0&\\_userid=10&md5=12ad92736d996f1da97c2e9c5aed8356](http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6T12-4K716DT-2&_coverDate=06%2F19%2F2006&_alid=457204692&_rdoc=1&_fmt=&_orig=search&_qd=1&_cdi=4878&_sort=d&_view=c&_acct=C000050221&_version=1&_urlVersion=0&_userid=10&md5=12ad92736d996f1da97c2e9c5aed8356)
179. **The Relationship Between Blood Pressure and C-Reactive Protein in the Multi-Ethnic Study of Atherosclerosis (MESA).** [This study confirms the existence of an independent association between hypertension and inflammation in both men and women.] Susan G. Lakoski MD, Mary Cushman MD, *Journal of the American College of Cardiology* Volume 46, Issue 10 , 15 November 2005, pp 1869-1874.  
[http://www.sciencedirect.com/science?\\_ob=ArticleURL&\\_udi=B6T18-4HD8B8W-9&\\_coverDate=11%2F15%2F2005&\\_alid=457161432&\\_rdoc=1&\\_fmt=&\\_orig=search&\\_qd=1&\\_cdi=4884&\\_sort=d&\\_view=c&\\_acct=C000050221&\\_version=1&\\_urlVersion=0&\\_userid=10&md5=41ee28feacb6799762011cc40fceb428](http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6T18-4HD8B8W-9&_coverDate=11%2F15%2F2005&_alid=457161432&_rdoc=1&_fmt=&_orig=search&_qd=1&_cdi=4884&_sort=d&_view=c&_acct=C000050221&_version=1&_urlVersion=0&_userid=10&md5=41ee28feacb6799762011cc40fceb428)

## Kidney Disease

180. **Effect of Periodontitis on Overt Nephropathy and End-Stage Renal Disease in Type 2 Diabetes.** [The purpose of this study was to investigate the effect of periodontitis on development of overt nephropathy, defined as macroalbuminuria, and end-stage renal disease (ESRD) in type 2 diabetes. Periodontitis predicts development of overt nephropathy and ESRD in individuals with type 2 diabetes. Whether treatment of periodontitis will reduce the risk of diabetic kidney disease remains to be determined.] Schultis WA, Weil EJ, et.al. *Diabetes Care* 30:306-311, 2007. <http://care.diabetesjournals.org/cgi/content/abstract/30/2/306>
181. **Importance of periodontal disease in the kidney patient.** [C-reactive protein (CRP), the major acute phase protein in man, has been found to predict all-cause and cardiovascular mortality in ESRD patients on hemodialysis maintenance therapy. Hepatic CRP synthesis is upregulated by proinflammatory cytokines released locally at sites of infection or inflammation, although many patients experience elevated CRP values in the absence of overt infection or inflammation. Destructive periodontal diseases in the general population have been associated with both an increased prevalence of atherosclerotic complications and an elevation in serum CRP values. In view of the prevalence of destructive periodontal diseases in the general population, and since periodontal evaluations are normally not performed as part of a medical assessment, destructive periodontal diseases may be an over looked source of inflammation in ESRD patients on hemodialysis therapy.] Craig R.G., Spittle M.A., *Blood Purif.* 2002;20(1):113-9. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=11803168&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11803168&dopt=Abstract)
182. **Periodontal disease is associated with renal insufficiency in the Atherosclerosis Risk In Communities (ARIC) study.** [Periodontitis, a chronic bacterial infection of the oral cavity, is a novel risk factor for atherosclerotic cardiovascular disease (CVD). Given the numerous shared risk factors for CVD and chronic kidney disease (CKD), we hypothesized that periodontitis also is associated with renal insufficiency in the Dental Atherosclerosis Risk in Communities study. This is the first study to show an association of periodontal disease with prevalent renal insufficiency. A prospective study is necessary to determine the exact nature of the observed relationship.] Kshirsagar, A.V., Moss K.L., et.al., *Am J Kidney Dis.* 2005 Apr;45(4):650-7 [.http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=15806467&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15806467&dopt=Abstract)
183. **Poor Nutritional Status and Inflammation: Linking Oxidative Stress and Inflammation in Kidney Disease.** [For end-stage renal disease (ESRD) patients, cardiovascular disease remains the single most common cause of excess morbidity and mortality. Furthermore, although the prevalence of traditional cardiovascular risk factors is high in the dialysis population, the extent and severity of associated cardiovascular morbidity and mortality remain disproportionate to traditional risk factor profiles. Consequently, considerable effort has been focused on "nontraditional" risk factors for cardiovascular events in this patient population. Among the examined nontraditional risk factors, increased oxidative stress as well as increased acute phase inflammation are postulated to be important contributors to uremic cardiovascular risk. Additional important uremic cardiovascular risk factors include malnutrition and endothelial dysfunction, both of which may be directly linked to the processes that cause increased oxidative stress and inflammation in uremia. In this context I review available data linking the pathogenesis of oxidative stress to acute phase inflammation and uremia. I also review data suggesting that oxidative stress in uremia directly contributes to the development of acute phase inflammation and that patients with higher levels of inflammation have higher levels of oxidative stress biomarkers. Similarly I review emerging data on the potential effects

of antioxidant therapy on inflammatory biomarkers, as well as data suggesting that strategies to lower acute phase inflammation may also improve biomarkers of oxidative stress. Theoretical constructs evaluating the linkage of oxidative stress and inflammation in uremia and their contribution to the pathogenesis of atherosclerosis are suggested.] Himmelfarb J. *Seminars In Dialysis, Volume 17 Issue 6 Page 449 - November 2004.* <http://www.blackwell-synergy.com/doi/abs/10.1111/j.0894-0959.2004.17605.x?journalCode=sdi>

## Lung Disease

184. **Involvement of Periodontopathic Anaerobes in Aspiration Pneumonia.** [Increasing evidence has linked the anaerobic bacteria forming periodontopathic biofilms with aspiration pneumonia in elderly persons.] Okuda K et al, *J Periodontology* 2005, Vol. 76, No. 11-s, pp2154-2160. <http://www.joponline.org/doi/abs/10.1902/jop.2005.76.11-S.2154>
185. **Respiratory Diseases.** [Scientists believe that through the aspiration process, bacteria can cause frequent bouts of infection in patients with COPD.] <http://www.perio.org/consumer/mbc.respiratory.htm>

## Obesity

186. **Elevation of serum C-reactive protein levels is associated with obesity in boys.** [This study aimed to reveal the relationships among C-reactive protein (CRP), obesity, blood pressure (BP), and serum lipids in children. This study revealed a significant relationship between CRP and obesity in children. Obese children tended to have high CRP levels, BP elevation, and slight dyslipidemia. These results support the findings that CRP is one of the useful indices of childhood obesity that would affect the progression to future atherosclerotic disease. We consider that a strategy of preventing obesity from childhood would contribute to a drop in the future incidence of metabolic syndromes.] Hiura M., Kikuchi T., *Hypertens Res.* 2003 Jul;26(7):541-6. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=12924621&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12924621&dopt=Abstract)
187. **Obesity Is an Important Determinant of Baseline Serum C-Reactive Protein Concentration in Monozygotic Twins, Independent of Genetic Influences.** [C-reactive protein (CRP) values predict atherothrombotic cardiovascular disease and type 2 diabetes mellitus. CRP was strongly related to total and central abdominal obesity, blood pressure, and lipid levels, independent of genetic influences. These relationships are likely to contribute significantly to prospective associations between CRP and type 2 diabetes and coronary events.] Greenfield J.R., Samaras K., *Circulation.* 2004;109:3022-3028. <http://circ.ahajournals.org/cgi/content/full/109/24/3022>
188. **Obesity related to periodontal disease.** [Obesity is significantly related to periodontal disease through the pathway of insulin resistance. Insulin resistance is a condition in which the body does not respond well to the action of insulin. Overweight people with an insulin-resistance index in the top 25 percent were nearly 50 percent more likely to have severe periodontal disease compared with those who had a high BMI and low insulin resistance. "We think bacteria from gum disease may interfere with fat metabolism, leading to elevated low-density lipoprotein cholesterol and total cholesterol," says Dr. Sara G. Grossi, lead author of the study. "Now we see a relationship between obesity, insulin resistance and periodontal disease in a large, population-based cohort. This relationship is important because obesity is an important risk factor for Type 2 diabetes and heart disease. It is possible that periodontal disease

contributes to increased morbidity in overweight or obese individuals." ] News. J Am Dent Assoc, Vol 131, No 6, 729. <http://jada.ada.org/cgi/content/full/131/6/729-a>

189. **Periodontal disease, obesity associated with heart disease marker: study .**  
**Periodontal disease, obesity associated with heart disease marker.** *ADA News*, 5/27/2003, citing Slade GD, Ghezzi EM, et al, Relationship Between Periodontal Disease and C-Reactive Protein Among Adults in the Atherosclerosis Risk in Communities Study, *Arch Intern Med*. 2003;163:1172-1179.  
<http://www.ada.org/prof/resources/pubs/adanews/adanewsarticle.asp?articleid=270>
190. **Pneumonia in nonambulatory patients. The role of oral bacteria and oral hygiene.**  
[A number of studies have shown that the mouth can be colonized by respiratory pathogens and serve as a reservoir for these organisms. Other studies have demonstrated that oral interventions aimed at controlling or reducing oral biofilms can reduce the risk of pneumonia in high-risk populations. Studies support the notion that institutionalized subjects are at greater risk of developing dental plaque colonization by respiratory pathogens than are community-dwelling subjects. There is a relationship between poor oral hygiene and bacterial pneumonia in special-care populations. Taken together, the evidence is substantial that improved oral hygiene may prevent pneumonia in vulnerable patients.] Scannapieco, FA., *JADA*, Vol.137, Oct 2006 Supplement, pp.21s-25s. [http://jada.ada.org/content/vol137/suppl\\_2/index.dtl](http://jada.ada.org/content/vol137/suppl_2/index.dtl)

## **Osteoporosis**

191. **The Relationship Between Bone Mineral Density and Periodontitis in Postmenopausal Women.** [Skeletal BMD is related to interproximal alveolar bone loss and, to a lesser extent, to clinical attachment loss, implicating postmenopausal osteopenia as a risk indicator for periodontal disease.] Tezal M, Grossi S.G., *J Periodontology* 2000, Vol. 71, No. 9, pp 1492-1498. <http://www.joponline.org/doi/abs/10.1902/jop.2000.71.9.1492>
192. **The Role of Osteopenia in Oral Bone Loss and Periodontal Disease.** [The relationship of osteopenia to oral bone loss and periodontal disease has been addressed in a limited number of studies. A review of current knowledge regarding this relationship is presented. Interpretation of the literature is complicated by the variety of methods used to assess osteopenia, oral bone mass, and periodontitis, as well as varying definitions of outcomes of interest. Results of a previously unpublished study are presented which suggest that severity of osteopenia is related to loss of alveolar crestal height and tooth loss in post-menopausal women.] Wactawski-Wende J, Grossi SG., et.al., *J Periodontol* Vol 67 #10, Oct 1996.  
<http://www.electronicipc.com/JournalEZ/detail.cfm?code=02250010671019>

## **Pregnancy**

193. **A Review of Premature Birth and Subclinical Infection.** [This article reviews the evidence linking subclinical infection and premature birth. Evidence of subclinical infection as a cause of preterm labor is raised by finding elevated maternal serum C-reactive protein and abnormal amniotic fluid organic acid levels in some patients in preterm labor. Biochemical mechanisms for preterm labor in the setting of infection are suggested by both in vitro and in vivo studies of prostaglandins and their metabolites, endotoxin and cytokines.] Gibbs RS, Romero R, et.al., *Am J Obstet Gynecol* 166:1515-28, 1992.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Abstract&list\\_uids=92280938](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Abstract&list_uids=92280938)

194. **Adverse Pregnancy Outcomes and Periodontal Disease.** [Periodontitis is a chronic inflammatory disease caused mainly by gram-negative bacteria. It is believed that periodontitis can contribute to adverse outcomes of pregnancy. Toxins or other products generated by periodontal bacteria in the mother can reach the blood circulation, cross the placenta, and harm the foetus. In addition, the response of the mother's immune system to the infection activates the release of inflammatory mediators, growth factors and other potent cytokines, which may trigger preterm labour.] World Health Organization, <http://www.whocollab.od.mah.se/expl/systpreterm.html>
195. **Exploring the relationship between periodontal disease and pregnancy complications.** [Obstetric complications not only are a significant health care expense, but also affect the well-being of the affected infants throughout life. Maternal infection with periodontal pathogens has a deleterious effect on fetal growth and viability. Treatments can be provided safely during pregnancy to improve the oral health of the mother. It is the responsibility of the dentist and the profession to inform patients about the biological plausibility that untreated periodontal disease may increase the risk not only of unfavorable pregnancy outcomes, but also of developing conditions that may affect the well-being of the offspring. There is no evidence of a down-side to providing care to mothers, which suggests that such treatment actually may be beneficial for two.] Bobetsis YA, Barros SP, et.al., *JADA*, vol 137 Oct 2006 Supplement, pp.7s-13s. [http://jada.ada.org/content/vol137/suppl\\_2/index.dtl](http://jada.ada.org/content/vol137/suppl_2/index.dtl)  
[http://jada.ada.org/cgi/content/full/137/suppl\\_2/7S](http://jada.ada.org/cgi/content/full/137/suppl_2/7S)
196. **Healthy Births Initiative Blueprint.** [The role that infections play in preterm birth (particularly very early preterm birth) has been clearly established, and the interactions that occur with maternal and fetal immunity is increasingly understood. Microbes can cause LBW and preterm birth directly or through activation of maternal and fetal immune processes. Infection causes white blood cells (T-helper lymphocytes, TH 1) to specialize and release proteins called cytokines (i.e., gamma-interferon, tumor necrosis factor and interleukins) that increase the immune response and serve as crucial mediators of the body's immune-inflammatory responses. Considerable information from human studies and animal models is available regarding the mechanisms through which immune functioning mediates LBW and PTB. As part of the body's response to infection, a cascade of maternal and fetal enzymes (metalloproteases) that may precipitate preterm labor and preterm premature rupture of membranes (PPROM) can be released. Infections such as bacterial vaginosis (BV), asymptomatic bacteruria, sexually transmitted infections and periodontal infections have all been associated with increased risk for preterm delivery. Current investigations suggest that genetic variation in response to infection (e.g., increased inflammatory response) may place susceptible women at increased risk. A mother's ability to resist infection during pregnancy is dependent upon such factors as stress, nutritional status, and personal habits (e.g., smoking, substance use, douching) as well as genetics. Infection and inflammation during pregnancy may have other adverse consequences for the infant. Pro-inflammatory cytokines implicated in LBW and PTB have also been implicated in the pathogenesis of cerebral palsy in premature infants and maternal depression.] Los Angeles Best Babies Collaborative. <http://www.first5la.org/docs/Projects/HB/LABBCHealthyBirthsBluePrint.pdf>
197. **Is there a link between periodontal disease and preterm birth?** [Mounting evidence suggests that a chronic oral infection may lead to an immune reaction that either triggers premature parturition or contributes to its onset. Researchers have measured gingival crevicular levels of PGE<sub>2</sub> and IL-1 $\beta$  in 48 mothers who delivered preterm, LBW infants and compared these levels to those found in control women.<sup>23</sup> They discovered that gingival crevicular fluid levels of PGE<sub>2</sub> were significantly higher in cases, compared to control women. In addition, among primiparous women with preterm, LBW infants, they found a significant

inverse association between birthweight and gestational age and gingival crevicular PGE<sub>2</sub> levels.] Bogess KA. *Contemporary OB?GYN Aug.1,2003.*

<http://www.cedip.cl/Temas/PTDandPERIODONT/Is%20there%20a%20link%20between%20periodontal%20disease%20and%20preterm%20birth.htm>

198. **Maternal periodontal disease and preterm low birthweight: case-control study.**

[Periodontal disease has been suggested to be an important risk factor for preterm low birthweight (PLBW). Here we report a case-control study of 236 cases (infants < 37 wks and weighing < 2499 g) and a daily random sample of 507 controls ( $\geq$  38 wks and weighing  $\geq$ 2500 g). Clinical periodontal indices were measured on the labor wards. Associated risk factors for periodontal disease and PLBW were ascertained by means of a structured questionnaire and maternity notes. The risk for PLBW decreased with increasing pocket depth (odds ratio [OR] 0.83, 95% confidence interval [CI] 0.68 to 1.00). After adjustment for maternal age, ethnicity, maternal education, smoking, alcohol consumption, infections, and hypertension during pregnancy, this decreased further (OR 0.78, 95% CI 0.64 to 0.99). We found no evidence for an association between PLBW and periodontal disease. Our results do not support a specific drive to improve periodontal health of pregnant women as a means of improving pregnancy outcomes.] Davenport ES, Williams CECS, et.al. *J Dent Res* 81(5): 313-318, 2002

<http://jdr.iadrjournals.org/cgi/content/abstract/81/5/313>

199. **Maternal Periodontal Disease Is Associated With an Increased Risk for Preeclampsia.**

[OBJECTIVE: To determine if maternal periodontal disease is associated with the development of preeclampsia. METHODS: A cohort of 1115 healthy pregnant women were enrolled at less than 26 weeks' gestation and followed until delivery. Maternal demographic and medical data were collected. Periodontal examinations were performed at enrollment and within 48 hours of delivery to determine the presence of severe periodontal disease or periodontal disease progression. Preeclampsia was defined as blood pressure greater than 140/90 on two separate occasions, and at least 1+ proteinuria on catheterized urine specimen. The potential effects of maternal age, race, smoking, gestational age at delivery, and insurance status were analyzed, and adjusted odds ratios for preeclampsia were calculated using multivariable logistic regression. RESULTS: During the study period, 763 women delivered live infants and had data available for analysis. Thirty-nine women had preeclampsia. Women were at higher risk for preeclampsia if they had severe periodontal disease at delivery (adjusted odds ratio 2.4, 95% confidence interval 1.1, 5.3), or if they had periodontal disease progression during pregnancy (adjusted odds ratio 2.1, 95% confidence interval 1.0, 4.4). CONCLUSION: After adjusting for other risk factors, active maternal periodontal disease during pregnancy is associated with an increased risk for the development of preeclampsia.] Bogess KA, Lief S, et.al. *Obstetrics & Gynecology* 2003;101:227-231.

<http://www.greenjournal.org/cgi/content/abstract/101/2/227>

200. **Maternal periodontitis and prematurity. Part I: Obstetric outcome of prematurity and growth restriction.**

[Oral Conditions and Pregnancy (OCAP) is a 5-year prospective study of pregnant women designed to determine whether maternal periodontal disease contributes to the risk for prematurity and growth restriction in the presence of traditional obstetric risk factors. Full-mouth periodontal examinations were conducted at enrollment (prior to 26 weeks gestational age) and again within 48 hours postpartum to assess changes in periodontal status during pregnancy. Maternal periodontal disease status at antepartum, using a 3-level disease classification (health, mild, moderate-severe) as well as incident periodontal disease progression during pregnancy were used as measures of exposures for examining associations with the pregnancy outcomes of preterm birth by gestational age (GA) and birth weight (BW) adjusting for race, age, food stamp eligibility, marital status, previous preterm births, first birth, chorioamnionitis, bacterial vaginosis, and smoking. Interim data from the first 814 deliveries demonstrate that maternal periodontal disease at antepartum and incidence/progression of

periodontal disease are significantly associated with a higher prevalence rate of preterm births, BW < 2,500 g, and smaller birth weight for gestational age. ...In summary, the present study, although preliminary in nature, provides evidence that maternal periodontal disease and incident progression are significant contributors to obstetric risk for preterm delivery, low birth weight and low weight for gestational age. These studies underscore the need for further consideration of periodontal disease as a potentially new and modifiable risk for preterm birth and growth restriction.] Offenbacher S, Lieff S, et.al. *Ann Periodontol*. 2001 Dec;6(1):164-74. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=11887460&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11887460&dopt=Abstract)

201. **Maternal Periodontitis and Prematurity, Part II: Maternal Infection and Fetal Exposure.** [Clinical data from the first 812 deliveries from a cohort study of pregnant mothers entitled Oral Conditions and Pregnancy (OCAP) demonstrate that both antepartum maternal periodontal disease and incidence/progression of periodontal disease are associated with preterm birth and growth restriction after adjusting for traditional obstetric risk factors. In the current study we present measures of maternal periodontal infection using whole chromosomal DNA probes to identify 15 periodontal organisms within maternal periodontal plaque sampled at delivery. In addition, maternal postpartum IgG antibody and fetal exposure, as indexed by fetal cord blood IgM level to these 15 maternal oral pathogens, was measured by whole bacterial immunoblots. The potential role of maternal infection with specific organisms within 2 bacterial complexes most often associated with periodontitis, conventionally termed "Orange" (*Campylobacter rectus*, *Fusobacterium nucleatum*, *Peptostreptococcus micros*, *Prevotella nigrescens*, and *Prevotella intermedia*) and "Red" (*Porphyromonas gingivalis*, *Bacteroides forsythus*, and *Treponema denticola*) complexes, respectively, to prematurity was investigated by relating the presence of oral infection, maternal IgG, and fetal cord IgM, comparing full-term to preterm (gestational age < 37 weeks). The prevalence of 8 periodontal pathogens was similar among term and preterm mothers at postpartum. There was a 2.9-fold higher prevalence of IgM seropositivity for one or more organisms of the Orange or Red complex among preterm babies, as compared to term babies (19.9% versus 6.9%, respectively,  $P = 0.0015$ , chi square). Specifically, the prevalence of positive fetal IgM to *C. rectus* was significantly higher for preterm as compared to full-term neonates (20.0% versus 6.3%,  $P = 0.0002$ , as well as *P. intermedia* (8.8% versus 1.1%,  $P = 0.0003$ ). A lack of maternal IgG antibody to organisms of the Red complex was associated with an increased rate of prematurity with an odds ratio (OR) = 2.2; confidence interval (CI) 1.48 to 3.79), consistent with the concept that maternal antibody protects the fetus from exposure and resultant prematurity. The highest rate of prematurity (66.7%) was observed among those mothers without a protective Red complex IgG response coupled with a fetal IgM response to Orange complex microbes (combined OR 10.3;  $P < 0.0001$ ). These data support the concept that maternal periodontal infection in the absence of a protective maternal antibody response is associated with systemic dissemination of oral organisms that translocate to the fetus resulting in prematurity. The high prevalence of elevated fetal IgM to *C. rectus* among premature infants raises the possibility that this specific maternal oral pathogen may serve as a primary fetal infectious agent eliciting prematurity. ] Madianos RPN, Lieff S, et.al. *Obstetrical & Gynecological Survey*. 58(7):438-339, July 2003. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=11887461&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11887461&dopt=Abstract)

202. **Oral Health in Women During Preconception and Pregnancy: Implications for Birth Outcomes and Infant Oral Health.** [Maternal oral health has significant implications for birth outcomes and infant oral health. Maternal periodontal disease, that is, a chronic infection of the gingiva and supporting tooth structures, has been associated with preterm birth, development of preeclampsia, and delivery of a small-for-gestational age infant. Periodontal disease is a destructive inflammatory condition of the gingiva and bone that supports teeth. It is

most commonly associated with a gram-negative anaerobic infection of these structures. Fluid that bathes the tooth at the gingival margin often contains inflammatory mediators and oral pathogens associated with periodontal disease. The mechanisms underlying this destructive process involve both direct tissue damage resulting from plaque bacterial products, and indirect damage through bacterial induction of the host inflammatory and immune responses. Extrapolation from these data suggested that 18% of the preterm, low birth weight infants born annually might be attributable to periodontal disease, and thus account for a significant proportion of the \$5.5 billion annual hospital costs associated with the care of preterm/low birthweight infants. These early studies led to the hypothesis that periodontopathic bacteria, primarily Gram-negative anaerobes, may serve as a source for endotoxin and lipopolysaccharides, which then increases local inflammatory mediators including PGE<sub>2</sub>, and cytokines, and that this increases systemic inflammatory mediators that can then lead to preterm birth.] Boggess KA, Edelstein BL, *Matern Child Health J.* 2006 September; 10(Suppl 7): 169–174. <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1592159>

203. **Periodontal Disease and Preterm Birth: Results of a Pilot Intervention Study.** [This trial indicates that performing SRP in pregnant women with periodontitis may reduce PTB in this population.] Jeffcoat, MK, Hauth JC, et al, *J Periodontol* 2003;74:1214-1218. <http://www.joponline.org/doi/abs/10.1902/jop.2003.74.8.1214?prevSearch=allfield%3A%28Jeffcoat+Pregnant%29>
204. **Periodontal Infection and Preterm Birth: Results of a Prospective Study.** [Babies born prematurely are at a significant risk of developing serious and lasting health problems. Preterm delivery, or PTD, is the major cause of neonatal mortality and of nearly one-half of all serious long-term neurological morbidity. Previous studies have suggested that chronic periodontal infection may be associated with preterm births. Chronic periodontitis has been proposed as a risk factor for preterm birth. The authors conducted a prospective study to test for this association. The authors' data show an association between the presence of periodontitis at 21 to 24 weeks' gestation and subsequent preterm birth. This study provides additional evidence that pre-existing periodontal disease in the second trimester of pregnancy increases the risk of preterm birth. The odds of increased prematurity were increased 4.5- to 7.0-fold.] Jeffcoat MK, Geurs NC, et al., *JADA* 2001; 132:875-880. <http://jada.ada.org/cgi/content/abstract/132/7/875>
205. **Periodontal Disease – The Emergence of a Risk for Systemic Conditions: Pre-term Low Birth Weight.** [There is compelling evidence that a link exists between pre-term low birth weight and periodontitis. A model explaining the plausible relationship is proposed based upon the concept of infection leading to a cascade of inflammatory reactions associated with pre-term labour and periodontal disease. Current evidence has pointed to an interest in dental intervention studies to control periodontal disease as one of the potential strategies to reduce pre-term labour.] Yeo BK, Lim LP, et. al. *Annals Academy of Medicine* January 2005, Vol. 34 No. 1. <http://www.annals.edu.sg/pdf200502/YeoBK.pdf>
206. **Periodontal Infection as a Possible Risk Factor for Preterm Low Birth Weight.** [Periodontal diseases are gram-negative anaerobic infections that can occur in women of childbearing age (18 to 34 years). These data indicate that periodontal diseases represent a previously unrecognized and clinically significant risk factor for preterm low birth weight as a consequence of either pre-term labor or preterm rupture of membranes.] Offenbacher S, Katz V., et.al., *J Periodontol.* 1996 Oct;67(10 Suppl):1103-13. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=8910829&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8910829&dopt=Abstract)

207. **Periodontal Therapy May Reduce Incidence of Preterm Births.** [Study shows that women with gingivitis who received periodontal therapy before 28 weeks of gestation had a significantly lower incidence of preterm low-birthweight babies than women who did not receive periodontal therapy. There is a significant association between gingivitis and preterm birth after adjusting for the major risk factors for preterm delivery, suggesting that gingivitis, the earliest form of periodontal disease, is an independent risk factor for preterm birth and low birthweight. If periodontal infection is diagnosed at any time during pregnancy, the treatment should be administered as soon as possible in order to reduce the risk of preterm birth and low birthweight.] *American Academy of Periodontology Media Release, Nov 2005*  
<http://www.perio.org/consumer/pregnancy-therapy.htm>
208. **Periodontal Therapy May Reduce the Risk of Preterm Low Birth Weight in Women With Periodontal Disease: A randomized Controlled Trial.** [Pregnant women who receive treatment for their periodontal disease can reduce their risk of giving birth to a low birth-weight or pre-term baby. Of the women who received treatment during pregnancy, 2 percent gave birth to either a low birth-weight or pre-term infant. By comparison, 10 percent of the women who received treatment after birth had either a low birth-weight or pre-term baby.] Lopez NJ, et al. *J Periodontology* 2002, Vol. 73, No. 8, Pages 911-924.  
<http://www.joponline.org/doi/abs/10.1902/jop.2002.73.8.911>
209. **Periodontal Therapy Reduces the Rate of Preterm Low Birth Weight in Women With Pregnancy-Associated Gingivitis.** [One hypothesis to explain the association between periodontal disease (PD) preterm/low birth weight (PT/LBW) is that PT/LBW may be indirectly mediated through translocation of bacteria or bacterial products in the systemic circulation. Periodontal treatment significantly reduced the PT/LBW rate in this population of women with pregnancy-associated gingivitis. Within the limitations of this study, we conclude that gingivitis appears to be an independent risk factor for PT/LBW for this population.] Lopez NJ, Da Silva I et.al, *J Periodontol* 2005, Vol. 76, No. 11-s:2144-2153.  
<http://www.joponline.org/doi/abs/10.1902/jop.2005.76.11-S.2144?journalCode=jop>
210. **Periodontitis, a marker of risk in pregnancy for preterm birth.** [Pregnant women with findings of elevated amniotic fluid levels of PGE<sub>2</sub>, IL-6 and IL-8 in the 15–20 weeks of pregnancy and with periodontitis are at high risk for premature birth. The implication of this is that periodontitis can induce a primary host response in the chorioamnion leading to preterm birth.] Dörtbudak O, Eberhardt R., *Journal Of Clinical Periodontology*. Volume 32 Page 45 - January 2005. <http://www.blackwell-synergy.com/links/doi/10.1111/j.1600-051X.2004.00630.x/abs/>
211. **Periodontitis and Plasma C-Reactive Protein During Pregnancy.** [Periodontitis has been associated with increased risk of adverse pregnancy outcomes and elevated C-reactive protein (CRP) concentrations in non-pregnant adults. These findings suggest that periodontitis may increase CRP levels in pregnancy. CRP could potentially mediate the association of periodontitis with adverse pregnancy outcomes.] Pitiphat W, †‡ Joshipura KJ, *Journal of Periodontology*, 2006.050193). <http://www.joponline.org/doi/abs/10.1902/jop.2006.050193>
212. **Polymorphism in the interleukin-1 gene complex and spontaneous preterm delivery.** [Objective: We examined the association between preterm delivery and polymorphisms at position +3953 of the interleukin-1[beta] gene (IL1B+3953) and in intron 2 of the interleukin-1 receptor antagonist gene (IL1RN). Study Design: This was a case-control study that involved 52 pregnancies that resulted in spontaneous preterm delivery before 34 weeks of gestation and 197 pregnancies that resulted in birth at term. Polymorphisms were determined by polymerase chain reaction and restriction fragment length polymorphism analysis. Results: Homozygous carriage of IL1B+3953 allele 1 by fetuses of African descent

was associated with a risk of preterm delivery (P =.033). Fetuses of Hispanic descent that carried IL1RN allele 2 were found to be at an increased risk for preterm premature rupture of membranes and subsequent preterm delivery(P =.021; odds ratio, 6.5; 95% CI, 1.25-37.7). Conclusion: There are associations of spontaneous preterm delivery with the fetal carriage of IL1B+3953\*1 and IL1RN\*2 alleles in African and Hispanic populations, respectively.] Genc MR, Gerber S, et.al. **American Journal of Obstetrics & Gynecology July 2002, 187:1.** <http://pt.wkhealth.com/pt/re/ajog/abstract.00000447-200207000-00024.htm;jsessionid=GFnPyPB6tdln2WTlIFrd4qChqpkqThfGf18hThLvZDcK4yy7p2YN!-377544086!-949856144!8091!-1>

213. **Poor periodontal health of the pregnant woman as a risk factor for low birth weight.** [We conclude that poor periodontal health of the mother is a potential independent risk factor for LBW.] Dasanayake AP, *Ann Periodontol* 1998 Jul;3(1):206-12. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list\\_uids=9722704](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=9722704)
214. **Potential Pathogenic Mechanisms of Periodontitis – Associated Pregnancy Complications.** [Maternal inflammatory response appears to be an important effector mechanism underlying preterm low-birth-weight infants. This response involves genetic as well as environmental exposure components. There is a growing body of evidence indicating that periodontitis may be a sufficient infectious challenge to result in PLBW. Data presented here indicates that perio disease (in hamster model) can induce elevations in intraamniotic PGE2 and TNF- $\alpha$  and result in fetal growth retardation; and that mothers with PLBW have a significant 2-fold elevation in the BCF-PGE2 levels and a plaque microbiota, which is consistent with progressive periodontitis. The similarities in the mixed anaerobic infection of vaginosis and Periodontitis and the striking parallels in inflammatory mediator responses suggest that there is a common underlying pathophysiologic pathway or mechanism that warrants further investigation of the linkage between these infections and PLBW.] Offenbacher S, Jared HL, et. al., *Annals of Periodontology* Vol. 3, No. 1, July 1998. <http://medweb.uni-muenster.de/institute/zmk/einrichtungen/par/bilder/offenbacher.pdf>
215. **Preterm low birth weight and periodontal disease among African Americans.** [African Americans consistently experience higher rates of preterm and low birth weight (LBW) deliveries than do whites. LBW and preterm infants are more likely to die before their first birthday and survivors may suffer from a number of health problems. Therefore, identification of modifiable risk factors for preterm deliveries and LBW has considerable public health significance. Pregnant women's poor periodontal health is emerging as one such factor. Maternal clinical periodontal status and bacteriologic and immunologic profiles related to periodontal disease have been associated with risk of fetal growth and preterm LBW, and periodontal treatment during pregnancy has reduced the incidence of preterm deliveries. This article reviews the literature on the above association and presents data from a previously published prospective study of predominantly African Americans to show that preterm LBW deliveries are associated with higher midtrimester maternal serum antibody levels against *Porphyromonas gingivalis*.] Dasanayake AP, Russell S. *The Dental clinics of North America*. 2003, vol. 47, No.1 pp.115-12., <http://cat.inist.fr/?aModele=afficheN&cpsid=14624279>
216. **Progressive Periodontal Disease and Risk of Very Preterm Delivery.** [The OCAP study demonstrates that maternal periodontal disease increases relative risk for preterm or spontaneous preterm births. Furthermore, periodontal disease progression during pregnancy was a predictor of the more severe adverse pregnancy outcome of very preterm birth, independently of traditional obstetric, periodontal, and social domain risk factors.] Offenbacher

S, Boggess KA, et. al. Obstetrics & Gynecology 2006;107:29-36.

<http://www.greenjournal.org/cgi/content/abstract/107/1/29>

217. **Research Presented Today Provides Further Evidence on the Importance of Good Oral Health in Pregnant Women.** [The more of the mouth affected with periodontal disease, the more likely a woman is to deliver a premature baby, according to an ongoing study of more than 2,000 pregnant women. The results point to further evidence that periodontal disease may be a significant risk factor for preterm births. Past studies have shown that women with periodontal disease may be up to seven times more likely to deliver a preterm low birth weight baby. Today at the American Academy of Periodontology's Specialty Conference on Periodontal Medicine in Washington, D.C., preliminary research was presented for the first time suggesting that the risk for women who have generalized periodontal disease (meaning it affects at least 30 percent of their mouth) is even higher. Data tells us the best advice continues to be that women considering pregnancy have a periodontal screening and get any problems with their oral health under control before becoming pregnant. Women who are already pregnant should not shy away from dental care. Dentists should perform scaling and root planing, along with any supportive therapy, in the second trimester for pregnant patients with periodontal disease.] Jeffcoat M., American Academy of Periodontology Specialty Conference on Periodontal Medicine in Washington, DC, May 7, 2000. Univ of Alabama Birmingham School of Dentistry. American Academy of Periodontology Press Release May 2000. [http://www.perio.org/consumer/women\\_risk.htm](http://www.perio.org/consumer/women_risk.htm)
218. **Study boosts suspected link between mothers' gum disease and both premature birth, low birth weight.** [Mothers who suffer from gum disease are significantly more likely to deliver their babies prematurely than women without that illness. In the five-year study, researchers evaluated periodontal disease in more than 850 women. This prospective study confirms our earlier case-control studies showing that both periodontal disease and periodontal disease progression during pregnancy have an effect on the fetus. Babies developing in women's wombs are being adversely affected by germs growing in their mothers' mouths such that they are born early or at lower than normal weight. Scientists find antibodies to specific organisms in placental blood at the time of delivery. One in 10 babies in the United States is born too small or too early, which is a major cause of sickness and mortality. This work is very important because it confirms a new and potentially modifiable risk factor that we should be able to reduce. Gum disease may be responsible for up to 18 percent of pre-term deliveries, he said the new study suggests. It's not just that periodontal disease is a surrogate marker for poor oral hygiene or other socioeconomic factors just sort of jumbled together," the scientist said. "The fact that we're finding specific organisms that can cause growth and delivery problems opens up a whole new avenue for preventive care.] Lieff, S., McKaig R.G., University of North Carolina at Chapel Hill, Duke University. [http://www.eurekalert.org/pub\\_releases/2002-03/uonc-sbs030502.php](http://www.eurekalert.org/pub_releases/2002-03/uonc-sbs030502.php)
219. **The association between Porphyromonas gingivalis-specific maternal serum IgG and low birth weight.** [Low birth weight infants are about 20 times more likely to die before their first birthday compared to normal birth weight infants. While the rate of LBW has been consistently higher among African Americans compared to whites, there has been a gradual increase in LBW for both African Americans and whites over the last 15 years. In an attempt to identify modifiable risk factors for LBW, we have previously reported that a pregnant woman's poor periodontal health may be an independent risk factor for low birth weight. Porphyromonas gingivalis (P.g.)-specific maternal serum IgG levels were higher in the LBW group compared to the normal birth weight (NBW) group. Women with higher levels of Pg.-specific IgG had higher odds of giving birth to LBW infants. This association remained significant after controlling for smoking, age, IgG levels against other selected periodontal pathogens, and race.

Conclusions: Low birth weight deliveries were associated with a higher maternal serum antibody level against *P. gingivalis* at mid-trimester.] Dasanayake AP, Boyd D, et.al., *Journal of periodontology* 2001, vol. 72, n°11, pp. 1491-1497.  
<http://cat.inist.fr/?aModele=afficheN&cpsid=13493073>

220. **The East London Study of Maternal Chronic Periodontal Disease and Preterm Low Birth Weight Infants: study design and prevalence data.** [The influence of subject-based and environmental factors on the balance between the subgingival microbial challenge and the host response in periodontal diseases illustrates the intimate link between oral and systemic health. From this stems the hypothesis that the persistent Gram-negative challenge and associated inflammatory sequelae in periodontal disease may have consequences extending beyond the periodontal tissues themselves. This paper addresses the design of a case-control study to examine the relationship between preterm low birth weight (PLBW) and maternal periodontal disease. We present preliminary data on the prevalence of these 2 conditions in a group of mothers at the Royal Hospitals Trust, London, U.K. Cases are defined as mothers delivering an infant weighing less than 2,500g before 37 weeks gestation and controls as mothers delivering an infant of more than 2,500g after 38 weeks. We estimated that a study involving 800 mothers (1:3 case:control) should have sufficient power to detect an association with a minimum odds ratio of 3 at the 5% significance level. Demographic details of 177 subjects demonstrated that they were representative of the local population, and the prevalence of PLBW was within the expected range. However, the extent and severity of periodontal disease were higher than predicted and may have reflected elevations in gingival inflammation associated with pregnancy. The final outcome of the study should help determine the need for further interventionist studies to demonstrate a causal relationship between periodontal disease and PLBW, as well as provide information on the prevalence of periodontal diseases in this study population.] Davenport ES, Williams CE, et.al. *Ann Periodontol.* 1998 Jul;3(1):213-21.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=9722705&dopt=Citation](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9722705&dopt=Citation)
221. **The Relationship Between Infections and Adverse Pregnancy Outcomes: An Overview.** [Preterm birth with its subsequent morbidity and mortality is the leading perinatal problem in the United States. Infants born before the thirty-seventh week of gestation account for approximately 6% to 9% of all births, but 70% of all perinatal deaths and half of all long-term neurologic morbidity. Current approaches focus on symptomatic treatment. Despite widespread use of drugs to arrest preterm labor (tocolytics), there has been no decrease in low birth weight or preterm infants in the last 20 years. It is likely that therapy directed at preventing or treating underlying causes would be more successful. Evidence from many sources links preterm birth to symptomatic infections, for example, of the urinary or respiratory tracts. In the last decade, great interest has been generated to support the hypothesis that subclinical infection is an important cause of preterm labor. Evidence to support this may be categorized as follows: histological chorioamnionitis is increased in preterm births; clinical infection is increased after preterm birth; there is significant association of some lower genital tract organisms and infections with preterm birth or preterm premature rupture of the membranes; there are positive cultures of amniotic fluid or membranes from some patients with preterm labor and preterm birth; there are markers of infections in preterm birth; bacteria or their products induce preterm birth in animal models; and some antibiotic trials have shown a lower rate of preterm birth or have deferred preterm birth. In the last 5 years, additional exciting information has suggested that not only is subclinical infection responsible for preterm birth but also many serious neonatal sequelae including periventricular leukomalacia, cerebral palsy, respiratory distress, and even bronchopulmonary dysplasia and necrotizing enterocolitis. In sum, a large body of clinical and laboratory information suggests that subclinical infection is

a major cause of preterm birth, especially those occurring before 30 weeks. This concept holds promise that new approaches can be developed to prevent prematurity.] Gibbs RS. *Annals of Periodontology* December 2001, Vol. 6, No. 1, Pages 153-163.

<http://www.joponline.org/doi/abs/10.1902/annals.2001.6.1.153?journalCode=annals>

## **Endodontics**

222. **Pathogenesis of apical periodontitis and the causes of endodontic failures.** [Apical periodontitis is a sequel to endodontic infection and manifests itself as the host defense response to microbial challenge emanating from the root canal system. It is viewed as a dynamic encounter between microbial factors and host defenses at the interface between infected radicular pulp and periodontal ligament that results in local inflammation, resorption of hard tissues, destruction of other periapical tissues, and eventual formation of various histopathological categories of apical periodontitis, commonly referred to as periapical lesions. The treatment of apical periodontitis, as a disease of root canal infection, consists of eradicating microbes or substantially reducing the microbial load from the root canal and preventing re-infection by orthograde root filling. The treatment has a remarkably high degree of success. Nevertheless, endodontic treatment can fail. Most failures occur when treatment procedures, mostly of a technical nature, have not reached a satisfactory standard for the control and elimination of infection. Even when the highest standards and the most careful procedures are followed, failures still occur. This is because there are root canal regions that cannot be cleaned and obturated with existing equipments, materials, and techniques, and thus, infection can persist. In very rare cases, there are also factors located within the inflamed periapical tissue that can interfere with post-treatment healing of the lesion. The data on the biological causes of endodontic failures are recent and scattered in various journals. This communication is meant to provide a comprehensive overview of the etio-pathogenesis of apical periodontitis and the causes of failed endodontic treatments that can be visualized in radiographs as asymptomatic post-treatment periapical radiolucencies.] Nair PN. *Crit Rev Oral Biol Med.* 2004 Nov 1;15(6):348-81.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=15574679&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15574679&dopt=Abstract)
223. **Comparative evaluation of endodontic irrigants against *Enterococcus faecalis* biofilms.** [The aim of this study was to compare the efficacy of root canal irrigants against *E. faecalis* biofilms using a novel in vitro testing system. Biofilms grown in a flow cell system were submerged in test irrigants for either 1 or 5 minutes. Statistical analysis revealed a significant relationship between test agent and percentage kill of the biofilm bacteria ( $P < 0.05$ ). No statistically significant relationship between time and percentage kill was found. The percentage kill of the biofilm bacteria was: 6% NaOCl (>99.99%), 1% NaOCl (99.78%), Smear Clear (78.06%), 2% chlorhexidine (60.49%), REDTA (26.99%), and BioPure MTAD (16.08%). Post-hoc analysis showed a significant difference between 1% and 6% NaOCl, and all other agents including Smear Clear, 2% chlorhexidine, REDTA, and BioPure MTAD ( $P < 0.05$ ). Within the parameters of this study, both 1% NaOCl and 6% NaOCl were more efficient in eliminating *E. faecalis* biofilm than the other solutions tested.] Dunavant TR, Regan JD, et.al. *J Endod.* 2006 Jun;32(6):527-31.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list\\_uids=16728243&dopt=abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list_uids=16728243&dopt=abstract) ; <http://www.aae.org/joe/abstracts/abst0606.htm>
224. **Lesions of Endodontic Origin and Risk of Coronary Heart Disease.** [A paucity of epidemiologic research exists regarding systemic health consequences of endodontic disease.

This study evaluated whether incident radiographically evident lesions of endodontic origin were related to development of coronary heart disease (CHD) among 708 male participants in the VA Dental Longitudinal Study. At baseline and every three years for up to 32 years, participants (who were not VA patients) received complete medical and dental examinations, including full-mouth radiographs. Cox regression models estimated the relationship between incident lesions of endodontic origin and time to CHD diagnosis. Among those  $\leq 40$  years old, incident lesions of endodontic origin were significantly associated with time to CHD diagnosis ( $p < 0.05$ ), after adjustment for covariates of interest, with hazard ratios decreasing as age increased. Among those  $> 40$  years old, no statistically significant association was observed. These findings are consistent with research that suggests relationships between chronic periodontal inflammation and the development of CHD, especially among younger men.] Caplan DJ, Chasen JB, et.al. *Dent Res* 85(11):996-1000, 2006. <http://jdr.iadrjournals.org/cgi/content/abstract/85/11/996>.

## Ulcers

225. **Are Dental Plaque, Poor Oral Hygiene, and Periodontal Disease Associated With *Helicobacter pylori* Infection?** [The microorganism *Helicobacter pylori* has been closely linked to chronic gastritis, peptic ulcer, gastric cancer, and mucosa-associated lymphoid tissue (MALT) lymphoma. Despite the current treatment regimens that lead to successful management of *H. pylori*-positive chronic gastritis, the reinfection rate is high. It has been suggested that one of the possible mechanisms of reinfection is the recolonization from dental plaque. *H. pylori* in dental plaque is seldom eliminated by *H. pylori*-eradication therapy, and this may act as a source for future reinfection. Hence, eradication of *H. pylori* from the dental plaque should be made an important part of comprehensive management of *H. pylori*-associated gastric diseases.] Anand PS, Nandakumar K. *Journal of Periodontology* 2006.050163. <http://www.joponline.org/doi/abs/10.1902/jop.2006.050163>

## Volatile Sulfur Compounds, Mouth Odor

226. **Antimicrobial mouthrinse as part of a comprehensive oral care regimen.** [Antimicrobial mouthrinses are safe and effective in reducing plaque and gingivitis, and they should be a part of a daily comprehensive oral health care regimen that includes brushing, flossing and rinsing to prevent or minimize periodontal disease.] Silverman S, Wilder R, *J Am Dent Assoc, Vol 137, No suppl\_3, 22S-26S*. [http://jada.ada.org/cgi/content/full/137/suppl\\_3/22S](http://jada.ada.org/cgi/content/full/137/suppl_3/22S)
227. **Effect of hydrogen sulfide and methyl mercaptan on the permeability of oral mucosa.** [Hydrogen sulfide (H<sub>2</sub>S) and methyl mercaptan (CH<sub>3</sub>SH) are the volatile sulfur compounds (VSC) that were investigated for a possible role in the etiology of periodontal disease. The results show that the permeability of porcine non-keratinized sublingual mucosa is increased by up to 75% or 103% following exposure to H<sub>2</sub>S and CH<sub>3</sub>SH, respectively. The effect may be attributed to VSC reaction with tissue components resulting in alteration in the integrity of the tissue barrier. Treatment of the mucosa with 0.22% ZnCl<sub>2</sub>, either prior to or after exposure to CH<sub>3</sub>SH, nullified the effect of CH<sub>3</sub>SH and restored the permeability to a state similar to that observed in control 95% air/5% CO<sub>2</sub> systems.] Ng W., Tonzetich J., *Journal of Dental Research, Vol 63, 994-997*. <http://jdr.iadrjournals.org/cgi/content/abstract/63/7/994>
228. **Efficacy of a Chlorine Dioxide-containing Mouthrinse in Oral Malodor.** [The objective of this study was to determine the efficacy of CloSYSII Oral Rinse in reducing oral malodor over a 96 hour period. This study employed serial organoleptic and Halimeter measurements to document the duration of action CloSYSII Oral Rinse (formerly Retardex) on oral malodor. The results show that a single 15-mL rinsing with the chlorine dioxide rinse, in its unflavored form, improves breath odor pleasantness, reduces breath malodor, and reduces

VSC concentrations in the mouth through 8 hours after use.] Frascella J. et al, TKL Research, Inc., Paramus, NJ., *Journal of Dental Research*, , (IADR Abstracts) 1999, p. 356, Article 2004. <http://www.rowpar.com/professionals/oralhealth/research/5.html>

229. **Formation of Methyl Mercaptan from L-Methionine by *Porphyromonas gingivalis*.** [Methyl mercaptan production by oral bacteria is thought to be one of the main causes of oral malodor. We examined the ability of periodontopathic *Porphyromonas gingivalis* to produce methyl mercaptan from L-methionine. These results suggest that methyl mercaptan not only is one of the sources of oral malodor, but may also play a role in the pathogenicity of *P. gingivalis*.] Yoshimura M., Nakano Y, et.al., *Infection and Immunity*, December 2000, p. 6912-6916, Vol. 68, No. 12. <http://iai.asm.org/cgi/content/abstract/68/12/6912>
230. **Management of Periodontitis with Oral Care Products.** [This study shows the effectiveness of the use of Rowpar's products, CloSYSII Toothpaste and CloSYSII Oral Rinse when used in a twice daily regimen as an effective aid for prevention of periodontitis and the maintenance of recall patients. 1,046 of the original 2,085 pockets were healed to normal probing depths. The relationship between reduction of VSC and the permeability of the epithelial barrier may be associated with the reduction in probing scores.] Chapek et al, *Compendium Vol. XV No 6, 740-746, 1994.* <http://www.rowpar.com/professionals/oralhealth/research/6.html>
231. **Managing the complexity of a dynamic biofilm.** [The pathogenic nature of the dental plaque biofilm can be diminished in the oral cavity by reducing the bioburden and effectively maintaining a normal oral flora via oral hygiene procedures that include daily toothbrushing, flossing and rinsing with an antimicrobial mouthrinse. An oral hygiene regimen that includes rinsing with an antimicrobial mouthrinse is a practical approach to the prevention and management of periodontal diseases. This strategy may have wider benefits when the link between periodontal disease and certain systemic diseases is considered.] Thomas JG, Nakaishi LA. *J Am Dent Assoc, Vol 137, Nov suppl\_3, 10S-15S.* [http://jada.ada.org/cgi/content/full/137/suppl\\_3/10S](http://jada.ada.org/cgi/content/full/137/suppl_3/10S)
232. **Production and origin of oral malodor: a review of mechanisms and methods of analysis.** [Organoleptic studies indicate that the oral cavity is usually the principal source of physiologic malodor associated with the early morning halitosis. This results from normal metabolic activity in the oral cavity and is accentuated in cases with periodontal involvement. Proteolysis and reduction of disulphide bonds precedes the formation of odor. The odor intensity of putrescent saliva and plaque head-space vapor has been correlated with the concentration of volatile sulphur compounds consisting of hydrogen sulphide, methyl mercaptan, dimethyl sulphide and dimethyl disulphide.] Tonzetich J. *Periodontol. 1977 Jan;48(1):13-20.* [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=264535&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=264535&dopt=Abstract)
233. **Production of volatile sulphur compounds in diseased periodontal pockets is significantly increased in smokers.** [Increased production of volatile sulphur compounds may represent a further mechanism of increased susceptibility to periodontitis in smokers and also help to explain the reported association between smoking and halitosis.] Khaira N, Palmer, R.M., et.al., *Oral Dis. 2000 Nov;6(6):371-5.* [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=11355269&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11355269&dopt=Abstract)
234. **Reduction of Bleeding on Probing by Oral Care Products.** [Bleeding can occur only with loss of integrity and continuity between epithelial cells. Penetration of bacterial antigens

will not occur with an intact epithelial barrier. VSC have been associated with increased permeability of the epithelial barrier. The reduction of bleeding on probing with the use of CloSYSII Toothpaste and CloSYSII Oral Rinse when used twice daily between recall visits suggests that these patients had returned to a more healthy periodontal state.] Chapek et al, *Compendium*, Vol. 16, No. 2, 1995, 188-196.

<http://www.rowpar.com/professionals/oralhealth/research/7.html>

235. **Sulphur By-Product: The Relationship between Volatile Sulphur Compounds and Dental Plaque-Induced Gingivitis.** [The purpose of this study was to evaluate the relationship between volatile sulphur compounds (VSC) and gingival health status, and to monitor the changes in VSC in early dental plaque-induced gingivitis. Sulfur levels were significantly higher on the non-brushing side at 4 of the 6 data collection intervals; therefore, sulfur levels may be associated with the initiation and progression of early plaque-induced gingivitis.] Zhou H, McCombs GB, Darby ML, et. al. *The Journal of Contemporary Dental Practice*, Volume 5, No. 2, May 15, 2004.  
[http://72.14.253.104/search?q=cache:bRxqez1\\_m\\_kJ:www.thejcdp.com/issue018/zhou/zhou.pdf+Sulfur+uptake+by+type+I+collagen+from+methyl+mercaptan,+dimethyl+disulfide+air+mixtures&hl=en&gl=us&ct=clnk&cd=5](http://72.14.253.104/search?q=cache:bRxqez1_m_kJ:www.thejcdp.com/issue018/zhou/zhou.pdf+Sulfur+uptake+by+type+I+collagen+from+methyl+mercaptan,+dimethyl+disulfide+air+mixtures&hl=en&gl=us&ct=clnk&cd=5)
236. **Sulfur uptake by type I collagen from methyl mercaptan/dimethyl disulfide air mixtures.** [The results provide evidence that the reaction of collagen with H<sub>2</sub>S and CH<sub>3</sub>SH/(CH<sub>3</sub>S)<sub>2</sub> mixture proceeded via the H<sub>2</sub>S and CH<sub>3</sub>SH thiol groups.] Johnson P.W. Tonzetich J., *Journal of Dental Research*, Vol 64, 1361-1364.  
<http://jdr.iadrjournals.org/cgi/content/abstract/64/12/1361>
237. **The capacity of subgingival microbiotas to produce volatile sulfur compounds in human serum.** [Hydrogen sulfide is formed by the subgingival microbiotas of periodontal pockets. The capacity of these microbiotas to form various volatile sulfur compounds in human serum was studied. Hydrogen sulfide was the predominant volatile sulfur compound, but also methyl mercaptan was formed in significant amounts.] Persson S, Claesson R. *Oral Microbiol Immunol*. 1989 Sep;4(3):169-72.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=2639302&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2639302&dopt=Abstract)
238. **The rationale for the daily use of an antimicrobial mouthrinse.** [There is a twofold rationale for daily use of antimicrobial mouthrinses: first, given the inadequacy of mechanical plaque control by the majority of people, as a component added to oral hygiene regimens for the control and prevention of periodontal diseases; second, as a method of delivering antimicrobial agents to mucosal sites throughout the mouth that harbor pathogenic bacteria capable of recolonizing supragingival and subgingival tooth surfaces, thereby providing a complementary mechanism of plaque control.] Barnett ML, *J Am Dent Assoc*, Vol 137, No suppl\_3, 16S-21S.  
[http://jada.ada.org/cgi/content/full/137/suppl\\_3/16S](http://jada.ada.org/cgi/content/full/137/suppl_3/16S)
239. **The Relationship Between Oral Malodor, Gingivitis, and Periodontitis. A Review.** [Volatile sulfur compounds (VSC) are a family of gases which are primarily responsible for halitosis, a condition in which objectionable odors are present in mouth air. An increasing volume of evidence is demonstrating that extremely low concentrations of many of these compounds are highly toxic to tissues. VSC may, therefore, play a role in the pathogenesis of inflammatory conditions such as periodontitis. Two members of this family, hydrogen sulfide (H<sub>2</sub>S) and methyl mercaptan (CH<sub>3</sub>SH), are primarily responsible for mouth odor. Although many bacteria produce H<sub>2</sub>S, the production of CH<sub>3</sub>SH, especially at high levels, is primarily restricted to periodontal pathogens. Direct exposure to either of these metabolites adversely affects protein synthesis by human gingival fibroblasts in culture. However, methyl mercaptan

has the greatest effect. Other in vitro experiments have demonstrated that cells exposed to methyl mercaptan synthesize less collagen, degrade more collagen, and accumulate collagen precursors which are poorly cross-linked and susceptible to proteolysis. CH<sub>3</sub>SH also increases permeability of intact mucosa and stimulates production of cytokines which have been associated with periodontal disease. VSC, and in particular methyl mercaptan, are therefore capable of inducing deleterious changes in both the extracellular matrix and the local immune response of periodontal tissues to plaque antigens.] Ratcliff PA, Johnson PW., *J Periodontol.* 1999 May;70(5):485-9 <http://www.joonline.org/doi/abs/10.1902/jop.1999.70.5.485> Ratcliff PA, Johnson PW. *J Periodontol.* 1999 May;70(5):485-9. Review.

240. **Volatile Sulfur Compounds and relation to Periodontal disease.** [Every mouth contains the components that produce volatile sulfur compounds (VSCs) bacterial, saliva, and proteins. VSCs are a major component in the development of periodontal diseases. There are three compounds that produce oral malodor: 1)- hydrogen sulphide, 2)-methyl mercaptan, & 3)- dimethyl sulphide. These compounds are the degradation end products from polypeptides. The maintenance of the tissue barrier is important, since toxic substances such as endotoxin and bacterial dextrans have been shown to be incapable of causing inflammation in healthy sulcular gingiva (Gaffar et al., 1981; Rizzo, 1968). VSCs have been shown to have a direct effect on protein synthesis by human gingival fibroblasts (Johnson and Tonzetich et al, 1980). VSCs play a major role in preparing tissues for the invasion of bacterial toxins. <http://dentalimplants-usa.com/Conditions/breath.html>
241. **What is Chlorine Dioxide?** [http://www.lennotech.com/chlorine\\_dioxide.htm](http://www.lennotech.com/chlorine_dioxide.htm); <http://www.epa.gov/pesticides/factsheets/chemicals/chlorinedioxidefactsheet.htm>; <http://www.clo2.com/>

### ***Laser Assisted Periodontal Therapy***

242. **Advantages of a pulsed CO<sub>2</sub> laser in direct pulp capping: a long-term in vivo study.** [The CO<sub>2</sub> laser seems to be a valuable aid in direct pulp capping; the efficiency of laser treatment can be increased by using a pulsed CO<sub>2</sub> laser.] Moritz A, Schoop U, et al. *Lasers Surg Med* 1998;22(5):288-93. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&list\\_uids=9671995&cmd=Retrieve&dopt=Citation&indexed=google](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&list_uids=9671995&cmd=Retrieve&dopt=Citation&indexed=google)
243. **Bactericidal effects of the neodymium:YAG laser: in vitro study.** [The effects of laser energy on three bacterial strains, Staphylococcus aureus, Escherichia coli, and Pseudomonas aeruginosa were studied utilizing the neodymium:YAG laser. Cell suspensions of each strain were divided into four groups. In group I, suspensions from each strain were exposed to laser energy densities of 555-3,333 J/cm<sup>2</sup>. In groups II and III, two artificial dyes, congo red or methylene blue, were added to the suspensions prior to lasing. In group IVa, no laser energy was used, and group IVb was used to measure the bactericidal thermal effects of the laser. It was concluded that: Low dosages of laser energy exceeding 1,667 J/cm<sup>2</sup> resulted in a 2 to 8 log decline in the number of viable bacterial colonies in vitro. Compared to the other two bacterial strains, P aeruginosa was the most sensitive to YAG laser irradiation. Addition of methylene blue, a dark-colored dye, enhanced the bactericidal effects of the YAG laser as indicated by the significantly reduced viability of P aeruginosa after irradiation with 2,222 J/cm<sup>2</sup>.] Schultz RJ, Harvey GP, et.al. *Lasers Surg Med.* 1986;6(5):445-8. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=3100891&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=3100891&dopt=Abstract)

244. **Effects of CO2 Laser Treatment on Fibroblast Attachment to Root Surfaces. A Scanning Electron Microscopy Analysis.** [The group of specimens treated by laser and scaling showed the highest number of fibroblastic cells and a prevalence of well attached fibroblasts higher than control group and scaling/root planing group. The SEM observation didn't show any damages such as cracks and fissures of root surfaces treated by laser and scaling. These findings could suggest that CO<sub>2</sub> laser treatment could be considered as an adjunctive tool to detoxify and to condition the root surfaces in periodontal treatment. CO<sub>2</sub> laser treatment in defocused, pulsed mode with a low power of 2W combined with mechanical instrumentation constitutes a useful tool to condition the root surface and increase fibroblast attachment to root surfaces.] Crespi, R, Barone, A, et al, *Journal of Periodontology* 2002; 73, No.11 pp 1308-1312.  
<http://www.joponline.org/doi/abs/10.1902/jop.2002.73.11.1308?journalCode=jop>
245. **Laser Curettage when combined with SRP gives Superior results to SRP alone when measured by probing scores.** [Laser assisted periodontal treatment when combined with SRP gives better healing and less patient discomfort than with SRP alone]. [Sulcular Debridement with Pulsed Nd: YAG Lasers in Dentistry](#) January 2002.  
<http://www.millenniumdental.com/research/jan-02.html>
246. **Nd:YAG Assisted Periodontal Curettage to Prevent Bacteremia Before Cardiovascular Surgery.** [Laser decontamination is more effective for reducing the occurrence of bacteremia than alternative methods.] *Dentistry Today*, March 1998. [Nd: YAG - Assisted Periodontal Curettage to Prevent Bacteremia Before Cardiovascular Surgery](#)".
247. **Laser de-epithelialization for enhanced guided tissue regeneration. A paradigm shift?** Rossmann JA; Israel M. (Department of Periodontics, Baylor College of Dentistry, Texas A&M University System Health Science Center at Dallas. *Dent Clin North Am* 2000 Oct;44(4):793-809  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=11048272&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11048272&dopt=Abstract)
248. **Periodontal tissue regeneration in beagle dogs after laser therapy.** [CO<sub>2</sub> laser treatment of class III furcation induced formation of new periodontal ligament, cementum and bone.] Crespi R, Covani U, et al. Hospital S. Raffaele, Milan, Italy. *Lasers Surg Med* 1997;21(4):395-402.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=9328987&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9328987&dopt=Abstract)
249. **The carbon dioxide laser as an aid in apicoectomy: an in vitro study.** [CO<sub>2</sub> laser treatment optimally prepares the tooth for final intraoperative filling because of sealing of the dentinal tubules, the resultant elimination of niches for bacteria and the sterilizing effect of the laser.] Moritz A, Gutknecht N, et al. *J Clin Laser Med Surg* 1997;15(4):185-8.
250. **The CO2 laser as an aid in direct pulp capping.** [The CO<sub>2</sub> laser seems to be a valuable aid in direct pulp capping.] Moritz A, Schoop U, et al. *J Endod* 1998 Apr;24(4):248-51.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=9641128&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9641128&dopt=Abstract)

## Microbiology

251. **Use of the carbon dioxide laser in retarding epithelial migration: a pilot histological human study utilizing case reports.** [This is the first reported observation of

human histologic evaluation using CO2 laser for de-epithelization and may warrant further study.] Israel M, ; Rossmann JA, et al. *J Periodontol* 1995 Mar;66(3):197-204.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=7776164&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=7776164&dopt=Abstract)

252. **"Red complex" (Bacteroides forsythus, Porphyromonas gingivalis, and Treponema denticola) in endodontic infections: a molecular approach.** [OBJECTIVE: The "red complex," composed of Bacteroides forsythus, Porphyromonas gingivalis, and Treponema denticola, is implicated in severe forms of periodontal diseases. The purpose of this study was to assess the occurrence of the red complex in root canal infections through the use of a sensitive technique-the 16S rDNA-directed polymerase chain reaction (PCR). STUDY DESIGN: Samples were obtained from 50 necrotic pulps with periradicular pathosis. Ten cases were diagnosed as acute periradicular abscesses. DNA was extracted from the samples and analyzed with a PCR-based identification assay. RESULTS: At least 1 member of the red complex was found in 33 of 50 cases. T denticola, P gingivalis, and B forsythus were detected in 44%, 30%, and 26% of the cases, respectively. The red complex was found in 4 of 50 cases. No particular signs or symptoms were associated with the presence of these bacterial species. CONCLUSIONS: Despite what is indicated in reports with respect to marginal periodontitis, red complex bacteria-either singularly or collectively-was not associated with any particular pattern of clinical symptoms. However, because the bacterial species from the red complex are recognized oral pathogens, their occurrence in root canal infections suggests that they may play a role in the pathogenesis of periradicular diseases.] Rocas IN, Siqueira JF Jr, et.al. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2001 Apr;91(4):468-71.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=11312465&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11312465&dopt=Abstract)

253. **Porphyromonas gingivalis, Treponema denticola, and Tannerella forsythia: the "red complex", a prototype polybacterial pathogenic consortium in periodontitis.** [ ] Holt SC, Ebersole JL. *Periodontol* 2000. 2005;38:72-122.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list\\_uids=15853938](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=15853938)

## **Nutrition**

254. **Clinical Evaluation of a Nutraceutical for the Treatment of Periodontal Disease.** Munoz, CA Kiger R. Loma Linda University. [PerioTherapy is effective at reducing gingivitis, bleeding and periodontal pockets, but not attachment levels.]

<http://www.yourcelebritysmile.com/pdf/pharmaden.pdf> ;

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=11913269&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11913269&dopt=Abstract)

255. **COQ10**

[http://www.vistamagonline.com/articles/page.php?tp=3&p=1&id=17&s=coq10\\_heart\\_therapy](http://www.vistamagonline.com/articles/page.php?tp=3&p=1&id=17&s=coq10_heart_therapy)

256. **Supplement Containing Vitamins C, E and Grape Seed Extract Improves Smokers' Response to Gum Disease Treatment.** [Researchers showed that giving smokers a supplement containing the antioxidant vitamins C and E and grape seed extract improved the response to treatment, shown by better gum attachment and improved oral health in general.] Grossi S., Department of Oral Biology, UB School of Dental Medicine.

<http://www.buffalo.edu/news/fast-execute.cgi/article-page.html?article=66410009>

257. **Grape seed extract induces apoptotic death of human prostate carcinoma DU145 cells via caspases activation accompanied by dissipation of mitochondrial membrane potential and cytochrome c release.** [Results suggest that GSE possibly causes mitochondrial damage leading to cytochrome c release in cytosol and activation of caspases resulting in PARP cleavage and execution of apoptotic death of human prostate cancer DU145 cells.] Agarwal C, Singh RP, *Carcinogenesis*. 2002 Nov;23(11):1869-76.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&itool=pubmed\\_docsum&list\\_uids=12419835&query\\_hl=8](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&itool=pubmed_docsum&list_uids=12419835&query_hl=8)
258. **Anti-inflammatory Activity of a High-molecular-weight Cranberry Fraction on Macrophages Stimulated by Lipopolysaccharides from Periodontopathogens.** [The continuous, high production of cytokines by host cells triggered by periodontopathogens is thought to be responsible for the destruction of tooth-supporting tissues. Macrophages play a critical role in this host inflammatory response to periodontopathogens. The aim of this study was to investigate the effect of (polyphenols) ... on the pro-inflammatory cytokine response of macrophages induced by lipopolysaccharides.... Results clearly indicate that the cranberry fraction was a potent inhibitor of the pro-inflammatory cytokine and chemokine responses induced by LPS. Their results indicated that red wine polyphenols significantly modulate several inflammatory components released by macrophages (a population of host immune cells) in response to bacterial stimuli. Specifically, polyphenols efficiently scavenged and inhibited free-radical generation by host immune cells by controlling intracellular proteins involved in their release. These anti-oxidant properties of red wine polyphenols could be useful in the prevention and treatment of inflammatory periodontal diseases as well as other disorders involving free radicals.] Bodet C. et al., Laval University, Montreal, Canada. *J Dent Research* 85[3]:235-239, 2006.  
<http://jdr.iadrjournals.org/cgi/content/abstract/85/3/235?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&author1=Bodet%2C+c&title=Anti-inflammatory+Activity+&andorexactitle=and&andorexactitleabs=and&andorexactfulltext=and&searchid=1&FIRSTINDEX=0&sortspec=relevance&resourcetype=HWCIT>  
[http://www.rxpgnews.com/research/dental/article\\_3641.shtml](http://www.rxpgnews.com/research/dental/article_3641.shtml)

## Arthritis & TMJ

259. **Clinical Significance of Cytokine Determination in Synovial Fluid.** [Cytokines are a complex family of small regulatory proteins able to mediate intercellular communication and play a crucial role in immunologic and inflammatory reactions. Many reports have demonstrated that some cytokines, in particular tumor necrosis factor  $\alpha$  (TNF $\alpha$ ) and interleukin (IL)-1 $\beta$ , IL-6, and IL-8, so-called proinflammatory, may have a major role in the pathogenesis of joint diseases. Thus, high levels of these substances have been found in inflammatory arthropathies, in particular in those characterized by a more aggressive and destructive outcome, such as rheumatoid arthritis, gout, and infectious arthritis. In keeping with their role, the determination of cytokines in synovial fluid may be proposed for clinical purposes, including diagnostic and prognostic assessments. Furthermore, as some of these cytokines may reflect disease activity, their determination may also be useful in the evaluation of therapy.] Punzi L, Calo L, et.al. *Critical Reviews in Clinical Laboratory Sciences* Volume 39, Number 1/January-February 2002. P 63-88.  
<http://taylorandfrancis.metapress.com/content/xl7eupq0p2j9k8cq/>
260. **Effects of tumor necrosis factor blockade on cardiovascular risk factors in psoriatic arthritis: A double-blind, placebo-controlled study.** [Objective: To conduct a robust, double-blind, placebo-controlled study examining the effects of tumor necrosis factor

(TNF) modulation on concentrations of traditional and novel cardiovascular disease risk factors in patients with an inflammatory condition. This study is the first to demonstrate that targeting the TNF pathway can significantly decrease Lp(a) and homocysteine levels and elevate Apo A-I and SHBG concentrations. These data support an important precursor role for high-grade inflammation in modulating these putative risk parameters. However, TNF blockade-induced increases in triglyceride and Apo B levels were unexpected and suggest that it is not possible, on the basis of biochemical changes in isolation, to suggest that cardioprotection would necessarily follow; rather, direct measures of atherosclerotic progression with TNF blockade (e.g., using carotid ultrasound) would be better.] Sattar N, Crompton P, et.al. *Arthritis & Rheumatism*, Vol 56, Issue 3, p 831-839. <http://www3.interscience.wiley.com/cgi-bin/abstract/114130672/ABSTRACT>

261. **Inhibition of activator protein-1 transcription factor activation by [omega]-3 fatty acid modulation of mitogen-activated protein kinase signaling kinases.** [Background: Lipopolysaccharide (LPS)-stimulated macrophages (M[Phi]) produce excess tumor necrosis factor (TNF), and the direct inhibition of I[kappa]B phosphorylation and its subsequent separation from the nuclear factor [kappa]B (NF[kappa]B)-I[kappa]B complex has been experimentally supported as a mechanism for [omega]-3 fatty acid (FA) inhibition of this TNF response. However, TNF production is a "late" event in the LPS-induced M[Phi] inflammatory cascade, and in addition to NF[kappa]B-associated pathways, a separate transcription factor, activator protein-1 (AP-1) is an important pathway for M[Phi] proinflammatory cytokine production. The mitogen-activated protein kinase (MAPK) cascade regulates both NF[kappa]B-I[kappa]B and AP-1-associated gene transcription through several cross-amplifying phosphorylation kinases, specifically p44/42 [ie, extracellular signal-regulated kinase (ERK) 1/2], p38, and c/jun N-terminal kinase (JNK)/stress-activated protein kinase (SAPK). The activation of these kinases occurs in the proximal MAPK cascade and activation modulates AP-1 activation. In this set of experiments, it was hypothesized that inhibition of MAPK signaling phosphorylation kinases by [omega]-3 fatty acids in a model of LPS-stimulated M[Phi]s would alter the activation of the proinflammatory cytokine transcription factor AP-1. ...Conclusions: [omega]-3 FA inhibited p44/42 and JNK/SAPK phosphorylation; however, p38 remained unchanged. Phosphorylation of p44/42 and JNK/SAPK are the immediate prior steps in AP-1 activation. Attenuated AP-1 activation and subsequent attenuated gene-level proinflammatory cytokine elaboration is anticipated after inhibition of these MAPK intermediates and is confirmed by the reduction in AP-1 activity. These results provide further evidence for the transcriptional level regulation in the elaboration of proinflammatory cytokines by [omega]-3 FA in this M[Phi] model.] Babcock TA, Kurland A, et.al. *Journal of Parenteral and Enteral Nutrition* 27:176-181, 2003.

[http://findarticles.com/p/articles/mi\\_qa3762/is\\_200305/ai\\_n9216984](http://findarticles.com/p/articles/mi_qa3762/is_200305/ai_n9216984)

262. **Inflammatory cytokines activity in temporomandibular joint disorders: a review of literature.** [Cytokines are important polypeptides mediators of acute and chronic inflammation. These molecules act as a complex immunological network, in which there are pro-inflammatory cytokines, such as interleukin-1 (IL-1), IL-6 and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), and anti-inflammatory mediators like IL-10 and transforming growth factor- $\beta$ . In spite of some controversial findings, in general high levels of pro-inflammatory cytokines have been correlated with signs and symptoms of temporomandibular disorders (TMD) such as internal derangement and osteoarthritis. These mediators promote degradation of cartilage and bone joint by inducing release of proteinases and other inflammatory molecules. Indeed, pro-inflammatory cytokines have been associated with temporomandibular joint (TMJ) tissue destruction. However, its mechanisms and pathophysiology have not been clearly delineated. In attempt to summarize the role of cytokines in TMD pathophysiology and its potential for medical intervention, the purpose of the current study was to review the literature concerning

the analysis]. Campos MIG, Campos PSF, et.al. *Braz J Oral Sci. July-September 2006 - Vol. 5 - Number 18* [http://www.fop.unicamp.br/brjorals/temp2/c18\\_Art1\\_inflammatory.pdf](http://www.fop.unicamp.br/brjorals/temp2/c18_Art1_inflammatory.pdf)

263. **Is there a relationship between rheumatoid arthritis and periodontal disease?** [Aim: The aim of this study was to determine whether there is a relationship between disease experience of rheumatoid arthritis and periodontal disease. Conclusions: Based on data derived from self-reported health conditions, and not withstanding the limitations of such a study, we conclude that there is good evidence to suggest that individuals with moderate to severe periodontal disease are at higher risk of suffering from rheumatoid arthritis and vice versa.] Mercado F, Marshall RI, et.al. *Journal of Clinical Periodontology Volume 27 Issue 4 Page 267 - April 2000.* <http://www.blackwell-synergy.com/doi/abs/10.1034/j.1600-051x.2000.027004267.x?journalCode=cpe>
264. **Soluble tumour necrosis factor receptors in synovial fluids from temporomandibular joints with painful anterior disc displacement without reduction and osteoarthritis.** [The objective of this study was to detect soluble-form tumour necrosis factor receptors (sTNFRs) in temporomandibular joint (TMJ) synovial fluid aspirates, and to compare the sTNFR concentrations between painful anterior disc displacement without reduction and osteoarthritis (ADDwoR/OA) and asymptomatic TMJs. Synovial fluid was sampled from the superior TMJ cavity of 11 painful ADDwoR/OA cases (mean age: 36.9 years) and 10 asymptomatic females (mean age: 24.7 years) by diluted aspiration. The concentrations of sTNFR-I and -II in the synovial fluid were measured using human sTNFR-I and -II enzyme-linked immunosorbent assays. The total protein concentrations in synovial fluids were measured using a bicinchoninic acid protein assay kit. All data were normalised to the total protein concentration of each sample. Two-way factorial analysis of variance and post hoc multiple comparison revealed that: (1) mean normalised sTNFR-I and -II concentrations were higher in TMJ synovial aspirates from ADDwoR/OA patients than from healthy controls; (2) in the ADDwoR/OA patients and the healthy controls, the sTNFR-I concentration in TMJ synovial aspirates was higher than the sTNFR-II concentration; and (3) high TMJ synovial aspirate sTNFR-II seemed to be associated with less TMJ pain and a less restricted range of mouth opening in the ADDwoR/OA patients. The concentrations of sTNFRs in TMJ synovial fluid are higher in the presence of painful ADDwoR/OA, which could modulate intracapsular inflammation.] Uehara J, Kuboki T, et.al. *Arch of Oral biology vol 49, Issue 2, P 133-142.* <http://www.aobjournal.com/article/PIIS0003996903002036/abstract>

## **Oral Hygiene Devices**

265. **Comparison of the Hydrabrush Powered Toothbrush with Two Commercially-Available Powered Toothbrushes.** Patters MR, Bland PS, et al. Department of Periodontology and Department of Pediatric Dentistry and Community Oral Health, University of Tennessee Health Science Center, College of Dentistry, Memphis, TN. *Journal of the International Academy of Periodontology, July 2005.* <http://www.perioiap.org/absjul05.htm>
266. **The effect of oral irrigation with a magnetic water treatment device on plaque and calculus.** [The measurements of the group using an irrigator with a magnetic device showed a 44% greater reduction in calculus volume and a 42% greater reduction in area over the group using an unmagnetized irrigator. There appears to be a statistically significant difference in supragingival accretion volumes between conventional irrigation and using an irrigator with a magnetic water treatment device.] Watt DL, Rosenfelder C, et al. *J Clin Periodontol 1993; 20: 3J4-317.* [http://www.hydrofloss.com/oral\\_health.htm#JOURNAL%20OF%20CLINICAL%20PERIODONTOLOGY](http://www.hydrofloss.com/oral_health.htm#JOURNAL%20OF%20CLINICAL%20PERIODONTOLOGY)

267. **The effectiveness of a magnetized water oral irrigator (Hydro Floss® ) on plaque, calculus and gingival health.** [Irrigation with magnetized water resulted in 64% less calculus compared to the control group.] Johnson KE, Sanders JJ, et al, *J Clin Periodontol* 1998; 25: 316-321.  
[http://www.hydrofloss.com/oral\\_health.htm#JOURNAL%20OF%20CLINICAL%20PERIODONTOLOGY](http://www.hydrofloss.com/oral_health.htm#JOURNAL%20OF%20CLINICAL%20PERIODONTOLOGY)
268. **A two-month study of the effects of oral irrigation and automatic toothbrush use in an adult orthodontic population with fixed appliances.** [Forty-seven adult orthodontic patients with fixed orthodontic appliances were divided into three study groups: (1) oral irrigation with automatic toothbrush, (n = 16); (2) oral irrigation with manual toothbrushing, (n = 16); (3) control group with continued normal toothbrushing only, (n = 15). Gingival and plaque indices, bleeding after probing, and gingival sulcus depths were assessed at baseline, 1-month, and 2-month periods. Marked and significant gingival and plaque improvements from baseline were measured in all three study groups. After 1 to 2 months use of the automatic toothbrush and/or the oral irrigation device, there was a significant reduction in plaque when compared with the control group who used only the manual toothbrush (p = 0.026). Also, there was a significant reduction in gingival inflammation (p = 0.045) and evidence for reducing bleeding after probing (p = 0.037). No significant differences were found in probe depths among the three study groups, however, use of both devices reduced the pocket depth significantly from baseline by 0.5 mm (p < 0.0002). For this population of orthodontic patients, significant reductions in plaque, gingival inflammation, and a tendency for reduced bleeding after probing occurred in both groups with the power device. These improvements were most attributable to the effect of the oral irrigation device.] Burch JG, Lanese R, et.al. *Am J Orthod Dentofacial Orthop.* 1994 Aug;106(2):121-6.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=8059746&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8059746&dopt=Abstract)
269. **Comparison of irrigation to floss as an adjunct to tooth brushing: effect on bleeding, gingivitis, and supragingival plaque.** [OBJECTIVE: The purpose of this twenty-eight day, randomized, single-blind clinical trial was to assess the efficacy of the addition of daily oral irrigation to both power and manual tooth brushing, compared to a traditional regimen of manual tooth brushing and flossing, to determine which regimen had the greatest effect on the reduction of gingival bleeding, gingivitis, and supragingival plaque. CONCLUSION: The results of this clinical trial indicate that when combined with manual or sonic tooth brushing, oral irrigation is an effective alternative to manual tooth brushing and dental floss for reducing bleeding, gingival inflammation, and plaque removal.] Barnes CM, Russell CM, et.al. *J Clin Dent.* 2005;16(3):71-7.  
[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=16305005&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=16305005&dopt=Abstract)