Bale/Doneen/Nabors response to the AHA and ADA statements regarding Periodontal Disease and Cardiovascular Disease.

The issue of the relationship between chronic inflammatory periodontal disease (PD) and cardiovascular disease has, and continues to be, a subject of intense research as well as much debate. While the literature continues to show an independent relationship between these two diseases, the issue of causation was addressed in a recent and important article by the American Heart Association. http://circ.ahajournals.org. The *Circulation AHA* article examined 537 peer-reviewed studies that addressed the relationship between periodontal disease and cardiovascular disease. Concluding remarks from this intense analysis were as follows: "Observational studies to date support an association between PD and asymptomatic vascular disease (ASVD) independent of known confounders. They do not, however, support a causative relationship." The American Dental Association (ADA) Council on Scientific Affairs agrees with these conclusions.

Albeit the American Heart Association (AHA) does acknowledge the value of good oral health and hygiene, they stop short of suggesting that a direct relationship between the two conditions exists. This article provides the opportunity to investigate the objective data to determine the positive aspects of the analysis. Bradley Bale, MD, Amy Doneen, MSN, ARNP, and Thomas W. Nabors, DDS, FACD have the following response to the paper and position statement of the AHA and ADA. In light of the science presented in their article coupled with the substantial burden CVD places upon our society, we cannot afford to wait for the acquisition of causality data to incorporate assessing and treating PD in an effort to minimize CV risk.

We must acknowledge that cardiovascular disease (CVD) remains the leading cause of death and disability in this country and is projected to have substantial growth in monetary expenditures and morbidity in years to come. It is well established that systemic inflammatory diseases contribute to the potential for plaque rupture/erosions which create thrombotic events resulting in plaque growth patterns, microvascular thrombus activity that manifests itself with end stage diseases such as vascular dementia and peripheral vascular disease or major symptomatic events such as heart attacks and strokes.*

In light of this recent AHA publication, we must investigate the data that establishes the relationship of periodontal disease (PD) and cardiovascular disease (CVD). Current data establishes PD as a variety of and continuum of inflammatory conditions. These infections of the gingival tissues and alveolar processes exhibit classic demonstration of chronic inflammation of varying degrees and potential systemic dissemination of pathogenic oral bacteria.

A significant challenge in evaluating a cause and effect relationship between these two diseases is that PD is not consistently nor universally defined. This results in substantial variation in definitive clinical diagnoses. An objective and uniform definition of PD from its biological phenotype would be helpful in order to establish a formal cause and effect relationship with CVD. In the recent AHA article, the interpretation of the data in various studies has been limited to a subjective definition of PD which creates a tenuous platform of relating PD to CVD. More

recent definitions of PD that includes DNA determination of pathogen burden are widely accepted and appear to add great value to determining severity of PD. Contrarily, the antibody titers of oral pathogens are highly variable as PD is a group of distinct diseases vs. a single disease. Additionally, PD (as defined by oral pathogen burden), demonstrates a trend in CV benefit when PD is effectively treated. In regards to defining if PD therapy reduces ASVD risk or CVD events, an additional obstacle for any cause and effect therapeutic study will be to control for all known confounding CV risk factors. There needs to be no statistically significant difference at baseline and at end of study with all of the known risk factors in the treatment group and the control group. Due to the huge number of known risk factors, this will be a daunting task.

The literature confirms that the inflammatory milieu resulting from PD contributes to the systemic vascular burden of inflammation, as documented by various biomarkers including highly sensitive c-reactive protein (hsCRP), lipoprotein-associated phospholipase A-2 (Lp-PLA2), fibrinogen, and myeloperoxidase (MPO). There is a paucity of data regarding PD and endothelial activity as documented by microalbumen/creatine urine ratio. Studies included in this review also confirmed that PD is independently correlated with carotid plaque (as evidenced by carotid intima media thickness) and CHD events. The authors also found data substantiating a strong association of PD with myocardial infarction and stroke. After reviewing all this data, they concluded there is Level A evidence that PD is independently associated with CVD.

The six treatment studies investigating a potential cause and effect relationship between PD and CVD have been riddled with obstacles that include a lack of uniform definition of PD, a lack of unified treatment protocol for PD, and a lack of unified definition of end point of therapy and a lack of objective measurement for effective treatment for PD. Protocol driven treatment response benefit is necessary in order to prove causality. Recognizing this challenge to prove a causal relationship, yet based on current data of independence of risk, we must consider the potential that periodontal infections may be significant contributors to systemic inflammation as measured by serum markers of inflammation.

We acknowledge that the causality of PD with CVD remains challenging due to a lack of formal outcome trials and based on the fact that the definition of PD lacks uniformity and cardiovascular plaque rupture is also a continuum of risk. However, the recent AHA review of the literature does indicate that PD is associated with atherosclerosis independent of known confounders. Additionally, the AHA meta-analysis cited that 8 of 8 studies that assessed PD (as documented by clinical exam) were positively associated with higher risk for heart attacks (MI). One study revealed a positive PD pathogen definition to be associated with MI. Two (of 2) studies revealed a direct serological study to be related to MI. The two cited studies showing a lack of association of PD with MI included a PD definition of tooth loss and self-reported PD, both of which are proven to be poor diagnostic criteria.

An association between PD and atherosclerosis is supported by Level A evidence (meaning that the data are derived from multiple randomized clinical trials). It is agreed that available data indicate a trend toward a benefit obtained from periodontal treatment induced suppression of systemic inflammation and improvement of inflammatory biomarkers.

We, Bale/Doneen/Nabors, believe that a strong association of periodontal disease and vascular disease exists with the trend for reduced systemic inflammation and improved endothelial health when effective periodontal therapy is achieved. We also recommend that the evaluation and treatment of periodontal disease along with appropriate medical care be included in any strategy for the prevention of cardiovascular disease. Both the medical and dental communities should realize that there are positive health benefits when both fields of medicine work in harmony for the prevention of atherosclerotic vascular disease. In light of the above we, Bale/Doneen/Nabors, believe any healthcare program designed to maintain CV wellness should assess individuals for PD and when present, it should be therapeutically managed as both an oral disease of significance as well as a possible strategy to reduce CV risk.

We formally thank the American Heart Association for their extensive literature review which confirms our recognition of the oral/systemic association.

We are pleased to announce that we will be delivering a one day CME course not only reviewing pertinent studies from the above review, but also other studies not mentioned in this review along with the latest breaking information available. Any healthcare provider who wishes to be armed with the latest science supporting incorporating PD into a practice focused on CV wellness should attend this course.

– Please join us for our CME course for Medical and Dental health practitioners:

Vascular Inflammation: The Systemic / Oral Connection, November 2, 2012.

Final arrangements are being made for this event.

*Armin Arbab-Zadeh, et. al. **Acute Coronary Events** *Circulation 4/*2012, 125:1147-1156